MINISTRY OF HEALTH

Ontario

Exceptional Access Program Reimbursement Criteria for Frequently Requested Drugs

January 1, 2025

Disclaimer

The information in this document is updated on a regular basis. Although we strive to ensure that all information is accurate at the time of posting, please be aware that some items may be subject to change from time-to-time.

The following list of drugs and indications that will be considered for funding under the Exceptional Access Program is not exhaustive. Physicians may wish to contact the EAP directly by phone at 416-327-8109 or 1-866-811-9893 or by email at EAPFeedback.MOH@ontario.ca to see if a specific drug product and or indication not listed below may be considered for EAP funding.

Pharmacists and prescribers should be informed of a drug product's official indications and recommended dosage as set out in Health Canada's approved product monograph. Some aspects of the public funding criteria may differ from the official indications and recommended dosage as described in the product monographs for drug products that may be funded based on case-by-case approval through the Exceptional Access Program. The Executive Officer's funding of drug products is informed by advice from expert committees that consider evidence regarding the safety, clinical efficacy, and cost-effectiveness of the drug products. Where there is a difference between a product monograph and the reimbursement criteria described in this document, the published criteria governs for the purpose of funding under the Ontario Drug Benefit Program.

The information provided in this document and website is intended for information purposes only and does not provide any medical diagnosis, symptom assessment, health counselling or medical opinion for individual users. This information also does not constitute medical advice for physicians or patients. For more detailed information on prescription drugs, please consult a qualified healthcare professional.

General Information about the Reimbursement Criteria for Frequently Requested Drugs and Indications

For a drug to be considered for funding, the EAP reimbursement criteria must always be met and the request approved prior to the initiation of treatment with the drug being requested, unless otherwise specified within the criteria. This includes:

- funding for continued treatment that was previously supplied through a clinical trial, or paid for by other means (such as a third party payer)
  Note: First time applications for the funding of ongoing treatments must meet **both** initial and renewal criteria for the drug being requested (unless otherwise specified)

- funding for a renewal beyond the previously approved initial period, unless otherwise specified.

Note that the terms “fund”, “funded”, or “funding” within this document are interpreted and applied by the Ministry in accordance with the clinical evidence used to establish the reimbursement criteria. The Ministry does not distinguish between the source of the drug funding (e.g. public or private payer[s]) in administering the EAP reimbursement criteria.

Consider the following:

The “non-funding” of specific combination treatments as identified by the criteria will not be reimbursed regardless of the funding source(s) of either therapy. *The funding criteria are established based on the reviewed clinical evidence through the submission process and are not to be misconstrued with the source(s) of funding.*

Example 1: If drug A has approved reimbursement criteria and drug B has approved reimbursement criteria but the combination therapy of drug A plus drug B has not been reviewed through the established process and/or has no reimbursement criteria, the EAP will not fund either drug individually or as combination therapy if the intended use is for combination therapy, regardless of the actual source of funding of either drug A or drug B.

Example 2: If drug A has approved reimbursement criteria and drug B does not have approved reimbursement criteria, and drug A used in combination with drug B does not have approved reimbursement criteria, funding for drug A will not be provided if the intent is to use drug A as combination with drug B, regardless of the source of funding for drug B.

The duration of funding of a regimen identified in the criteria is in accordance with the duration of therapy supported by the clinical evidence and is not related to or dependent on source(s) of funding.

Example 1: If the approved reimbursement criteria states that “The Ministry will fund drug C for a period of 3 years” and drug C was already used by the patient for 2 years funded by another payer (e.g. private payer, manufacturer, out-of-pocket), the Ministry will only be obliged to fund drug C for the remaining one year if the request meets the approved EAP reimbursement criteria. Such a limitation in the duration of funding is aligned with the clinical evidence provided to the Ministry at the time of the review.

For a limited number of requests where expert opinion is required, the requests are reviewed by an external reviewer who is a medical expert in the field.

Where available, a link has been provided to the information page containing details of the Committee to Evaluate Drugs (CED) review and subsequent the Executive Officer's funding decision for the particular drug and indication. Information on whether the drug and indication can be considered through the Telephone Request Service (TRS) is also included.

EAP requests may be submitted for numerous other drugs not listed below, or for drugs listed below but for different indications. However, EAP funding will only be considered for drugs and indications that have been reviewed by the CED and approved for funding by the Executive Officer. For more information, please refer to the main EAP webpage.

Some of the drugs considered through EAP are also listed on the ODB Formulary for a different indication as Limited Use (LU) benefit. You can check whether the drug is listed by searching the
e-Formulary.

For details on how the EAP reimbursement criteria are developed, please refer to the main EAP webpage.

To assist physicians applying for exceptional access, the ministry has developed a standard form.

Use of form is not mandatory but does facilitate provision of all relevant information. Where applicable, please ensure that all relevant clinical information is provided demonstrating that the patient meets the reimbursement criteria.

Note: The dosage form and strength of the product that has been approved for reimbursement consideration are those that have been approved by the Committee to Evaluate Drugs (CED). In most cases, these are the dosage forms and strengths submitted to the CED by the manufacturer for consideration, however, it may not be inclusive of all dosage forms and strengths available through the manufacturer.

The Biosimilar Policy - Biologic Exemptions through The Exceptional Access Program

Biosimilar Switching Policy

The Ontario government is expanding its biologic drug coverage policy to further promote the use of biosimilars funded through the Ontario Drug Benefit (ODB) program. As a key health system partner, the Ministry of Health ("the ministry") is seeking support from pharmacists in the implementation of this policy. These changes support the Ministry's objectives of creating a modern and sustainable drug system that continues to offer high-quality treatment, while allowing the government to fund more new drug therapies, bring innovation to the health care system and continue its work to deliver better, connected patient care.

Please note that effective in 2025, all future transitions will continue to follow the policy described in the EO Notice on Biosimilar Policy dated on July 17, 2024.

https://www.ontario.ca/files/2024-07/moh-executive-officer-notice-en-2024-07-17.pdf

Please visit the Ministry website to view the more detailed information pertaining to each biologic originator/biosimilar announcement in the Executive Officer Communication Notices. Frequently Asked Questions pertaining to each biologic/drug at the time of implementation are also found on the Ministry website.

https://www.ontario.ca/page/ontario-public-drug-programs-executive-officer-communications

You can find the limited use criteria associated with funded biosimilars on the e-formulary or the latest version of the Ontario Drug Benefit Formulary. The searchable electronic formulary is available at the following URL on the Drugs and Devices Division's website:

https://www.formulary.health.gov.on.ca/formulary/

November 29, 2024 update of the Biosimilar policy

Effective November 29, 2024, Ontario has added two additional biologic drugs to the biosimilar policy: Xgeva® (denosumab) and Prolia®(denosumab). Please note that future transitions will continue to follow the policy described in the EO Notice on Biosimilar Policy dated on July 17, 2024.

Biosimilars versions of the two impacted originators were listed on the ODB Formulary as Limited Use (LU) benefits on **August 30, 2024** and as such access to these biologics became subject to a **"New Start Rule"**. In accordance with this New Start Rule, ODB

program recipients who are treatment naïve to denosumab will only receive coverage for the biosimilar versions, provided they meet the applicable LU criteria for the products.

ODB program recipients who are already using Xgeva® or Prolia® are subject to a **"Transition Rule"**. This 9-month transition period **begins on November 29, 2024 and ends on August 29, 2025**. At the end of this transition period, Xgeva® and Prolia® will not be funded under the ODB program, subject to certain exceptions.

In accordance with the "Transition Rule", treatment-experienced recipients on Prolia® accessed as a LU benefit will have 9 months to transition to a biosimilar version, subject to certain exceptions.
ODB program recipients who have coverage for Xgeva® through the EAP will be required to transition to a biosimilar version by the expiry date of their existing EAP approval or August 29, 2025, whichever is earlier, unless their continued coverage for Xgeva® is approved through the EAP based on a medically necessary exemption (see below). ODB program recipients who have an early expiry date for their EAP approval of Xgeva® between November 29, 2024 and March 1, 2025, will have the end date changed to March 2, 2025 to provide additional time to obtain a prescription.

During the transition period for Xgeva® and Prolia®, prescribers with patients requiring specific medically necessary exemptions to this policy may include the corresponding temporary LU codes (as applicable for Prolia® palliative care patients) on their prescriptions, but only if the patient is currently established on the originator. To remain on the originator for other types of medically necessary exemptions for Prolia® and for all exemptions for Xgeva®, prescribers will be required to submit their request to the EAP for case-by-case consideration. Prescribers are encouraged to submit EAP requests through SADIE or by fax as soon as possible during the transition period to avoid a gap in coverage.

Within the biosimilar policy, it should be noted that requests for a medically necessary exemption must include documentation that a recipient had been funded for the originator biologic under the ODB program and has tried up to two biosimilar versions (where applicable) and has experienced an adverse effect that is documented and submitted on the Health Canada side effect reporting form. A copy of each Health Canada side effect reporting form must be included in the EAP request.

July 31, 2024 update

Additional 4 Originator Products to undergo Biosimilar Switch Policy.

Effective **July 31, 2024** Ontario added four additional biologic drugs to the biosimilar policy: Lucentis® (Ranibizumab), Stelara® (Ustekinumab), Lovenox® (Enoxaparin), and Neupogen® (Filgrastim). Please note that additional transitions will follow the updated Biosimilar Policy as outlined in the EO Notice dated July 17, 2024 titled "Biosimilar Policy - Update".

Biosimilar versions of the originator biologics are currently listed on the Formulary and treatment-naïve recipients are required to start on the biosimilar product (the "New Start Rule"). Under "the Transition Rule" recipients who have already initiated therapy with the originator biologic (treatment-experienced) will have 6 months (from July 31, 2024 to January 31, 2025) to transition to a biosimilar version of the biologic in order to receive ODB program coverage for the biologic, subject to certain exceptions.

During the transition period of July 31, 2024 to January 31, 2025 for the above listed products, prescribers with patients requiring specific medically necessary exemptions to this policy may include the corresponding temporary Limited Use codes (as applicable for some products for pregnancy and palliative care patients) on their prescriptions, but only if the patient is currently established on the originator. For other types of medically necessary exemptions to remain on the originator, prescribers will need to submit their request to the EAP for case-by-case consideration. Prescribers are encouraged to submit EAP requests through SADIE or by fax as soon as possible during the transition period to avoid a gap in coverage.

First drugs for the Biosimilar Switch Policy with transition period March 30, 2023 to December 30, 2024 extended to end of January 2025 for some requests.

Reimbursement for Remicade®, Enbrel®, Humira®, Rituxan®, and Copaxone® (not a biologic but a complex molecule included under this policy) through the Ontario Drug Benefit (ODB) program is provided only for eligible ODB recipients who are treatment experienced on a case-by-case basis. All patients must meet specified initiation criteria and renewal criteria associated with the treatment depending on the duration of use of the biologic by the patient. This requirement must be met irrespective of whether the drug was originally funded through a private health insurance plan, a clinical trial, compassionately by another payer, accessed in another country or jurisdiction, or paid for out-of-pocket and it is intended to optimize consistency and equity of funding for Ontarians in accordance with the evidence-review processes.

Patients who are treatment naïve to the biologic are funded for the biosimilar version for its Health Canada approved indications. The biosimilar version of these drugs can be accessed as a limited use benefit upon meeting specified criteria for their Health Canada approved indications. If a request does not meet the LU criteria on the ODB formulary, case-by-case consideration may be provided through the EAP.

Patients must be provided with a new prescription and meet the Limited Use Criteria or Exceptional Access Program criteria to be publicly reimbursed for either the biologic originator or its biosimilar versions. The biosimilar version is generally available for all its Health Canada approved indications on the ODB formulary as a limited use benefit. Additionally, requests for a biologic for indications where Health Canada has not granted notice of compliance for the biologic originator or the biosimilar versions, if approved for funding through a case-by-case process, will be granted access to the biologic originator and the biosimilar versions.

What are the changes in drug coverage for biologics?

In general, effective March 31, 2023, the ODB program will start transitioning coverage for Copaxone®[1], Enbrel®, Humalog®[2], Humira®, Lantus®, NovoRapid®, Remicade®, and Rituxan® to their biosimilar versions. As new biosimilars enter the Canadian market, these biosimilars and their corresponding originator biologic drugs may be included as part of this policy change.

Effective December 29, 2023, coverage for these originator biologic drugs through the ODB program will not be available for patients and the ODB program will only provide coverage for the biosimilar version of these drugs for all ODB program recipients, with limited exemptions (see below). In general, for ODB program recipients who are already on these biologic drugs, there is up to a 9-month transition period (see below for more information).

Note: The ministry is aware of the ongoing Admelog shortage. The ministry will continue to monitor the situation. Prescribers will be expected to transition patients once the supply issues are resolved. The ministry will continue to communicate with healthcare providers.

This biosimilars switching policy does not apply to coverage outside of the ODB program, including private drug plans and prescriptions paid out-of-pocket. However, the biosimilar switching policy will apply to patients transitioning from other coverage types to the ODB program; such patients who are on originator biologic drugs subject to the biosimilar switching policy will need to transition to a biosimilar version to receive coverage for these biologic drugs under the ODB program, with exemptions.

Transition period

ODB program recipients on any of the drugs listed above will be required to transition to a biosimilar version to continue receiving coverage for their medication under the ODB program, unless they meet a medically necessary exemption. A transition period of up to nine months, beginning March 31, 2023, will be granted for ODB program recipients (including existing Exceptional Access Program (EAP) recipients) to provide an opportunity for patients and their health care professionals to discuss biosimilar transition.

EAP approvals for Copaxone®, Enbrel®, Humira®, Remicade® or Rituxan® expiring between March 31, 2023, and June 29, 2023, will be extended to June 30, 2023. The purpose of this extension is to give prescribers adequate time to contact their patients and discuss the transition to the biosimilar version or to determine if the patient may require a medically necessary exemption.

---

[1] Glatect® and Copaxone® are non-biologic complex drugs (NBCDs), however, the biosimilars switching policy will apply to their funding. As a result, in this document, references to an originator biologic include Copaxone® and references to a biosimilar include Glatect®.

[2] Humalog® 200 **units**/mL KwikPen® 200U/mL Inj Sol-Pref Pen 5x3mL Pk (DIN 02439611) is excluded from the biosimilar switching policy. No biosimilar is available for this strength.

Patients with EAP approvals for Copaxone®, Enbrel®, Humira®, Remicade® or Rituxan® expiring *after* June 29, 2023, will be required to transition to a biosimilar by the expiry date of their EAP approval OR December 28, 2023, whichever is earlier, in order to continue receiving ODB program coverage for these biologics.

Prescribers are being asked to contact their patients to discuss transitioning to a biosimilar version of their medication and will need to write a new prescription. Prescribers should access the biosimilar for their patients on the ODB Formulary by using an eligible Limited Use (LU) code as applicable.

Medically Necessary Exemptions for Formulary Biologics

Medically necessary exemptions to this policy may be granted on a case-by-case basis through the EAP. Note that patients are generally expected to trial at least two biosimilars of the originator biologic before a request to the EAP will be considered to resume funding of the originator product.

During the transition period of March 31, 2023, to December 28, 2023, prescribers with patients requiring medically necessary exemptions to this policy for Lantus®, NovoRapid®, and Humalog® may include the corresponding temporary LU codes on their prescriptions, but only if the patient is currently established on the originator biologic. As of December 29, 2023, the temporary LU codes will be removed and any medically necessary exemptions for Lantus®, NovoRapid®, and Humalog® will need to be submitted to the EAP for case-by-case consideration. Prescribers are encouraged to submit EAP requests as soon as possible during the transition period to avoid a gap in coverage.

As of December 29, 2023, access to Enbrel® and Humira® for plaque psoriasis will be discontinued and that indication will be removed from the ODB Formulary. Requests for patients requiring medically necessary exemptions to this policy for Enbrel® or Humira® for plaque psoriasis will need to be submitted to the EAP.

Table of Contents

ANEMIA

Darbepoetin
Brand(s): Aranesp
DOSAGE FORM/ STRENGTH: Prefilled syringes: 150 mcg, 200 mcg, 300 mcg, 500 mcg

(Requests **for the treatment of chemotherapy-induced anemia in patients with malignant cancer** DO NOT require an EAP submission. Please refer to the ODB e-formulary to determine if the patient satisfies the criteria for use.)

For the treatment of anemia secondary to chronic renal disease in those who are not eligible under the Special Drugs Program, approval can be given if the patient meets the following criteria:

Estimated glomerular filtration rate (GFR) less than 30 mL/min **AND**

Baseline hemoglobin level less than 100 g/L **AND**

Mean corpuscular volume (MCV) level between 75 fL and 120 fL

All requests MUST indicate the reason why the patient is ineligible for the Special Drugs Program.

Duration of Approval: 6 months

Renewals will be provided to patients where the hemoglobin levels have improved by 15 g/L after 3 months of therapy.

Renewals must specify the name of the drug and dose requested and MUST be accompanied by bloodwork that includes a recent hemoglobin level. Also, please identify if the patient has received transfusions after the first 2 weeks of therapy with darbepoetin and the date (s) that the transfusion(s) occurred.

Duration of Approval: 12 months

For the treatment of anemia secondary to myelodysplastic syndrome (MDS) in patients who meet the following criteria:

- MDS confirmed by the bone marrow report AND
- With a hemoglobin count less than 100 g/L AND
- Endogenous erythropoietin level of less than 500 U/L AND
- Mean corpuscular volume (MCV) level between 75 fL and 120 fL.

Submissions must include the date(s) for the above blood work.

Darbepoetin
Brand(s): Aranesp
DOSAGE FORM/ STRENGTH: Prefilled syringes:150 mcg, 200 mcg, 300 mcg, 500 mcg

For patients with an MCV level below 75 fL or above 120 fL, the physician must provide a discussion of how reversible causes of anemia were ruled out to enable further consideration of the submission.

Duration of Approval: 6 months

Renewals will be provided to patients where the hemoglobin levels have improved by 15 g/L after 3 months of therapy.

Renewals must specify the name of the drug and dose requested and MUST be accompanied by bloodwork that includes a recent hemoglobin level. Also, please identify if the patient has received transfusions after the first 2 weeks of therapy with darbepoetin and the date(s) that the transfusion(s) occurred.

Duration of Approval: 12 months

For the treatment of anemia secondary to myelodysplastic syndrome (MDS) in patients who meet the following criteria:

- MDS confirmed by the bone marrow report AND
- With a hemoglobin count less than 100 g/L AND
- Endogenous erythropoietin level of less than 500 U/L AND
- Mean corpuscular volume (MCV) level between 75 fL and 120 fL.

Submissions must include the date(s) for the above blood work.

For patients with an MCV level below 75 fL or above 120 fL, the physician must provide a discussion of how reversible causes of anemia were ruled out to enable further consideration of the submission.

Duration of Approval: 6 months

Renewals will be provided to patients where the hemoglobin levels have improved by 15 g/L after 3 months of therapy.

Renewals must specify the name of the drug and dose requested and MUST be accompanied by bloodwork that includes a recent hemoglobin level. Also, please identify if the patient has received transfusions after the first 2 weeks of therapy with darbepoetin and the date(s) that the transfusion(s) occurred.

Duration of Approval: 12 months

Epoetin Alpha

Brand(s): Eprex

DOSAGE FORM/ STRENGTH: Prefilled syringes: 1,000 IU, 2,000 IU, 3,000 IU, 4,000 IU 5,000 IU per 0.5 mL, 6,000 IU/0.6 mL, 8,000 IU/0.8 mL, 10,000 IU/mL, 20,000 IU/0.5 mL, 40,000 IU/mL; Check the formulary and/or e-formulary for funded products

For the treatment of anemia secondary to chronic renal disease in those who are not eligible under the Special Drugs Program, approval can be given if the patient meets the following criteria:

- Estimated glomerular filtration rate (GFR) less than 30 mL/min **AND**
- Baseline hemoglobin level less than 100 g/L **AND**
- Mean corpuscular volume (MCV) level between 75 fL and 120 fL

All requests MUST indicate the reason why the patient is ineligible for the Special Drugs Program.

Renewals will be provided to patients where the hemoglobin levels have improved by 15 g/L after 3 months of therapy.

Renewals must specify the name of the drug and dose requested and MUST be accompanied by bloodwork that includes a recent hemoglobin level. Also, please identify if the patient has received transfusions after the first 2 weeks of therapy with epoetin alpha and the date(s) that the transfusion(s) occurred.

For the treatment of anemia secondary to myelodysplastic syndrome (MDS) in patients who meet the following criteria:

- MDS confirmed by the bone marrow report **AND**
- With a hemoglobin count less than 100 g/L **AND**
- Endogenous erythropoietin level of less than 500 U/L **AND**

Mean corpuscular volume (MCV) level between 75 fL and 120 fL.

Submissions must include the date(s) for the above blood work.

For patients with an MCV level below 75 fL or above 120 fL, the physician must provide a discussion of how reversible causes of anemia were ruled out to enable further consideration of the submission

Duration of Approval: 6 months

Renewals will be provided to patients where the hemoglobin levels have improved by 15 g/L after 3 months of therapy.

Epoetin Alpha

Brand(s): Eprex
DOSAGE FORM/ STRENGTH: Prefilled syringes: 1,000 IU, 2,000 IU, 3,000 IU, 4,000 IU, 5,000 IU per 0.5mL; 6,000 IU/0.6 mL; 8,000 IU/0.8 mL;10,000 IU/mL; 20,000 IU/0.5 mL, 40,000 IU/mL

Renewals must specify the name of the drug and dose requested and MUST be accompanied by bloodwork that includes a recent hemoglobin level. Also, please identify if the patient has received transfusions after the first 2 weeks of therapy with epoetin alfa and the date(s) that the transfusion(s) occurred.

Duration of Approval: 6 months

Pre-operative use at a dose up to 40,000 IU weekly prior to single hip, double knee, or single ("redo") knee surgery in patients who meet the following criteria;

- Hemoglobin between 100 – 130 g/L inclusive AND
- Mean corpuscular volume (MCV) level between 75 fL and 120 fL inclusive

Request not meeting these criteria will be assessed on a case-by-case basis.

Duration of Approval: Up to 4 doses preoperatively

For the treatment of anemia in palliative cancer patients. Individuals will be assessed on a case-by-case basis. Submissions must include the rationale for using epoetin alpha over transfusion.

Requests **for the treatment of chemotherapy-induced anemia in patients with malignant cancer** DO NOT require an EAP submission. Please refer to the e-formulary to determine if the patient satisfies the criteria for use.

Iron sucrose

Brand(s): Venofer, PMS Iron Sucrose
DOSAGE FORM/ STRENGTH: 20 mg/mL Injectable

For the treatment of iron-deficiency anemia confirmed by bloodwork where the patient has a demonstrated intolerance[1] to oral iron therapy[2] OR has not responded to adequate therapy with oral iron[2].

[1]Intolerance must be described.

[2]Provide name of iron salt, dose, duration of therapy, response etc.

Duration of Approval: 1 year

Renewals will be considered on a case-by-case basis.

Duration of Approval: 2 years

Ferric derisomaltose (also known as iron isomaltoside 1000)

Brand(s): Monoferric
DOSAGE FORM/ STRENGTH: 100 mg elemental iron/mL Injectable

Requests for iron derisomaltose (formerly iron isomaltoside 1000) (Monoferric) 100 mg/mL that do not meet the Limited Use Criteria on the Ontario Drug Benefit formulary may be considered for funding on a case-by-case basis by the EAP.

Lenalidomide

Brand(s): Revlimid
DOSAGE FORM/STRENGTH: 2.5 mg, 5 mg, 10 mg, 15 mg, 20 mg, 25 mg capsule

Effective with the April 29, 2022 formulary update, lenalidomide for the treatment of anemia due to myelodysplastic syndrome (MDS) may be accessed upon meeting limited use criteria on the Ontario Drug Benefit Formulary.

Luspatercept
Brand(s): Reblozyl
DOSAGE FORM/ STRENGTH: 25 mg, 75 mg vials
Effective date: February 27, 2023

Beta-thalassemia associated anemia

Initiation Criteria

For the treatment of red-blood cell (RBC) transfusion-dependent anemia associated with beta-thalassemia in patients who meet ALL the following criteria:

1. 18 years of age and older; AND

2. Has 'transfusion-dependent' beta-thalassemia associated anemia defined as:

    a. Requiring 6 to 20 RBC units in the 24 weeks prior to initiating luspatercept; AND
    b. Has not had a transfusion-free period greater than 35 days in the 24 weeks prior to initiating treatment with luspatercept; AND

3. Treatment is prescribed by a clinician with expertise in the management of beta-thalassemia.

Notes:

1. The patient's RBC transfusion record within the 24 weeks prior to treatment initiation with luspatercept must be provided.

2. Renewal requests must include the patient's RBC transfusion record within the 6 months (approximately 24 weeks) of the coverage period in order to compare baseline and on-treatment RBC transfusion burden and other relevant laboratory/bloodwork results.

Exclusion criteria

1. Patients with a diagnosis of Hemoglobin S/beta-thalassemia.
2. Patients with a diagnosis of alpha-thalassemia.

Discontinuation criteria:

Luspatercept should be discontinued in patients who have not achieved a reduction in RBC transfusion burden after using 3 consecutive escalated doses (9 weeks) at 1.25 mg/kg in accordance with the product monograph.

Luspatercept
Brand(s): Reblozyl
DOSAGE FORM/ STRENGTH: 25 mg, 75 mg vials

Renewal criteria

Renewals will be considered for patients who are able to achieve or maintain at least a 33% reduction of RBC transfusion burden compared to the pre-luspatercept baseline RBC transfusion burden AND who do not meet the discontinuation criteria AND who have not developed unacceptable toxicities from treatment with luspatercept

At each renewal, the RBC transfusion burden over 24 weeks of treatment will be compared against the baseline RBC transfusion burden measured in the 24 weeks prior to initiation of treatment with luspatercept.

Approved dosage:

Usual starting dose of 1mg/kg to a maximum of 1.25 mg/kg or 120 mg per dose (whichever is reached first) administered subcutaneously every 3 weeks

Duration of Approvals (initial and renewals): 6 months

<u>Transfusion-dependent anemia associated with myelodysplastic Syndromes</u>

Initiation criteria

For the treatment of red-blood cell (RBC) transfusion-dependent anemia associated with myelodysplastic Syndromes (MDS) in patients who meet ALL the following criteria:

1. 18 years of age or older; AND

2. Diagnosed with very low- to intermediate-risk MDS with ringed sideroblasts in accordance with the Revised International Prognostic Scoring System (IPSS-R); AND

3. Has ‘transfusion-dependent’ MDS associated anemia defined as requiring an average of 2 RBC units over 8 weeks in the 16 weeks prior to initiating luspatercept; AND

4. Failed or not appropriate to be treated with an erythropoietin stimulating agent (ESA) for their MDS-associated anemia (see Note 3 and 4); AND

5. Good performance status of 0 to 2; AND

6. Treatment is prescribed by a clinician with expertise in the management and treatment of MDS.

Luspatercept
Brand(s): Reblozyl
DOSAGE FORM/ STRENGTH: 25 mg, 75 mg vials

Notes:

1. The patient's RBC transfusion record within the 24 weeks prior to treatment initiation with luspatercept must be provided.

2. Renewal requests must include the patient's RBC transfusion record within the 6 months (approximately 24 weeks) of the coverage period in order to compare baseline and on-treatment RBC transfusion burden and other relevant laboratory/bloodwork results.

3. Initial applications should include details of the ESAs that have been used (i.e. Name of treatment, dose(s), duration of use, response.)

4. Patients considered inappropriate for ESA therapy may include those who are predicted to have less than a 25% chance of responding to an ESA, or those with contraindications, or have a history of unacceptable toxicities to an ESA.

5. Patients must not have had a thrombotic event (e.g. stroke, deep venous thrombosis, pulmonary or arterial embolism) in the 6 months prior to treatment initiation with luspatercept.

Exclusion criteria

1. Patients with a diagnosis of MDS-associated anemia due to Isolated 5q deletion.

2. Patients with high-risk categories of MDS.

3. Patients diagnosed with Acute Myeloid Leukemia (AML) or whose disease has transformed to AML.

Discontinuation Criteria:

1. Luspatercept should be discontinued in patients who have not achieved a reduction in RBC transfusion burden after using 3 consecutive escalated doses (9 weeks) at 1.75 mg/kg in accordance with the product monograph.

2. Progression of MDS to a higher risk category or transformation to AML.

Luspatercept
Brand(s): Reblozyl
DOSAGE FORM/ STRENGTH: 25 mg, 75 mg vials

Renewal Criteria:

Initial renewals will be approved for patients who achieve RBC transfusion independence over a minimum of 16 consecutive weeks within the first 24 weeks of treatment initiation with luspatercept AND who do not meet the discontinuation criteria AND who have not developed unacceptable toxicities to luspatercept.

Subsequent renewals will be approved for patients who maintain their transfusion independence while on treatment and who have not developed unacceptable toxicities to luspatercept.

Patients who are not transfusion independent at the time of the initial or subsequent renewal but who have experienced a 50% or more reduction in RBC transfusion burden over a period of 16 weeks compared to the pre-luspatercept baseline RBC transfusion burden during the period of coverage (i.e. approximately 24 weeks), will be considered on a case-by-case basis.

(CBCs, other relevant bloodwork, and transfusion records during the coverage period should be included with the application.)

Approved dosage:

Usual starting dose of 1mg/kg to a maximum of 1.75 mg/kg or 168 mg per dose (whichever is reached first) administered subcutaneously every 3 weeks

Duration of Approvals (initial and renewals): 6 months

ANTICOAGULANTS

Enoxaparin biosimilars are general benefits on the Ontario drug benefit formulary and do not require EAP approval.

Other Low Molecular Weight Heparins (LMWHs) (e.g. dalteparin, tinzaparin, fraxiparine) are currently listed on the ODB Formulary as Limited Use (LU) benefits for the treatment of deep venous thrombosis (DVT) and pulmonary embolism (PE) in certain patient groups. Please consult the Formulary for further details.

Dalteparin

Brand(s): Fragmin
DOSAGE FORM/ STRENGTH: Check formulary or e-formulary for funded products

For peri-operative bridging for patients who require long-term warfarin therapy and must temporarily discontinue it before and after surgery, and who are at moderate- to high-risk for an embolic event while off warfarin.

Standard Approval Duration: As requested up to a maximum of **10 days** before the date of surgery **plus up to 7 days** after surgery.

For post-operative prophylaxis of DVT for patients who had hip or knee surgery, and cannot use warfarin.

Standard Approval Duration: As requested up to a maximum of **30 days** starting on the day of surgery.

For the post-operative prophylaxis of venous thromboembolism following abdominal or pelvic surgery for cancer in patients who do not have a history of or risk factors for heparin-induced thrombocytopenia.
Standard Approval Duration: Maximum of 30 days

For extended treatment of symptomatic acute venous thromboembolism (VTE) in patients with cancer for whom warfarin treatment is not appropriate on a case-by-case basis.

Standard Approval Duration: 6 months

Tinzaparin
Brand(s): Innohep
DOSAGE FORM/ STRENGTH: Check formulary or e-formulary for funded products

For **peri-operative bridging** for patients who require long-term warfarin therapy and must temporarily discontinue it before and after surgery, and who are at moderate- to high-risk for an embolic event while off warfarin.

Standard Approval Duration: As requested up to a maximum of **10 days** before the date of surgery **plus up to 7 days** after surgery.

For **post-operative prophylaxis of DVT** for patients who had hip or knee surgery, and cannot use warfarin.

Standard Approval Duration: As requested up to a maximum of **30 days** starting on the day of surgery.

For the post-operative prophylaxis of venous thromboembolism following abdominal or pelvic surgery for cancer in patients who do not have a history of or risk factors for heparin-induced thrombocytopenia.

Standard Approval Duration: Maximum of 30 days

Fondaparinux
Brand(s): Arixtra and generic
DOSAGE FORM/ STRENGTH: 2.5 mg

For the post-operative prophylaxis of venous thromboembolism following abdominal or pelvic surgery for cancer.

Standard Approval Duration: Maximum of 30 days

Fondaparinux
Brand(s): Arixtra (2.5mg) and Generic (2.5mg and 7.5mg) Check formulary or e-formulary for funded products
DOSAGE FORM/ STRENGTH: 2.5 mg and 7.5 mg

For the treatment of **venous thromboembolism (VTE)** [deep vein thrombosis (DVT), pulmonary embolism (PE)] in the setting of acute heparin induced thrombocytopenia (HIT)

Duration: 1 month if patient is able to transition to warfarin OR up to 1 year for patients who cannot be managed on warfarin*

Fondaparinux

Brand(s): Arixtra (2.5mg) and Generic (2.5mg and 7.5mg) Check formulary or e-formulary for funded products
DOSAGE FORM/ STRENGTH: 2.5mg and 7.mg Injection

For the treatment of venous thromboembolism (VTE) [deep vein thrombosis (DVT), pulmonary embolism (PE)] in patients with previous HIT who cannot use rivaroxaban

Duration: 1 month if patient is able to transition to warfarin OR up to 1 year for patients who cannot be managed on warfarin*

** Patients may not be able to use warfarin as extended treatment or prophylaxis of VTE due to contraindication, previous clinical failure, inability to swallow/ take oral medications, immobility, inability to monitor INR, etc. The reasons why warfarin is not appropriate must be clearly described.*

Renewal of funding for the above indications may be considered on a case-by-case basis with documented clinical rationale that includes details pertaining to patient's risks for recurrent VTE, risks of bleeding, update on whether warfarin therapy may now be considered, and response to therapy.

For peri-operative bridging for patients with history of HIT who require long-term warfarin therapy and must temporarily discontinue it before and after surgery, and who are at moderate- to high-risk for an embolic event while off warfarin.

Duration: As requested up to a maximum of 10 days before the date of surgery plus up to 7 days after surgery

Renewal of funding will NOT be considered for this indication.

Nadroparin

Brand(s): Fraxiparine
DOSAGE FORM/ STRENGTH: Check formulary or e-formulary for funded products

For the post-operative prophylaxis of venous thromboembolism following abdominal or pelvic surgery for cancer in patients who do not have a history of or risk factors for heparin-induced thrombocytopenia.

Standard Approval Duration: Maximum of 30 days

ANTICONVULSANTS

Lamotrigine (chewable)
Brand(s): Lamictal
DOSAGE FORM/ STRENGTH: 5 mg chewable tablet

For the adjunctive therapy for children over 2 years of age who are suffering from refractory seizures associated with Lennox-Gastaut syndrome, and who have previously tried other antiepileptic drugs.

Duration of Approval: 1 year

Oxcarbazepine
Brand(s): Trileptal
DOSAGE FORM/ STRENGTH: 150 mg, 300 mg, and 600 mg tablet 60 mg/mL

For the treatment of partial seizures in adults and in children aged 6 years and older who have had an inadequate response or intolerance* to at least 3 other formulary agents (prior or current use) including carbamazepine.

* Intolerance must be described in detail.

Warning: Life-threatening dermatological reactions, including Stevens Johnson Syndrome and toxic epidermal necrolysis, and multi-organ hypersensitivity reactions have been associated with the use of oxcarbazepine. More information may be found on the Health Canada webpage:
http://www.hc-sc.gc.ca/dhp-mps/medeff/advisories-avis/prof/trileptal_hpc-cps_e.html

Duration of Approval: Lifetime

Rufinamide
Brand(s): Banzel
DOSAGE FORM/ STRENGTH: 100 mg, 200 mg, 400 mg

For the treatment of seizures associated with Lennox-Gastaut Syndrome (LGS) in patients who meet the following criteria:

- Patient is 4 years of age or older; AND
- the Patient is currently on two or more anti-epileptic drugs (AEDs) without optimal seizure control; AND
- the Patient has failed an adequate trial[1] of lamotrigine AND topiramate; AND
- the Patient is in the care of a physician experienced in managing seizures.

[1]If an adequate trial of lamotrigine and/or topiramate is not possible due to intolerance or contraindication, a less costly AED that is listed as a benefit on the Ontario drug benefit formulary must be tried in its place

Dose: Maximum daily dose is 1,300 mg per day for patients less than 30 kg; and 3,200 mg per day for patients 30 kg or greater

Exclusion Criteria.

Funding will not be approved for the following circumstances:

- Banzel used first line for LGS; OR

Treatment of partial seizures

Duration of Approval: Lifetime

Stiripentol
Brand(s): Diacomit
DOSAGE FORM/ STRENGTH: 250 mg capsule, 250 mg/pack powder for suspension, 500 mg capsule, 500 mg/pack powder for suspension

For the treatment of patients with severe myoclonic epilepsy in infancy (Dravet syndrome) who meet the following criteria;

i) the patient has refractory generalized tonic-clonic seizures; AND

ii) the patient requires Diacomit (Stiripentol) for use in combination with clobazam and valproate as adjunctive therapy for the seizures; AND

iii) the patient's seizures are not adequately controlled with clobazam and valproate alone; AND

iv) the request is submitted by a neurologist or pediatrician.

Case-by-case consideration through external review will be permitted for circumstances not meeting the above criteria.

Duration of Approval: Lifetime

ANTIDIABETIC AGENTS

Pioglitazone
Brand(s): Actos , Generics
DOSAGE FORM/ STRENGTH: 15 mg, 30 mg, 45 mg tablet

For the treatment of type 2 diabetes in patients who require;

- Dual combination therapy of diabetes AND demonstrate inadequate glycemic control (HbA1c of >7%) on maximal doses of metformin (2000 mg/day) OR

- Dual combination therapy of diabetes AND demonstrate inadequate glycemic control (HbA1c of >7%) on maximal* doses of sulfonylurea and demonstrated intolerance / contraindication to metformin OR

- Triple combination therapy of diabetes and who demonstrate inadequate glycemic control on maximal** doses of metformin and a sulfonylurea AND only if the physician has offered insulin as an alternative option first, and the patient has refused or is not able to take insulin. Note: Both the physician and patient must be aware that thiazolidinediones (TZDs), are not indicated for use in triple therapy.

***Those with one or more of the following contraindications/ precautions to therapy with pioglitazone/rosiglitazone will not be considered

- Patients with type 1 diabetes
- Patients who will be using this as monotherapy
- Combination use with a nitrates
- Combination use with insulin
- Patients with any stage of heart failure (i.e. NYHA Class I, II, III, IV)
- Patients at high risk for bone fracture (i.e. post-menopausal women with previously confirmed osteoporosis or osteopenia)
- Patients with recent history (in the past 3 months) of an ischemic cardiovascular event (myocardial infarction, unstable angina)

* Note: For the purpose of the EAP submission, maximal dose of sulfonylurea is considered to be glyburide 10 mg/day, gliclazide 160mg/day OR Diamicron MR 60mg/day, OR glimepiride (Amaryl) 4 mg/day and aximal dose of metformin is considered to be 2000 mg/day.

Duration of Approval: 5 years

Renewals as well as requests for ongoing treatment in patients previously provided these drugs by other means will be considered for those patients who have NOT developed a contraindication/precautionary use*** in the intervening period AND have demonstrated a recent HbA1c level ≤7% while on treatment

Duration of Approval: 5 years

Repaglinide
Brand(s): GlucoNorm
DOSAGE FORM/ STRENGTH: 0.5 mg, 1 mg, 2 mg tablet

For the treatment of type 2 diabetes in patients with:

- Inadequate glycemic control (HbA1c >7%) using maximal* doses of a sulfonylurea AND metformin (2000mg/day) **OR**
- Inadequate glycemic control and demonstrated intolerance or contraindication to metformin and who are on maximal* doses of a sulfonylurea **OR**
- Inadequate glycemic control and demonstrated intolerance or contraindication to a sulfonylurea (glyburide, gliclazide or glimepiride) and are on maximal** doses of metformin **OR**
- Demonstrated intolerance or contraindication to both a sulfonylurea (glyburide, gliclazide or glimepiride) AND metformin **OR**
- Adequate glycemic control (HbA1c ≤ 7%) who develops intolerance or contraindication to sulfonylurea (glyburide, gliclazide or glimepiride) or metformin **OR**
- HbA1c ≤ 7% but with greater than 50% of fasting blood glucose (FBG >7mmol/L) or post-prandial plasma glucose (PPG >10mmol/L) levels not within target range and using maximally tolerated doses of a sulfonylurea and metformin.

*** Note:** For the purpose of the EAP submission, maximal dose of sulfonylurea is considered to be glyburide 10mg/day, gliclazide 160 mg/day or Diamicron MR 60 mg/day, OR glimepiride

(Amaryl) 4 mg/day.

****Note**: For the purpose of the EAP submission, maximal dose of metformin is considered to be 2000 mg/day

Duration of Approval: 5 years

Rosiglitazone
Brand(s): Avandia
DOSAGE FORM/ STRENGTH: 2 mg, 4 mg, 8 mg tablet

For the treatment of type 2 diabetes mellitus in patients with:

- Inadequate glycemic control (HbA1c >7%) from ALL other oral antidiabetic agents* funded through one of the Ontario Drug Benefit Programs, in monotherapy or in combination OR
- Where ALL other oral antidiabetic agents are inappropriate due to contraindications or intolerance AND
- The patient has refused or is not able to take insulin AND
- There is no known contraindication to rosiglitazone

* Oral antidiabetics include the following agents;

  - glyburide
  - metformin
  - gliclazide (Diamicron, Diamicron MR)
  - sitagliptin (Januvia)
  - saxagliptin (Onglyza)
  - repaglinide (GlucoNorm)
  - pioglitazone (Actos)

Note: A trial with acarbose is not a mandatory requirement.

Note: It is not necessary for patients to have tried the following oral antidiabetic agents that are currently not funded by the OPDP for the purposes of obtaining rosiglitazone:

  - glimepiride (Amaryl)
  - nateglinide (Starlix)

Duration of Approval: 5 years

Renewals will be considered where patients have benefited and continue to benefit from rosiglitazone treatment as demonstrated by recent HbA1c levels ≤7% while on treatment with rosiglitazone AND in those who continue to have no known contraindication(s) to rosiglitazone.

Duration of Approval: 5 years

Orlistat
Brand(s): Xenical
DOSAGE FORM/ STRENGTH: 120 mg capsule

For the treatment of type 2 diabetes in a patient with:

- Inadequate glycemic control (i.e., HbA1c > 7.0%) on maximal oral antidiabetic medications* **AND**
- Body Mass Index ≥ 27 **AND**
- Demonstrated failure to a trial of nutritional/dietary counselling and exercise programs

* Note: Maximal dose of sulfonylurea is considered to be glyburide 10mg/day, gliclazide (160mg/day or Diamicron MR

60 mg/day) OR glimepiride (Amaryl) 4mg/day.

Note: Maximal dose of metformin is considered to be 2000 mg/day

Duration of Approval: 1 year

Renewals will be considered for those with demonstrated response to treatment reported as at least 5% weight loss and improvement in glycemic control (i.e., HbA1c <7.0% or HbA1c reduction of more than 0.5%)

Duration of Approval: 12 months (First Renewal)

ANTI-INFECTIVES

Aztreonam
Brand(s): Cayston
DOSAGE FORM/ STRENGTH: 75 mg/vial powder for solution

For the treatment of chronic infection with *Pseudomonas aeruginosa* (PsA)infection in patients with a diagnosis of Cystic Fibrosis who meet all the following criteria:

(a) Patient has a documented diagnosis of cystic fibrosis;

(b) Patient has a chronic infection with Pseudomonas aeruginosa (PsA) that has been confirmed by 2 (two) positive sputum cultures taken at least 1 month apart that are both positive for PsA;

(c) the Patient's clinical condition is deteriorating despite treatment with inhaled tobramycin;

(d) the Patient has moderate to severe impairment of lung function defined by baseline FEV1 < 75% of predicted; and

(e) the Patient is ≥ 6 years old.

Exclusion Criteria: Aztreonam (Cayston) will not be funded in the following circumstances.

- Aztreonam will not be funded in combination with tobramycin inhalation
- Aztreonam will not be funded for bronchiectasis indications outside of proven cystic fibrosis;
- Aztreonam will not be funded outside of the cystic fibrosis population
- Aztreonam will not be funded for patients with mild cystic fibrosis;
- Aztreonam will not be funded for the purpose of convenience

Approved Dosage. The approved dosage for Aztreonam (Cayston) under the EAP is as follows:

Inhale 75 mg three times daily used in a repeated 28 day cycle that involves administration of aztreonam for 4 weeks of treatment followed by 4 weeks off aztreonam therapy.

Duration of Approval: 1 year

Renewals will be considered in patients who demonstrate ongoing response to therapy.

Duration of Approval: 1 year

Aztreonam
Brand(s): Cayston
DOSAGE FORM/ STRENGTH: 75 mg/vial powder for solution

Approved Dosage. The approved dosage for Aztreonam (Cayston) under the EAP is as follows:

Inhale 75 mg three times daily used in a repeated 28 day cycle that involves administration of aztreonam for 4 weeks of treatment followed by 4 weeks off aztreonam therapy.

Renewals will be considered in patients who demonstrate ongoing response to therapy.

Duration of Approval: 1 year

Dalbavancin
Brand(s): Xydalba
DOSAGE FORM/ STRENGTH: 500 mg vial for injection
Effective date: May 31, 2024

Dalbavancin for the treatment of adults diagnosed with an acute bacterial skin and skin structure infection (ABSSSI) (e.g. cellulitis/erysipelas, major cutaneous abscess, wound infection) due to methicillin resistant staphylococcus aureus (MRSA) infection is funded as a Limited use benefit on the ODB formulary upon meeting specified funding criteria.

Retreatment within 30 days from the initial dose may be considered on a case-by-case basis through the Exceptional access program (EAP). Please submit the culture and sensitivity report and other relevant clinical details regarding the patient's infection presentation including the dose, duration, and approximate date of treatment of all anti-infectives used to manage the infection.

Patients are not eligible if they have ABSSSI associated with any of the following types of infections:

- *Known or suspected osteomyelitis or septic arthritis*
- *Infections complicated by the presence of prosthetic materials that would not be removed such as permanent cardiac pacemaker battery packs, or those involving joint replacement prosthesis*
- *Self-limited infections such as isolated folliculitis and isolated furuncles or other infections that have a high cure rate after surgical incision alone*
- *Patients who have had more than 2 surgical interventions or are expected to need more than 2 surgical interventions (defined as surgery that cannot be performed at the bedside) for the SSSI*
- *Skin and skin structure infection with arterial insufficiency, such as deep diabetic foot ulcers, decubitus ulcers, and ischemic ulcers*
- *Necrotizing fasciitis, gas gangrene*
- *Burns greater than 20% of total body surface*

Dalbavancin
Brand(s): Xydalba
DOSAGE FORM/ STRENGTH: 500 mg vial for Injection

EAP funding criteria for Dalbavancin (Xydalba) if retreatment is required within 30 days of doses provided through the Limited use mechanism.

For the retreatment of adult patients with acute bacterial skin and skin structure infections (ABSSSI) meeting the following criteria:

1. Confirmed culture and sensitivity test showing that the patient continues to have one or more susceptible isolates of methicillin resistant staphylococcus aureus (MRSA) in spite of having had a treatment course of dalbavancin at least 2 weeks prior; AND

2. Patient is deemed to be at high risk of nonadherence to a standard antibiotic treatment for MRSA ABSSSI or treatment with standard antibiotic treatment for MRSA ABSSSI is not feasible.
   OR
   Treatment with dalbavancin rather than a standard antibiotic regimen for MRSA ABSSSI will avoid the need for hospitalization OR will limit the need for prolonged hospitalization;

   AND
3. Full or partial response and improvement is seen within the first 28 days from the initial dose; AND

4. Request is from an infectious disease specialist or has been requested in consultation with an infectious disease specialist (provide consult notes).

Requests that are not from an infectious disease specialist may be reviewed on a case-by-case basis.

Notes:

1. Submit the culture and sensitivity report and other relevant clinical details including the dose, duration, and approximate date of treatment of all anti-infectives used to manage the infection.

Approved additional dose for ABSSSI: Up to 1500 mg intravenously (IV), administered either as a single dose OR A two dose regimen of 1000 mg IV followed one week later by 500 mg IV.

Daptomycin

Brand(s): Cubicin RF and generic daptomycin (Refer to the formulary for funded list)
DOSAGE FORM/ STRENGTH: 500 mg/10 mL powder for injection

Note that initial requests for Daptomycin may be accessed through the EAP's Telephone Request Service for some of the below indications (see latter part of this document under TRS).

For the treatment of patients experiencing the following types of infections due to methicillin-resistant Staphylococcus aureus (MRSA) bacteria;

i) Staphylococcus aureus bloodstream (SAB) infection including right-sided Staphylococcus aureus infective endocarditis (SARIE); AND/OR

ii) Osteomyelitis; AND/OR

iii) Device-related osteoarticular or prosthetic joint infections; AND/OR

iv) Diabetic foot infections.

Additionally, the patient must have failed to adequately respond to, be intolerant[1] to, or have a contraindication to vancomycin.

[1]Intolerance due to Red Man Syndrome. If the physician asserts that the patient is intolerant to vancomycin due to red man's syndrome, additional clinical details of the patient's intolerance, including rate of infusion and the use of antihistamines and other histamine blockers prior to therapy with vancomycin.

Duration of Approval: Up to 8 weeks

Renewals will be considered on a case-by-case basis. (Physicians must submit adequate clinical information to justify the need for ongoing therapy with daptomycin.)

Duration of Approval: Case-by-case

Exclusion Criteria:

- Daptomycin is not funded for patients with MRSA-related pneumonia;
- Daptomycin is not funded for patients with skin/skin structure infections other than diabetic foot infections caused by MRSA.

Daptomycin

Brand(s): Cubicin RF, generic daptomycin products (refer to the formulary list)
DOSAGE FORM/ STRENGTH: 500 mg/10 mL powder for injection

For the treatment of invasive infections[1] caused by vancomycin-resistant enterococcus (VRE) in patients who meet the following criteria:

1. VRE infection is confirmed by blood or tissue culture and sensitivity report
2. Patient is unable to use linezolid as a result of at least ONE of the following reasons:
    i) has developed resistance to linezolid as confirmed by the microbiology sensitivity report
    ii) has experienced intolerance[2] to linezolid (for example: severe gastric symptoms, myelosuppression, peripheral neuropathy requiring medical intervention, lactic acidosis)
    iii) has a contraindication[2] to linezolid

    OR

    Prescribed by an infectious disease expert for a patient who is able to use linezolid but where the bacteriostatic effect of linezolid may not be deemed to be clinically optimal due to other patient factors or comorbidities (e.g., immunocompromised, neutropenic).

[1]Not approved for colonization (e.g., nares, skin, stool)

[2]Intolerances and contraindications to linezolid must be fully described in the EAP application.

Recommended dose: 8 to 12 mg/kg daily for VRE with adjustments based on renal function

Duration of approval: *Note that the below are examples of durations for reimbursement of some common VRE infections. This is not an all-inclusive list.*

Urinary tract infections: up to 10 days

Bacteremia: up to 14 days

Endocarditis: up to 6 weeks

Osteomyelitis: up to 8 weeks

Requests for longer durations of funding will be considered case-by-case through external review and must be accompanied by a recent microbiology sensitivity report to confirm sensitivity to daptomycin.

Fidaxomicin (May be accessed through the telephone request service)

Brand(s): Dificid
DOSAGE FORM/ STRENGTH: 200 mg tablet

For the treatment of Clostridium difficile infection (CDI) in patients who meet the EAP criteria for vancomycin use, but where the patient:

- has experienced a third or subsequent episode within 6 months of treatment with vancomycin for prior episode(s), with no previous trial of fidaxomicin; OR
- has experienced treatment failure* with oral vancomycin for the current CDI episode; OR
- has had a documented allergy (immune-mediated reaction) to oral vancomycin; OR
- has experienced a severe adverse reaction or intolerance** to oral vancomycin treatment that resulted in the discontinuation of vancomycin therapy.

**Treatment failure is defined as 7 days of vancomycin therapy without acceptable clinical improvement.*

***Details of severe adverse reaction or intolerance must be provided and should be clinically related to oral administration of vancomycin.*

Re-treatment criteria:

- Re-treatment with fidaxomicin will only be considered for an early relapse occurring within 30 days of the completion of the most recent fidaxomicin course.
- Relapse/ recurrence occurring beyond 30 days after the completion of the most recent fidaxomicin course will require a trial with vancomycin, unless there is a documented allergy, severe adverse reaction or intolerance to prior oral vancomycin use.

Note: Fecal biotherapy (“stool transplantation”), if available, should be encouraged for this patient population.

Approved dose and duration: 200 mg twice a day for 10 days

Isavuconazole
Brand(s): Cresemba
DOSAGE FORM/ STRENGTH: 100 mg capsule, 200 mg Injection Solution

NOTE: **Prescribers must submit the laboratory results to confirm the patient's infection** and include drugs and drug regimens that have been used for the patient's condition, including the response to prior therapies and other relevant clinical information. Please also confirm that the patient does not meet the exclusion criteria.

For the treatment of invasive aspergillosis in patients meeting the following criteria:

- 18 years of age and older; AND
- Patient has failed, experienced intolerance to, or has contraindications to voriconazole; AND
- Isavuconazole is prescribed by or in consultation with an infectious disease specialist. (Include consult note with the request)

Exclusion criteria:

Patients with familial short QT syndrome.

Approval Duration: 3 months

Renewals will be considered on a case-by-case basis.

For the treatment of invasive mucormycosis in patients meeting the following criteria:

- 18 years of age and older; AND
- Isavuconazole is prescribed by or in consultation with an infectious disease specialist. (Include consult note with the request)

Exclusion criteria:

Patients with familial short QT syndrome.

Approval Duration: 3 months

Renewals will be considered on a case-by-case basis

Recommended dose:

200mg administered intravenously or orally every 8 hours for 6 doses followed by a maintenance dose of 200mg daily starting 12 to 24 hours after the last loading dose.

Oral therapy should be considered as a preferred option when clinically appropriate. A loading dose is not required when switching from intravenous to oral treatment or vice versa.

Letermovir
Brand(s): Prevymis
DOSAGE FORM/ STRENGTH: 240mg and 480mg tablet; 240mg and 480mg Injection

For the prophylaxis of cytomegalovirus (CMV) infection in adult patients who have received an allogeneic hematopoietic stem cell transplant (HSCT) meeting the following criteria:

- Age 18 years and older; AND
- Patient is a CMV-seropositive recipient [R+] meeting one of the following circumstances;
  - Recipient using umbilical cord blood as the stem cell source; OR
  - Patient is a haploidentical recipient; OR
  - Recipient of T-cell depleted grafts; OR
  - Recipient with documented history of CMV disease prior to transplantation; OR
  - Recipient requiring high-dose steroids (defined as the use of greater than or the same as 1 mg/kg/day of prednisone or an equivalent dose of another corticosteroid) or other immunosuppression for acute graft versus host disease (GVHD); OR
  - Recipients treated with antithymocyte globulin (ATG) for conditioning, or
  - Recipient treated with ATG for steroid-refractory acute GVHD treatment.
- Patient must have undetectable CMV viremia at baseline (results should be from samples collected within a week of transplant date); AND
- Treatment is prescribed by a clinician with expertise in the management of HSCT (e.g. medical oncologist, hematologist, infectious disease specialist)

Exclusion criteria:
- Treatment of CMV with letermovir is not funded.
- Patients receiving autologous hematopoietic stem cell transplant
- Concomitant use with antiviral drugs used for the management of CMV (e.g. ganciclovir, valganciclovir)

Notes: Patients should be transitioned to oral letermovir as soon as clinical circumstances permit to optimize cost-effectiveness

Funded dosage:

A maximum dose of 480mg administered orally or intravenously per day to be started within 28 days of transplant (i.e.as early as the day of transplant and no later than 28 days post-transplant). (240mg when co-administered with cyclosporine)

Approval duration: A maximum duration of funding of 100 days (includes both in-hospital and out-patient utilization) will be provided per patient per HSCT procedure.

Levofloxacin hemihydrate
Brand(s): Quinsair
DOSAGE FORM/ STRENGTH: 240mg/ 2.4mL solution for inhalation

For the management of adult cystic fibrosis patients with chronic pulmonary *Pseudomonas aeruginosa* (*P.aeruginosa*) infections who meet the following criteria:

- Documented diagnosis of Cystic Fibrosis; AND
- Patient is 18 years of age or older; AND
- Chronic infection with *Pseudomonas aeruginosa* (PsA) [confirmed by 2 (two) PsA positive sputum cultures taken at least 1 month apart]; AND
- Patient has failed treatment with inhalational tobramycin and demonstrates deteriorating clinical condition despite treatment with inhaled tobramycin; AND
- Request is from a prescriber experienced in the diagnosis and treatment of cystic fibrosis.

Exclusion criteria:

- Use in combination (sequential or cycled during off-treatment periods) with other inhaled antibiotics to treat *P.aeruginosa* will not be funded.
- Funding will not be provided for conditions outside of cystic fibrosis.

Approval duration: 1 year

Renewal requests:

Patient demonstrates response to therapy.

Approval duration: 1 year

Maribavir

Brand(s): Livtencity
DOSAGE FORM/ STRENGTH: 200 mg tablet
Effective date: July 8, 2024

Initiation criteria:

For the treatment of post-transplant cytomegalovirus (CMV) infection in adult patients who meet the following criteria;

1. Diagnosed with laboratory confirmed post-transplant cytomegalovirus (CMV) viremia; AND
2. Treatment is refractory to valganciclovir and/or ganciclovir (Note 1); AND
3. Prescribed by clinicians with experience and expertise in transplant medicine, transplant infectious disease, or infectious diseases.

Discontinuation criteria:

Maribavir must be discontinued in patients meeting one or more of the following:

1. No change or an increase in CMV viral load after at least 2 weeks of maribavir treatment
2. Confirmed CMV genetic mutation associated with resistance to maribavir

Exclusion criteria:
(Patients meeting any of the below criteria will not be funded.)

1. Maribavir will not be funded in combination with valganciclovir or ganciclovir.

Notes:

1. Patients who are intolerant to, resistant to, or have contraindications to valganciclovir and/or ganciclovir may be considered on a case-by-case basis if they have been refractory to CMV treatments (e.g. foscarnet or cidofovir) that are not funded under the ODB program.
2. Maribavir should not be used for prevention of CMV as there is limited data to support its efficacy in this clinical setting.
3. Retreatment with maribavir may be considered for patients who have a recurrence of CMV viremia after a previous successful course of therapy with maribavir.
4. Pediatric patients younger than 18 years of age may be considered on a case-by-case basis for requests from a prescriber specialized in the care of pediatric transplant patients.

Maribavir
Brand(s): Livtencity
DOSAGE FORM/ STRENGTH: 200 mg tablet

Recommended dose:

400mg twice daily

Duration of Approval: 3 months

Renewal criteria:

Requests for ongoing treatment of maribavir for continuation of therapy longer than 3 months will be considered on a case-by-case basis through an expert review in patients who do not meet the discontinuation or exclusion criteria.

All relevant clinical information to support the use of maribavir for an extended duration beyond 3 months, including laboratory results for resistance testing and the overall treatment plan must be provided.

Duration of Approval of Renewals: Up to 3 months

Posaconazole
Brand(s): Posanol
DOSAGE FORM/ STRENGTH: 100 mg tablet, 40 mg/mL Suspension

For the prophylaxis of Aspergillus and Candida infections in patients who have recently (within the past 3 months) undergone an allogeneic bone marrow transplant.

Duration of Approval: Limited to 4 months

For the prophylaxis of invasive fungal infections in patients who have previously (3 months or longer) undergone an allogeneic stem cell transplant and are experiencing moderate to severe graft-versus-host-disease (GVHD) will be considered on a case-by-case basis.

Note: Please provide details of the patient's clinical condition including all medications used to treat the condition with your request application.

Duration of Approval: Up to 4 months

Renewals will be considered on a case-by-case basis for patients who continue to experience ongoing symptoms of moderate to severe GVHD. Please provide information regarding infections that were experienced while on therapy (as applicable) including the names of medications and treatments being used to manage GVHD.

Duration of Approval: Case-by-case

For the treatment of invasive aspergillosis* in patients who are refractory or intolerant to voriconazole OR who have documented contraindication to voriconazole.

*Invasive aspergillosis should be confirmed by fungal culture.

Note: Requests without a positive fungal culture must be accompanied by a consultation note from an infectious disease expert with details of how the diagnosis was made and will be considered on a case-by-case basis.

Duration of Approval: 3 months

Renewals will be considered on a case-by-case basis.

Posaconazole
Brand(s): Posanol
DOSAGE FORM/ STRENGTH: 100 mg tablet, 40 mg/mL Suspension

For the treatment of mucormycosis** in patients who have failed, have a contraindication to, or experienced intolerance to amphotericin B; OR

Duration of Approval: 3 months

For the step-down treatment of mucormycosis** in patients who have been initially treated with amphotericin B but cannot tolerate long-term therapy with this agent.

**Mucormycosis infection must be confirmed by fungal culture.

Note: Requests without a positive fungal culture but where the diagnosis of mucormycosis is documented by an infectious diseases consult and other tools (e.g, radiology reports, histopathology, etc.) will be considered on a case-by-case basis.

Duration of Approval: 3 months

Renewals will be considered for patients who are responding to therapy but who have not experienced clinical resolution of their condition. Note that requests for renewal must be accompanied by supporting clinical information (Infectious disease consultation/radiology report)

Duration of Approval: 3 months

Duration of Approval of subsequent renewal: Case-by-case

Tipranavir
Brand(s): Aptivus
DOSAGE FORM/ STRENGTH: 250 mg capsules
Updated April 29, 2022

Initiation criteria

Reimbursement of Aptivus will be considered on a case-by-case basis in patients meeting the following criteria:

- are 18 years of age or older AND
- have failed (or failed to tolerate – nature of intolerance must be specified) at least two previous protease-inhibitor (PI) containing regimens AND
- genotyping/phenotyping indicates that response to tipranavir/ritonavir is likely AND
- tipranavir will be used with at least one other antiretroviral medication (in addition to ritonavir) for which sensitivity has been demonstrated on resistance testing (the intended regimen must be stated).

Approval period: 1 year

Tipranavir
Brand(s): Aptivus
DOSAGE FORM/ STRENGTH: 250 mg caps

Renewals criteria

Renewal of funding will be considered for patients who are responding to therapy and who have a viral load that is undetectable **or** CD4 count that is increasing or is stable (i.e., two recent CD4 counts are at least within 20% of one another).

Requests to EAP should include the following information:

- The complete regimen with which Aptivus will be used.
- A chronology of the past PI regimens that the patient has tried and reason(s) for discontinuation (i.e. virologic failure or intolerance to include viral loads and CD4 at the time of discontinuation)

If discontinuation was the result of an intolerance, include the nature of intolerances experienced as applicable.

- A copy of resistance testing results, genotype/phenotype tests as applicable.
- A copy of the most recent viral load and CD4 count obtained during the past three months.

Valganciclovir
Brand(s): Valcyte and Generics
DOSAGE FORM/ STRENGTH: 450 mg tablet, 50mg/mL pd for oral solution

For the treatment of moderate to severe symptomatic congenital CMV (cCMV) in newborns who meet the following criteria:

- Prescribed **by or in consultation with a pediatric ID specialist** (from one of the 5 treatment centres in Ontario: London, Hamilton, Toronto, Kingston, Ottawa; or Winnipeg for the North Western region of Ontario[1])
- Confirmed diagnosis of cCMV within the first 3 weeks of birth by:
  - PCR (urine, saliva or quantitative serum CMV); OR
  - Positive culture results (urine or saliva)
- Treatment to start within one month of birth
- Evidence of one or more of the following symptoms:
  - CNS disease (e.g., seizures, microcephaly, imaging abnormalities associated with CMV)
  - Eye disease (e.g., chorioretinitis)
  - Severe life-threatening organ dysfunction (specify/describe)
- Regular monitoring of labs for toxicity while on therapy

Valganciclovir

Brand(s): Valcyte and Generics
DOSAGE FORM/ STRENGTH: 450 mg tablet, 50 mg/mL pd for oral solutions

Approval Duration: maximum 6 months at 16mg/kg/dose BID (with dose adjustments in renal dysfunction, < 32 weeks gestational age, etc.)

Renewals: No extensions will be provided unless extenuating circumstances for severely affected infants. Case-by-case review with rationale for continued treatment (must include pediatric ID specialist consult note)

All other requests not meeting the above criteria will be reviewed on a case-by-case basis including:

- Initiation of treatment after one month of age
- Evidence of sensorineural hearing loss (SNHL) only (i.e., no other symptom described above)
- Isolated/multiple findings of mild symptoms such as: intrauterine growth retardation (IUGR), thrombocytopenia, elevated liver enzymes, jaundice, hepatitis

[1]List of treatment centres and addresses:

- Children's Hospital of Eastern Ontario, 401 Smyth Road, Ottawa ON K1H 8L1
- Kingston General Hospital, 76 Stuart Street, Kingston ON K7L 2V7
- The Hospital for Sick Children, 555 University Avenue, Toronto ON M5G 1X8
- McMaster Children's Hospital, 1200 Main Street West, Hamilton ON L8N 3Z5
- London Health Sciences Center, 339 Windermere Road, London ON N6A 5A5

Vancomycin

Brand(s): Vancocin and other generics (Note that only specific DINs are reimbursed by the EAP)
DOSAGE FORM/ STRENGTH: 125 mg capsules, 250 mg capsules (on case-by-case basis only)

Effective September 30, 2019, Vancomycin oral tablets for the treatment of Uncomplicated Clostridium difficile infection may be accessed upon meeting Limited Use Criteria on the Ontario Drug Benefit Formulary.

Vancomycin Injection to be used as an oral solution for Clostridium Difficile Infection may be accessed through the Telephone Request Service.

Case-by-case consideration for requests not meeting the Limited Use criteria (e.g. higher doses, longer durations, tapering regimens exceeding the dosing limits under LU, complicated C.Difficile Infections) may be considered through external review. Please submit requests to EAP providing adequate and relevant clinical detail to support the request.

Voriconazole
Brand(s): VFend
DOSAGE FORM/ STRENGTH: 50 mg, 200 mg tablets, 200 mg/vial injection

For the treatment of patients who have culture positive candidemia, due to *Candida* species, AND with documented resistance to fluconazole.

This will be for patients whose therapy is initiated in the hospital by a hospital physician and who require continuation of therapy when they are discharged as an outpatient. Oral tablets will be authorized for those with a properly functioning gastrointestinal (GI) tract and the parental injection will be authorized for those who do not have a properly functioning GI.

Case-by-case consideration for other indications will be provided.

Duration of Approval: 1 month

ANKYLOSING SPONDYLITIS DRUGS

Adalimumab – See Formulary for funded biosimilars
Brand(s): Humira and formulary listed biosimilars
DOSAGE FORM/ STRENGTH: 40mg/0.8mL prefilled syringe, 40mg/0.8mL and 20 mg/0.2 mL prefilled pens for subcutaneous injection

Certolizumab
Brand(s): Cimzia
DOSAGE FORM/ STRENGTH: 200 mg/mL prefilled syringe and autoinjector

Etanercept – See Formulary for funded biosimilars
Brand(s): Enbrel and formulary listed biosimilars
DOSAGE FORM/ STRENGTH: 25mg/vial and 50mg prefilled syringe for subcutaneous injection

Golimumab
Brand(s): Simponi
DOSAGE FORM/ STRENGTH: 50 mg/0.5 ml prefilled syringe and autoinjector

Infliximab- See Formulary for funded biosimilars
Brand(s): Remicade and formulary listed biosimilars
DOSAGE FORM/ STRENGTH: 100mg/10mL intravenous infusion

Secukinumab
Brand(s): Cosentyx
DOSAGE FORM/ STRENGTH: 150 mg/mL prefilled syringe and 150 mg/mL prefilled pen

Refer to the Executive Officer Communications on the Ministry website for the Ministry's Biosimilar Policy including frequently asked questions and updates for the biosimilar policy updates. http://www.health.gov.on.ca/en/pro/programs/drugs/opdp_eo/eo_communiq.aspx

Effective March 31, 2023, the ODB program will start transitioning coverage for Copaxone®, Enbrel®, Humalog®, Humira®, Lantus®, NovoRapid®, Remicade®, and Rituxan® to their biosimilar versions.

Effective December 29, 2023, coverage for these originator biologic drugs through the ODB program will not be available for patients and the ODB program will only provide coverage for the biosimilar version of these drugs for all ODB program recipients, with limited exemptions. In general, for ODB program recipients who are already on these biologic drugs, there is up to a 9-month transition period (see the biosimilar switch policy described on page 6 to 8 of this document).

It should be noted that after the date when a biosimilar becomes publicly funded for an approved indication, patients initiated on an originator biologic for this same provincially funded indication through support from a manufacturer's patient support program, will be expected to be provided ongoing access of the originator biologic through the patient's original payer mechanism (e.g. manufacturer's patient support program) or to switch to an ODB funded biosimilar version upon meeting specified criteria. The Ministry will no longer consider funding of originator biologics that are part of the biosimilar policy with limited exemptions on or after December 29, 2023.

For the treatment of ankylosing spondylitis (AS) OR psoriatic spondylitis (PS) in patients who have severe active disease with:

- Age of disease onset 50 years of age or younger; **AND**
- Low back pain and stiffness for greater than 3 months that improves with exercise and not relieved by rest; **AND**
- Failure to respond to or documented intolerance to adequate trials of 2 non-steroidal anti-inflammatory drugs (NSAIDs) for at least 4 weeks each; **AND**
- BASDAI score of ≥ 4 for at least 4 weeks while on standard therapy; **AND**
- A list of current concomitant medications related to the AS/PS, including pain medications (if relevant) with dosing regimens provided.

*NSAIDs include coxibs; use of DMARDS instead of NSAIDs not acceptable

The information submitted with the request must include the following:

- A list of current concomitant medications related to the AS/PS, including pain medications (if relevant). Please include dosing regimens.
- Details of review of radiographic reports for severe active disease.
    - X-ray or CT scan report stating the presence of "SI joint fusion" or "SI joint erosion" OR
    - MRI report stating the presence of "inflammation" or "edema" of the SI joint
    - Actual radiographic reports must be submitted with the request. If the radiographic reports do not specify the above, the request will be reviewed by external medical experts.

Additional information that should be provided if applicable:

- Schober measurement and chest expansion measurement
- Evidence of restricted spinal mobility

- If the patient has AS/PS with predominantly peripheral joint involvement, additional information pertaining to trials of DMARDs must be provided, and these requests will be reviewed by external medical experts.

Duration of Approval: 1 year

Renewal will be considered for patients with objective evidence of at least a 50% reduction in BASDAI score or ≥ 2 absolute point reduction in BASDAI score. Please provide an update on concomitant medications for AS/PS and whether there has been a reduction in pain medication for AS/PS since initiating the biologic (if applicable).

For renewals beyond the second year, objective evidence of preservation of treatment effect must be provided.

The planned dosing regimen for the requested biologic should be provided.

The recommended doses for the treatment of AS/PS are:

- Adalimumab 40 mg every two weeks
- Certolizumab 400mg at 0, 2, and 4 weeks followed by maintenance therapy of 200 mg every 2 weeks or 400 mg every 4 weeks.
- Etanercept 25 mg twice weekly or 50 mg once weekly
- Golimumab 50mg once a month
- Infliximab 3-5mg/kg/dose at 0, 2 and 6 weeks followed by maintenance therapy of up to 5mg/kg/dose every 6 to 8 weeks
- Secukinumab 150 mg sc at weeks 0, 1, 2, and 3 followed by monthly maintenance dosing starting at week 4.

Duration of Approval: First renewal: 1 year, Second and subsequent renewals: 5 years

Upadacitinib
Brand(s): Rinvoq
DOSAGE FORM/ STRENGTH: 15 mg Extended Release tablet
Effective date: August 8, 2024 (AS)

Upadacitinib for Ankylosing Spondylitis

Initiation Criteria:

For the treatment of ankylosing spondylitis (AS) in patients who have severe active disease confirmed by radiographic report with:

- 18 years of age and older; and
- Age of disease onset ≤ 50 year; and
- Low back pain and stiffness for > 3 months that improves with exercise and not relieved by rest; and
- Failure to respond to or documented intolerance to adequate trials of 2 non-steroidal anti-inflammatory drugs (NSAIDs*) for at least 4 weeks each; and
- BASDAI score of ≥ 4 for at least 4 weeks while on standard therapy; and
- A list of current concomitant medications related to the AS/PS, including pain medications (if relevant) with dosing regimens provided.

*NSAIDs include coxibs; use of DMARDS instead of NSAIDs not acceptable

The information submitted with the request must include the following:

- A list of current concomitant medications related to the AS, including pain medications (if relevant). Please include dosing regimens.
- Details of review of radiographic reports for severe active disease.
    - X-ray or CT scan report stating the presence of “SI joint fusion” or “SI joint erosion” OR
    - MRI report stating the presence of “inflammation” or “edema” of the SI joint
    - Actual radiographic reports must be submitted with the request. If the radiographic reports do not specify the above, the request will be reviewed by external medical experts

Additional information that should be provided if applicable:

- Schober measurement and chest expansion measurement
- Evidence of restricted spinal mobility
- If the patient has AS/PS with predominantly peripheral joint involvement, additional information pertaining to trials of DMARDs must be provided, and these requests will be reviewed by external medical experts.

Upadacitinib
Brand(s): Rinvoq
DOSAGE FORM/ STRENGTH: 15 mg ER Tablet

First Renewal:

Renewal will be considered for patients with objective evidence of at least a 50% reduction in BASDAI score or ≥ 2 absolute point reduction in BASDAI score. (Please provide an update on concomitant medications for AS/PS and whether there has been a reduction in pain medication for AS/PS since initiating the biologic, if applicable.)

Second and subsequent renewals:

For renewals beyond the second year, objective evidence of preservation of treatment effect must be provided.

Exclusion criteria (for Initials and Renewals):

1. Combination therapy with another biologic or JAK inhibitor treatment used to treat ankylosing spondylitis or other rheumatological condition will not be funded.

Approved dose: 15 mg once daily

Approval duration:

Initial: 1 year

First renewal: 1 year

Second and subsequent renewal: 2 years

ASTHMA

Benralizumab
Brand(s): Fasenra
DOSAGE FORM/ STRENGTH: 30 mg/mL Injection (PFS), 30 mg/ml Autoinjector
Updated: April 12, 2021

For the treatment of severe eosinophilic asthma in adult patients who meet ALL the following criteria:

a) Patient is at least 18 years old; AND
b) Benralizumab is being used as an add-on maintenance therapy; AND
c) Patient is inadequately controlled with high dose inhaled corticosteroids, defined as greater than or equal to 500mcg of fluticasone propionate or equivalent daily, and one or more additional asthma controller(s), such as long-acting beta-agonists; AND
d) Patient has a blood eosinophil count equal to or greater than 300 cell/µL within the past 12 months, and has experienced two or more clinically significant asthma exacerbations, defined as worsening of asthma resulting in administration of systemic corticosteroids for at least 3 days, or an emergency room visit, or hospitalization, in the past 12 months; **OR**

   Patient has a blood eosinophil count of equal to or greater than 150 cells/µL, and is receiving maintenance treatment with oral corticosteroids, defined as greater than the equivalent of prednisone 5 mg per day; AND

e) Patient is not using any other biologics to treat asthma, such as mepolizumab or omalizumab; AND
f) Patient has completed a baseline assessment of asthma symptom control using a validated asthma control questionnaire such as the Asthma Control Questionnaire (ACQ) or the Asthma Control Test (ACT) prior to initiation with Fasenra.
g) Request is submitted by a specialist in respirology, or allergy/clinical immunology, or by a physician with expertise in the treatment of asthma, unless the request confirms that the Patient does not have access to such specialists, in which case the request may be submitted by an Authorized Prescriber

Approved dose for initiation: 30mg sc injection administered once every 4 weeks for the first 3 doses followed by once every 8 weeks thereafter.

Approval duration of initiation and initials: 1 year

Renewals will be considered on a case-by-case basis for patients who do not meet any of the following stopping criteria:

- Patient's 12-month follow-up asthma control questionnaire score using the same validated asthma control questionnaire completed at baseline does not show improvement, such as a decrease of less than 0.5 points on the ACQ or an increase of less than 3 points on the ACT;

Benralizumab
Brand(s): Fasenra
DOSAGE FORM/ STRENGTH: 30 mg/mL Injection (Autoinjector and Prefilled syringe)

- Patient's subsequent asthma control questionnaire scores have not been maintained at the score seen following the first 12-months of therapy;

- the number of clinically significant exacerbations, defined as worsening of asthma resulting in administration of systemic corticosteroids for at least 3 days, an emergency room visit or hospitalization, has increased within the previous 12 months; and
- Patient failed to achieve or maintain at least a 25% decrease from baseline in the maintenance oral corticosteroid dose at 12 months of initiation of benralizumab and thereafter.

  Approved dose for renewals: 30mg sc once every 8 weeks.

  Approval duration for renewals: 1 year

Dupilumab
Brand(s): Dupixent
DOSAGE FORM/ STRENGTH: 200 mg/ 1.14 mL Prefilled syringe and prefilled pen, 300 mg/ 2mL prefilled syringe and prefilled pen
Effective Date: May 17, 2023

Initiation Criteria:

For the treatment of severe asthma in patients meeting the following criteria;

1. Patient is aged 6 years old or older; AND

2. Dupilumab is being used as an add-on maintenance therapy; AND

3. Patients 6 to 11 years of age with a type 2 or eosinophilic phenotype and a documented blood eosinophil count equal to or greater than 150 cells/μL within the past 12 months

   OR

   Patients 12 years of age or older with a type 2 or eosinophilic phenotype and a documented blood eosinophil count equal to or greater than 150 cells/μL within the past 12 months and/or has oral corticosteroid (OCS) dependent asthma; AND

Dupilumab
Brand(s): Dupixent
DOSAGE FORM/ STRENGTH: 200 mg/1.14 mL and 300mg/2mL (Prefilled syringe and prefilled pen)

4. Asthma is inadequately controlled using optimal treatment.

    i) For patients 6 to 11 years of age, this is defined as high dose inhaled corticosteroids (ICS) (greater than or equal to 400 mcg fluticasone priopionate daily or equivalent) alone OR medium- to high dose ICS plus 1 controller (e.g. a long-acting beta-agonists) AND experiencing at least one severe exacerbation (defined as having been treated with a systemic corticosteroid, hospitalized, or having visited an emergency department for worsening asthma) in the past 12 months

    ii) For patients 12 years and older, this is defined as using high dose ICS (greater than or equal to 500 mcg of fluticasone propionate or equivalent daily), and 1 or more additional asthma controller(s) (e.g., LABAs)[1]

5. Patient is not using any other biologics to treat asthma; AND

6. A baseline assessment of asthma symptom control using a validated asthma control questionnaire must be completed prior to initiation of dupilumab treatment.

7. Request is submitted by a specialist in respirology, or allergy/clinical immunology, or by a physician with expertise in the treatment of asthma, unless the request confirms that the patient does not have access to such specialists, in which case the request may be submitted by an authorized prescriber.

[1]Patients with type 2 or eosinophilic phenotypes are considered to be inadequately controlled if they have worsening of asthma resulting in administration of systemic corticosteroids for at least 3 days, or an emergency room visit, or hospitalization, in the past 12 months

Renewal criteria:

Renewals will be considered on a case-by-case basis for patients 6 years of age or older with type 2 or eosinophilic asthma who do not meet any of the following discontinuation/stopping criteria:

Dupilumab
Brand(s): Dupixent
DOSAGE FORM/ STRENGTH: 200 mg/1.14 mL and 300mg/2mL (Prefilled syringe and prefilled pen)

- Patient's 12-month follow-up asthma control questionnaire score using the same validated asthma control questionnaire completed at baseline does not show improvement, such as a decrease of less than 0.5 points on the ACQ or an increase of less than 3 points on the ACT;

- Patient's subsequent asthma control questionnaire scores have not been maintained at the score seen following the first 12-months of therapy;

- The number of clinically significant exacerbations defined as worsening of asthma resulting in administration of systemic corticosteroids, an emergency room visit or hospitalization, has increased within the previous 12 months.

Renewals will be considered on a case-by-case basis for patients 12 years of age or older on maintenance treatment with OCS dependent asthma who do not meet any of the following stopping criteria:

- there has been no decrease in the OCS dose in the first 12 months of treatment
- the reduction in the dose of OCS achieved after the first 12 months of treatment is not maintained or improved subsequently

Approval duration of initial and renewals: 1 year

Mepolizumab
Brand(s): Nucala
DOSAGE FORM/ STRENGTH: 100 mg/mL Injection (Prefilled syringe, Prefilled Autoinjector)
Effective date: March 15, 2018: Updated: July 23, 2019

For the treatment of severe eosinophilic asthma in adult patients who meet ALL the following criteria:

i) Patient is at least 18 years old; AND
ii) Mepolizumab is being used as an add-on maintenance therapy; AND
iii) Patient is inadequately controlled with high dose inhaled corticosteroids, defined as greater than or equal to 500mcg of fluticasone propionate or equivalent daily, and one or more additional asthma controller(s), such as long-acting beta-agonists; AND

iv) Patient has a blood eosinophil count equal to or greater than 300 cell/μL within the past 12 months, and has experienced two or more clinically significant asthma exacerbations, defined as worsening of asthma resulting in administration of systemic corticosteroids for at least 3 days, or an emergency room visit, or hospitalization, in the past 12 months;
OR
Patient has a blood eosinophil count of equal to or greater than 150 cells/μL, and is receiving maintenance treatment with oral corticosteroids, defined as greater than the equivalent of prednisone 5 mg per day; AND

v) Patient is not using any other biologics to treat asthma, such as benralizumab or omalizumab; AND

vi) Patient has completed a baseline assessment of asthma symptom control using a validated asthma control questionnaire such as the Asthma Control Questionnaire (ACQ) or the Asthma Control Test (ACT) prior to initiation with Nucala.

vii) Request is submitted by a specialist in respirology, or allergy/clinical immunology, or by a physician with expertise in the treatment of asthma, unless the request confirms that the Patient does not have access to such specialists, in which case the request may be submitted by an Authorized Prescriber

Initial approval duration: 1 year

Mepolizumab
Brand(s): Nucala
DOSAGE FORM/ STRENGTH: 100 mg/mL Inj. (Prefilled safety syringe, Prefilled Autoinjector)

Renewals will be considered on a case-by-case basis for patients who do not meet any of the following stopping criteria:

a) Patient's 12-month follow-up asthma control questionnaire score using the same validated asthma control questionnaire completed at baseline does not show improvement, such as a decrease of less than 0.5 points on the ACQ or an increase of less than 3 points on the ACT;

b) Patient's subsequent asthma control questionnaire scores have not been maintained at the score seen following the first 12-months of therapy;

c) the number of clinically significant exacerbations, defined as worsening of asthma resulting in administration of systemic corticosteroids for at least 3 days, an emergency room visit or hospitalization, has increased within the previous 12 months; and

d) Patient failed to achieve or maintain at least a 25% decrease from baseline in the maintenance oral corticosteroid dose at 12 months of initiation of mepolizumab and thereafter.

Renewal approval duration: 1 year

Montelukast

Brand(s): Singulair
DOSAGE FORM/ STRENGTH: 5 mg, 10 mg tablet
Updated criteria: October 28, 2010

For the treatment of asthma patients who cannot manage the use of an inhalation device despite assistance with a spacer (e.g. physically or mentally disabled patients or pediatric patients).

Duration of Approval: 5 years

OR

For the treatment of asthma in children and adolescents whose asthma cannot be controlled on ICS alone and where the condition remains uncontrolled despite using full doses of ICS with addition of LABA, and with assurance of good adherence and inhaler technique

Duration of Approval: 5 years (up until age of 18)

Renewal of requests that meet the above criteria will be provided where the following apply:

- Current medications and dosages must be clearly specified; AND

Objective evidence of positive response from treatment (spirometry OR decrease in health care utilization) must be provided

Duration of Approval: 5 years (up until age of 18)

Omalizumab

Brand(s): Xolair
DOSAGE FORM/ STRENGTH: 150 mg vial and 150 mg/mL prefilled syringe and 75 mg/0.5mL prefilled syringe (Asthma indication only)
Effective date: December 28, 2011; Updated April 27, 2017 (CIU)
Updated: November 23, 2021 (PFS format), October 30, 2023 (new PFS)

For the treatment of severe uncontrolled asthma in patients who meet the following criteria:

- Has within the past 12 months required hospitalization for asthma OR has required two or more urgent visits for asthma to a physician or an emergency department OR has had two or more courses of high-dose oral corticosteroids in the past 12 months; AND
- Is age 12 years or older; AND
- Has demonstrated a positive skin test or in vitro reactivity to a perennial aeroallergen; AND
- Has a baseline IgE level between 30 and 700 IU/mL (inclusive) ; AND
- Has an actual body weight between 20 kg to 150 kg (inclusive); AND
- Is receiving treatment with a high-dose inhaled corticosteroid* in addition to a long-acting inhaled beta 2-agonist. (Note: the patient can be on other concomitant therapies as well); AND
- Is deemed to be adherent and is using his/her inhaled corticosteroid and long-acting beta agonist daily as prescribed; AND
- Is using proper inhaler technique (with a spacer if required); AND
- The request for Xolair is made by the patient's specialist in respirology or allergy/clinical immunology. (Note: Individual consideration can be given for extenuating circumstances where access to these specialists is not possible.)

* High-dose inhaled corticosteroids are considered the use of more than 1000 mcg of beclomethasone dipropionate (BDP) equivalents daily.

Omalizumab

Brand(s): Xolair

DOSAGE FORM/ STRENGTH: 150 mg vial, 150 mg/mL PFS, 75mg/0.5 mL PFS (asthma only)

To avoid delays in the assessment of the request, physicians should provide the following information within their request submission.

1. The number of hospitalizations for asthma in the past 12 months.
2. The number of asthma exacerbations requiring urgent visits to a physician or emergency department in the past 12 months.
3. The average number of night-time awakenings in a one week period. (reflective of control in last 12 months).
4. The average number of puffs/day of short-acting beta-agonists within a one week period (reflective of control in last 12 months).
5. The number of courses of prednisone (or acute increases in prednisone dose if the patient is already using chronic daily prednisone) for asthma exacerbation in the past 12 months.
6. The FEV_1 pre and post bronchodilator.
7. Patient's actual body weight.
8. The serum IgE level.
9. Results of a positive allergy testing by skin prick test or IgE RAST.
10. A list of all of the patient's current asthma medications including drug name and doses.
11. Confirmation that the patient's asthma is currently uncontrolled despite optimal therapy (including confirmation of proper inhaler technique), patient adherence to current therapy, and the removal of allergic and environmental triggers or the reduction of such triggers to the fullest extent possible.

Omalizumab

Brand(s): Xolair

DOSAGE FORM/ STRENGTH: 150 mg/ vial, 150 mg/mL PFS, 75mg/0.5 mL PFS (asthma only)

Note that contraindications and intolerance to inhaled corticosteroids and/or long-acting beta agonists will not be considered as a justification to request Xolair funding.

Duration of Approval: 1 year

Renewal of requests for Xolair will be considered in patients who have a positive clinical response to the drug and who are expected to continue to do so. Renewals will be considered on a case-by-case basis and should be accompanied by the following information:

1. The number of hospitalizations for asthma in the past 12 months
2. The number of asthma exacerbations requiring urgent visits to a physician or Emergency Department in the past 12 months
3. The number of courses of prednisone (or acute increases in prednisone dose if patient is already using chronic daily prednisone) for asthma exacerbations in the past 12 months.
4. The number of nighttime awakenings (over a several week period post-introduction of therapy)
5. The average number of puffs/day of short-acting beta-agonists used per day (over a several week period post-introduction of therapy)
6. The FEV_1 pre and post bronchodilator
7. All current asthma medications taken by the patient including drug names and dosing schedule.

Duration of Approval: Up to 1 year

Tezepelumab
Brand(s): Tezspire
DOSAGE FORM/ STRENGTH: 210 mg/1.91 mL PFS and prefilled pen
Effective date: November 27, 2023

Initiation Criteria:

For the treatment of severe asthma in patients meeting the following criteria;

1. Patient is 12 years of age or older; AND
2. Tezepelumab is being used as an add-on maintenance therapy; AND
3. Patient's asthma is inadequately controlled with high-dose inhaled corticosteroids (ICSs), defined as greater than or the same as 500 mcg of fluticasone propionate or equivalent daily, and one or more additional asthma controller(s) (e.g., long acting beta agonists (LABAs)) (Note 1 and 2); AND
4. Experienced 2 or more clinically significant asthma exacerbations in the 12 months prior to the start of tezepelumab (Note 3);

   (The approximate dates/timelines and a brief description of at least two asthma exacerbations and how they were managed (e.g. urgent care visit, hospitalization, corticosteroids, drug therapy changes etc) must be included with the request application).

   AND
5. Tezepelumab is not being used in combination with other biologics used to treat asthma.

6. Request is submitted by a specialist in respirology, or allergy/clinical immunology, or by a physician with expertise in the treatment of asthma, unless the request confirms that the patient does not have access to such specialists, in which case the request may be submitted by an authorized prescriber.

Notes:

1. A baseline assessment of asthma symptom control using a validated asthma control questionnaire (i.e. ACQ or ACT) before initiation of tezepelumab treatment must be completed and submitted with the initial application. The effects of treatment should be assessed every 12 months using the same asthma control questionnaire that was used as baseline to evaluate response to treatment with Tezepelumab when requesting renewal of funding.
2. The names, doses, and approximate timelines and durations of use of all drugs used for the treatment of the patient's asthma must be included in the application. This includes information regarding the maintenance of interim use of oral corticosteroids to manage the patient's asthma.
3. A clinically significant asthma exacerbation is defined as a worsening of asthma that required one of the following:
   i) Required treatment with a burst of systemic corticosteroid (SCS) therapy for at least 3 days or a single depot-injectable corticosteroid dose

Tezepelumab
Brand(s): Tezspire
DOSAGE FORM/ STRENGTH: 210 mg/1.91 mL Prefilled syringe and Prefilled pen

ii) Resulted in an Urgent care or Emergency department visit which required treatment with systemic corticosteroid therapy
iii) Resulted in inpatient hospitalization due to asthma
iv) For patients on a stable maintenance dose of oral corticosteroid, the exacerbation resulted in a temporary increase in dose of the corticosteroid for at least 3 days.

Patients with one severe asthma exacerbation resulting in hospitalization within the 12 months before initiation of tezepelumab may be considered on a case-by-case basis.

Renewal Criteria:

Renewals will be considered on a case-by-case basis for patients who do not meet any of the following discontinuation/stopping criteria:

1. Patient's 12-month follow-up asthma control questionnaire score using the same validated asthma control questionnaire completed at baseline does not show improvement, such as a decrease of less than 0.5 points on the ACQ or an increase of less than 3 points on the ACT;

2. The asthma control questionnaire score achieved after the first 12 months of therapy has not been maintained subsequently.

3. The number of clinically significant asthma exacerbations has increased within the previous 12 months.

4. In patients on maintenance treatment with oral corticosteroids (OCSs), there has been no decrease in the OCS dose in the first 12 months of treatment with tezepelumab

5. In patients on maintenance treatment with OCSs, the reduction in the dose of OCS is not maintained or improved after the first 12 months of tezepelumab treatment.

Approval duration of initial and renewals: 1 year

Recommended dose: 210 mg subcutaneous injection every 4 weeks

BLOOD MODIFIERS

Deferasirox
Brand(s): Exjade
DOSAGE FORM/ STRENGTH: 125 mg, 250 mg, 500 mg tablet
Brand(s): Jadenu
DOSAGE FORM/ STRENGTH: 90 mg, 180 mg, 360 mg tablet

Effective on January 31, 2022, deferasirox is available on the Ontario Drug Benefit formulary as a general benefit.

Eculizumab
Brand(s): Soliris
DOSAGE FORM/ STRENGTH:10 mg/mL (300 mg per vial)

For the treatment of patients with Paroxysmal Nocturnal Hemoglobinuria (PNH) meeting the following criteria**:**

The diagnosis of Paroxysmal Nocturnal Hemoglobinuria (PNH) has been made based on the following confirmatory results:

- Flow cytometry/FLAER exam with granulocytes clone ≥ 10% **AND**
- LDH > 1.5 ULN

AND at least one of the following:

- A thrombotic or embolic event which required the institution of therapeutic anticoagulant therapy,
- Minimum transfusion requirement of 4 units of red blood cells in the previous 12 months,
- Chronic or recurrent anemia where causes other than hemolysis have been excluded and demonstrated by more than one measure of less than or equal to 70 g/L or by more than one measure of less than or equal to 100 g/L with concurrent symptoms of anemia,
- Pulmonary insufficiency: Debilitating shortness of breath and/or chest pain resulting in limitation of normal activity (New York Heart Association Class III) and/or established diagnosis of pulmonary arterial hypertension, where causes other than PNH have been excluded,
- Renal insufficiency: History of renal insufficiency, demonstrated by an eGFR less than or equal to 60 mL/min/1.73 m^2, where causes other than PNH have been excluded,

Eculizumab
Brand(s): Soliris
DOSAGE FORM/ STRENGTH: 10 mg/mL (300 mg per vial)

- Smooth muscle spasm: Recurrent episodes of severe pain requiring hospitalization and/or narcotic analgesia, where causes other than PNH have been excluded.

The dose of eculizumab that will be considered is:

600 mg once per week for the first 4 weeks, then from week five of treatment, 900 mg once every 2 weeks

Duration of Approval: 6 months

Renewals will be considered for patients who;

- Demonstrate clinical improvement while on therapy or
- Where therapy has been shown to stabilize the patient's condition

Requests for renewal should be accompanied by confirmation of granulocyte clone size (by flow cytometry).

Further, subsidized treatment may continue unless one or more of the following situations apply:

i) The patient or treating physician fails to comply adequately with treatment or measures, including monitoring requirements, taken to evaluate the effectiveness of the therapy;

ii) If therapy fails to relieve the symptoms of disease that originally resulted in the patient being approved for subsidized treatment;

Other eligibility requirements:

Note: All patients must receive meningococcal vaccination with a tetravalent vaccine at least two weeks prior to receiving the first dose of eculizumab.

Exclusion criteria for both initial and renewal requests:

i) Small granulocyte clone size - the treatment of patients with a granulocyte clone size below 10% will not be eligible for treatment; **OR**

ii) Aplastic anemia with two or more of the following: neutrophil count below 0.5 x 10^9/L, platelet count below 20 x 10^9/L, reticulocytes below 25 x 10^9/L, or severe bone marrow hypocellularity; **OR**

Eculizumab
Brand(s): Soliris
DOSAGE FORM/ STRENGTH: 10 mg/mL (300 mg per vial)

iii) Patients afflicted with PNH and another life-threatening or severe disease where the long term prognosis is unlikely to be influenced by therapy (for example acute myeloid leukemia or high-risk myelodysplastic syndrome); **OR**

iv) The presence of another medical condition that might reasonably be expected to compromise a response to therapy.

Preamble:

A confirmed diagnosis of atypical hemolytic uremic syndrome (aHUS) is required for eculizumab funding. The information below is to provide clinicians with context for how a diagnosis of aHUS will be assessed for funding consideration. Details to address these issues should be provided in the funding request.

While some patients may already have a confirmed aHUS diagnosis, by clinical history and/or genetic testing, the majority of patients presenting with thrombotic microangiopathy (TMA) have no prior diagnosis of aHUS. For most patients presenting with a TMA, it is not possible to confidently separate aHUS from the vast majority of other conditions causing TMA until after appropriate testing and treatment have occurred. The majority of patients who have TMA suffer from Thrombotic Thrombocytopenic Purpura (TTP) (30-40%), or a

secondary form of TMA (e.g., pregnancy, HIV, collagen vascular disease, drugs, malignancy, stem cell transplant, malignant hypertension) (> 50%), or hemolytic uremic syndrome due to a Shiga toxin (>5%). In most cases, patients who suffer from TTP will have an ADAMTS-13 of less than 10%. If TTP has been ruled out and any secondary causes have been treated and the patient still has a persisting unexplained TMA with ADAMTS-13 ≥10%, the patient would be presumed to suffer from aHUS. Patients who present with ADAMTS-13 of ≥10% and who are unresponsive to plasma therapy (>4 plasma exchanges) and do not have a known secondary explanation would also be presumed to suffer from aHUS.

In the absence of a confirmed diagnosis of aHUS, there is nothing in these criteria that changes the clinical expectation for appropriate use of plasma exchange/plasma infusion in the management of patients presenting with TMA.

Initiation Criteria

A patient must meet all three of the following criteria to obtain funding for initial treatment with eculizumab:

1. Confirmed diagnosis* of atypical hemolytic uremic syndrome (aHUS) at initial presentation, defined by:

Eculizumab
Brand(s): Soliris
DOSAGE FORM/ STRENGTH: 10 mg/mL (300 mg per vial)

a. Presence of an unexplained non- disseminated intravascular coagulation thrombotic microangiopathy (TMA); AND

b. Baseline ADAMTS-13 activity ≥ 10% on blood samples taken prior to plasma exchange or plasma infusion (PE/PI);

Note:

If the sample for ADAMTS-13 was not collected prior to PE or PI, platelet counts > 30 x 10^9/L and eGFR < 50 mL/min/1.73m^2 at TMA presentation will be accepted as predictive of ADAMTS-13 ≥10% in TMA patients. In this case, measurement of ADAMTS-13 can be taken 1-2 weeks following the last PE. The ADAMTS-13 result must be provided within 30 days of commencement of eculizumab and at least 1 week after the last PE. A one-month interim funding for eculizumab will be provided.

AND

c. STEC-negative test in patients with a history of bloody diarrhea in the preceding two weeks; AND

d. Other diagnoses and causes of TMA must be ruled out, as per preamble.

2. Evidence of ongoing active and progressing TMA as defined by:

   a. Thrombocytopenia (platelet count <150 x 10^9/L) that is not explained by some other cause including secondary TMA; AND hemolysis as indicated by the documentation of two of the following: red blood cell (RBC) fragmentation (schistocytes) on the blood film; low or absent haptoglobin; or lactate dehydrogenase (LDH) above normal; OR

   b. Tissue biopsy confirming TMA in patients who do not have evidence of platelet consumption and hemolysis.

      Note: Review by external clinical expert may be required to assess requests for patients with ongoing TMA that may not clearly meet the above criteria.

3. Evidence of at least one of the following documented clinical features of active organ damage or impairment:

   a. Kidney impairment as demonstrated by one of the following:

      - A decline in estimated glomerular filtration rate (eGFR) or a rise in serum creatinine (SrCr) of >20% in a patient with pre-existing renal impairment; OR

Eculizumab
Brand(s): Soliris
DOSAGE FORM/ STRENGTH: 10 mg/mL (300 mg per vial)

- SrCr > upper limit of normal (ULN) for age or eGFR < 60mL/min in patients who have no history of pre-existing renal impairment (i.e., who have no baseline eGFR measurement); OR
- SrCr > the age-appropriate ULN in pediatric patients (subject to advice from a pediatric nephrologist); or
- Renal biopsy;

OR

b. Onset of neurological impairment related to TMA (e.g., visual field defect, hemiparesis, sensory loss, asymmetric limb weakness, confusion, loss of consciousness/coma, new onset seizure).

Note: Patients who have extra-renal complications related to TMA (e.g., TMA-related cardiac impairment, TMA-related gastrointestinal impairment, or TMA-related pulmonary impairment) will be reviewed by an external clinical expert.

Continuation Criteria (at 6 months)

After six months of eculizumab therapy, a further six month of funding will be considered if the patient demonstrates treatment response, defined as:

Hematological normalization (platelet count, LDH, haptoglobin); AND

- An improvement or stabilization of eGFR (or SrCr); AND
- Stabilization of neurological or extra-renal impairment if these complications were originally present.

Continued treatment with eculizumab will not be funded beyond six months if a patient has experienced treatment failure, defined as:

- Dialysis-dependent at six months, and failed to demonstrate resolution or stabilization of neurological or extra-renal complications if these were originally present; OR
- On dialysis for ≥ four of the previous six months while receiving eculizumab and failed to demonstrate resolution or stabilization of neurological or extra-renal complications if these were originally present; OR

- Worsening of kidney function with a reduction in eGFR or increase in SrCr ≥ 25% from baseline.

Approval duration: 6 months

Continuation Criteria (at 12 months):

1. Ongoing treatment response as defined in the 6-month continuation criteria; AND

2. The patient has limited organ reserve defined as:

    - Significant cardiomyopathy, neurological, gastrointestinal or pulmonary impairment related to TMA; or

    - Grade 4 or 5 chronic kidney disease (eGFR <30mL/min). (Note: Patients who are dialysis- dependent with no significant extra-renal manifestations persisting are not considered).

There may be other exceptional circumstances where the patient has a high risk of recurrence and in whom consequences of a relapse are significant (e.g., complement Factor H genetic mutation, multiple clinical presentations of active TMA). These will be reviewed on a case-by-case basis by an external clinical expert.

For patients in whom a pause in therapy is recommended, funding will be left in place for 3 months so that eculizumab can be quickly restarted upon evidence of recurrence per recommencement criteria.

Approval duration: 12 months

Recommencement Criteria:

A patient previously diagnosed with aHUS and who responded to treatment with eculizumab and has not failed eculizumab is eligible to restart eculizumab if the following clinical conditions are met:

- Significant hemolysis as evidenced by presence of schistocytes on the blood film, or low or absent haptoglobin, or LDH above normal;

AND EITHER

- Platelet consumption as measured by either ≥ 25% decline from patient baseline or thrombocytopenia (platelet count <150,000 x 10^9/L);

OR

Eculizumab
Brand(s): Soliris
DOSAGE FORM/ STRENGTH: 10 mg/mL (300 mg per vial)

- TMA-related organ impairment (e.g., unexplained rise in serum creatinine with onset of urine dipstick positive for hemoglobin) including on recent biopsy.

Note:

1. Raised LDH alone is not a sufficient reason to recommence eculizumab, but thrombocytopenia with one marker of hemolysis (such as raised LDH, presence of schistocytes, or low/absence of haptoglobin) is an accepted reason to recommence.

2. Kidney transplantation/dialysis is not a contraindication to recommencement.

A patient who becomes eligible to restart eculizumab, in accordance with the above criteria, will be assessed every 6 months for treatment response or failure.

Approval duration: 6 months

Patients undergoing kidney transplantation:

For patients with a confirmed aHUS diagnosis who are undergoing kidney transplantation, eculizumab funding will be provided for the time period immediately prior to (or at time of) transplant. Treatment must be started immediately prior to or at time of transplant.

Approval duration: 6 months

All funding requests must come from, or be submitted in consultation with, a pediatric nephrologist, a nephrologist, a pediatric hematologist or a hematologist.

Deferiprone

Brand(s): Ferriprox
DOSAGE FORM/ STRENGTH: 1000 mg Tablet; 1000 mg MR tablet; 100 mg/mL oral solution
Effective date: October 17, 2016 Updated: August 30, 2017(oral solution); February 7, 2024 (MR tab)

For the treatment of patients with transfusional iron overload due to thalassemia syndromes who cannot be adequately treated with deferoxamine or deferasirox.

Notes:

Combination iron chelation therapy with Ferriprox will be considered on a case-by-case basis.

Therapy should be initiated and maintained by physicians experienced in the treatment of chronic iron overload due to blood transfusions.

Duration of Approval: 5 years

Renewals will be considered for Patients who continue to require iron chelation therapy and has had a consistent response to therapy (demonstrated by a reduction in baseline liver iron concentration (LIC) levels).

The following documentation is required:

- A transfusion record from the past year; and
- LIC levels – baseline (pre-treatment) and since initiation of treatment. The most recent LIC level should be from within the previous year.

Duration of Approval: 5 years

Eltrombopag
Brand(s): Revolade
DOSAGE FORM/ STRENGTH: 25 mg, 50 mg tablet
Effective date: May 1, 2012

For the treatment of refractory chronic idiopathic thrombocytopenic purpura (ITP) with bleeding complications in patients who meet the following criteria:

- Patient has undergone a splenectomy[1]; AND
- Patient has tried and is unresponsive to other treatment modalities[2].

[1]Requests for Revolade where the requesting physician has stated that the patient is not a candidate for splenectomy will be assessed on a case-by-case basis. The requesting physician must provide rationale for why a splenectomy cannot be considered, and where possible, to include a preoperative/surgical evaluation on the patient's surgical risks to splenectomy, to include consideration of risks of laparoscopic and open surgical interventions if these are available. This evaluation must come from a physician who is not the requesting physician.

[2]Appropriate first-line treatment modalities may include:

- Corticosteroids
- IV anti-D
- Intravenous immune globulin (IVIG)

[2]Appropriate second-line treatment modalities include:

- Azathioprine
- Cyclosporine
- Cyclophosphamide
- Mycophenolate
- Rituximab
- Danazol
- Dapsone

Eltrombopag
Brand(s): Revolade
DOSAGE FORM/ STRENGTH: 25 mg, 50 mg tablet

Note: Patients need to have failed at least two of the second-line therapies listed above prior to requesting Revolade. Dosage: 50 mg once daily to a maximum of 75 mg once daily.

Duration of Approval: 1 year

Renewal of requests for Revolade will be assessed on a case-by-case basis

Note: Revolade therapy beyond 1 year of continuous treatment has not been studied. After 1 year of continuous treatment, therapeutic options should be reassessed.

Duration of Approval: 1 year

Icatibant
Brand(s): Firazyr
DOSAGE FORM/ STRENGTH: 30 mg/3 mL prefilled syringe
Effective date: November 5, 2015

For the treatment of acute attacks of type I or type II hereditary angioedema (HAE) in adults with lab confirmed c1-esterase inhibitor deficiency if the following conditions are met:

a. Treatment of acute non-laryngeal attacks of at least moderate severity; OR

b. Treatment of acute laryngeal attacks; AND

c. Must be prescribed by physicians (e.g. immunologists, allergists or hematologists) with experience in the treatment of HAE.

Notes:

- Documentation of diagnosis (e.g. patient and family history, symptoms, lab test results) must be provided.

- For acute non-laryngeal attacks, documentation of severity (frequency, location, and degree of swelling) must be provided

Doses for acute treatment are limited to a single dose for self-administration per attack.

Duration of Approval: Lifetime

Lanadelumab
Brand(s): Takhzyro
DOSAGE FORM/ STRENGTH: 300 mg/2mL inj and 300 mg/2mL Prefilled Syringe
Effective date: February 2, 2021, Updated January 14, 2022

Initiation Criteria:

For the routine prevention of attacks of hereditary angioedema (HAE) in patients meeting ALL the following criteria:
- Is at least 12 years of age; AND
- Has HAE type I or II; AND
- Has experienced at least three HAE attacks within any four-week period requiring treatment with an acute injectable therapy (e.g. Icatibant, C1-INH); AND
- Must be prescribed by physicians (e.g. immunologists, allergists or hematologists) with experience in the diagnosis and management of HAE.

Lanadelumab
Brand(s): Takhzyro
DOSAGE FORM/ STRENGTH: 300 mg/2mL

NOTE: For patients who are already on long-term prophylactic treatment of angioedema (e.g. C1-INH) and intend to transition to lanadelumab, please provide historical HAE attack rates and treatment details.

Discontinuation Criteria:

Reimbursement will be discontinued in patients who either respond inadequately or exhibit loss of response, defined as follows:

- Inadequate response: No reduction in the number of HAE attacks that require treatment with an acute injectable therapy during the first three months of treatment with Takhzyro.
- Loss of response: An increase in the observed number of HAE attacks requiring acute injectable treatment compared to the number before initiating treatment with lanadelumab.

Exclusion Criteria: Patient is using lanadelumab with other medications used for the long-term prophylactic treatment of angioedema (e.g. C1-INH).

Renewal Criteria: Renewals will be considered in patients who do not meet the discontinuation criteria.

NOTE(S):

- *An assessment of a response to treatment should be conducted three months after initiating treatment with lanadelumab.*
- *Following the initial three-month assessment, patients should be assessed for continued response to lanadelumab every six months.*

Recommended dose: 300 mg administered subcutaneously (SC) every 2 weeks. The dose should not be escalated to more than 300 mg every two weeks in cases of inadequate response or loss of response. Dosing interval of 300 mg SC every 4 weeks may be considered if the patient is well-controlled (e.g. attack free) for more than six months.

Approval duration of initials and renewals: 4 months initial, 6 months first renewal, 12 months subsequent renewals

Case by Case Consideration: for patients not meeting the requirement of 3 HAE attacks in the initiation criteria but with HAE attacks associated with significant functional impairment and risk of mortality (e.g. laryngeal attacks).

Pegcetacoplan
Brand(s): Empaveli
DOSAGE FORM/ STRENGTH: 1080 mg/20 mL vial Injection
Effective date: May 15, 2024

Initial requests:

For the treatment of paroxysmal nocturnal hemoglobinuria (PNH) in patients meeting ALL the following criteria;

1. 18 years of age or older; AND

2. Has had an inadequate response (Note 1) to at least one C5 complement inhibitor therapy (i.e. eculizumab, ravulizumab) used at a stable dose for at least 3 months OR has experienced an intolerance to a C5 complement inhibitor (Note 2); AND

3. Prior to the initiation of C5 complement inhibitor treatment (or if the patient has not had an adequate trial of C5 complement therapy and is initiating pegcetacoplan due to adverse reactions to a C5 complement inhibitor therapy), the patient meets the following criteria to confirm the diagnosis of PNH at initial presentation before the use of complement inhibitors;

   a. Patient has documentation (provide a copy of the reports) of BOTH of the following confirmatory results:
      - Flow cytometry/ Fluorescent aerolysin (FLAER) exam with clone count (i.e. granulocyte or monocyte) equal to or greater than 10%
      - Lactate dehydrogenase (LDH) greater than 1.5 upper limit of normal (ULN)

AND

   b. AT LEAST ONE of the following clinical features:

- Has experienced a thrombotic or embolic event which required the institution of therapeutic anticoagulant therapy.
- Has a minimum transfusion requirement of 4 units of red blood cells in the previous 12 months.
- Has chronic or recurrent anemia where causes other than hemolysis have been excluded and demonstrated by more than one measure of hemoglobin less than or equal to 70 g/L OR more than one measure of hemoglobin less than or equal to 100 g/L with concurrent symptoms of anemia.
- Has pulmonary insufficiency: Debilitating shortness of breath and/or chest pain resulting in limitation of normal activity (New York Heart Association Class III) and/or established diagnosis of pulmonary arterial hypertension, where causes other than PNH have been excluded.

Pegcetacoplan
Brand(s): Empaveli
DOSAGE FORM/ STRENGTH: 1080 mg/20 mL vial for Injection

- Has renal insufficiency: History of renal insufficiency, demonstrated by an eGFR less than or equal to 60 mL/min/1.73 m^2, where causes other than PNH have been excluded.
- Has smooth muscle spasm: Recurrent episodes of severe pain requiring hospitalization and/or narcotic analgesia, where causes other than PNH have been excluded;

AND

4. Pegcetacoplan is prescribed by or in consultation with a hematologist; AND

5. Pegcetacoplan is not being used in combination with another complement inhibitors (e.g. eculizumab or ravulizumab) except in the first 4 weeks of treatment.

Notes:

1. An inadequate response is defined as documentation of persistent anemia with hemoglobin levels < 105 g/L (10.5 g/dL) despite an adequate trial of C5 inhibitor treatment (i.e. eculizumab, ravulizumab) reaching a stable dose for at least 3 months and when causes other than extravascular hemolysis have been excluded, or if the patient has intolerable adverse events from use of a funded C5 inhibitor treatments (i.e. eculizumab and ravulizumab).

2. Please ensure that the full details of the adverse effects and intolerances are provided on your request. If the adverse event experienced by the patient to the C5 inhibitor is not considered to be cross-sensitive within the C5 inhibitor class, then both funded C5 inhibitors must be trialed.

3. Prescribers should submit relevant bloodwork to support the diagnosis including CBC, transfusion records, bone marrow report, flow cytometry/FLAER exam report, LDH levels, and as possible, recent consult notes.

4. Prescribers should comply with the most current National Advisory Committee on Immunization (NACI) recommendations for meningococcal vaccination in patients with complement deficiencies to reduce the risk of serious infection. Appropriate vaccination for meningococcal disease should be administered at least 2 weeks prior to receiving the first dose of **pegcetacoplan** and if this is not possible, refer to the product monograph for mitigating instructions.

5. Funding will not be considered if the patient or treating physician fails to comply adequately with treatment or measures, including monitoring requirements, required to evaluate the effectiveness of the therapy with pegcetocoplan.

Pegcetacoplan
Brand(s): Empaveli
DOSAGE FORM/ STRENGTH: 1080 mg/20 mL vial for Injection

Renewal criteria:

Renewals will be considered in patients who demonstrate clinical improvement or disease stabilization of PNH compared to baseline clinical results and symptoms prior to the initiation and use of pegcetacoplan.

(Note that the baseline may be those results after C5 complement inhibitor treatment was deemed to be inadequate OR if a patient was deemed intolerant to C5 inhibitors, it may be the baseline PNH results before an adequate use of complement therapy.)

As part of the renewal of funding, confirmation of clone size (by flow cytometry) should be submitted with the request. Granulocyte and monocyte clone size should be included to compare against the baseline results.

Exclusion criteria (applies to both initials and renewals)

Patients meeting one or more of the following are not approved for funding under the Ontario drug benefit program:

1. Previously experienced treatment failure with pegcetacoplan administered for the treatment of PNH.

2. Pegcetacoplan will not be funded in combination with another complement inhibitor. Use of combination will only be permitted during the first 4 weeks during transitioning of treatment.

3. Small granulocyte clone size - the treatment of patients with a granulocyte clone size below 10% will not be eligible for treatment.

4. Aplastic anemia with two or more of the following: neutrophil count below 0.5 x 10^9/L, platelet count below 20 x 10^9/L, reticulocytes below 25 x 10^9/L, or severe bone marrow hypocellularity.
5. Patients diagnosed with another life threatening or severe disease where the long term prognosis is unlikely to be influenced by therapy (e.g. acute myeloid leukemia or high-risk myelodysplastic syndrome).

6. The presence of another medical condition that might reasonably be expected to compromise a response to therapy.

Pegcetacoplan
Brand(s): Empaveli
DOSAGE FORM/ STRENGTH: 1080 mg/20 mL vial for Injection

Approved doses:

Please refer to the product monograph for pegcetacoplan for further details about administration of the subcutaneous infusion using a commercially available syringe system infusion pump.

1080 mg subcutaneous infusion twice weekly on Day 1 and Day 4 of each treatment week.

The dosing regimen may be changed to 1080 mg every third day (i.e. Day 1, Day 4, Day 7, Day 10, Day 13, and so forth) if a subject has a lactate dehydrogenase (LDH) level greater than 2 × the upper limit of normal (ULN) on twice weekly dosing.

In the event of a dose increase, monitor LDH twice weekly for at least 4 weeks.

Dosage for patients switching to Empaveli from C5 inhibitors

For the first 4 weeks, pegcetacoplan is administered as twice weekly subcutaneous doses of 1080 mg in addition to the patient's current dose of C5 inhibitor treatment to minimize the risk of hemolysis with abrupt treatment discontinuation.

After 4 weeks, the patient can discontinue C5 inhibitor while continuing on monotherapy with pegcetacoplan.

Approval duration of initials: 6 months

Approved dosing of renewals: 1 year

Ravulizumab

Brand(s): Ultomiris
DOSAGE FORM/ STRENGTH: 300 mg/30 mL, 300 mg/3 mL,1100 mg/11 mL vial
Effective date: March 1, 2024

Initial requests:

For the treatment of paroxysmal nocturnal hemoglobinuria (PNH) in patients meeting all the following criteria;

1. Age one month or older; AND

2. Has a confirmed diagnosis of PNH at initial presentation based on meeting the following;

   a. Patient has documentation (provide a copy of the reports) of both of the following confirmatory results**:**

   - Flow cytometry/ Fluorescent aerolysin (FLAER) exam with clone count (i.e granulocyte or monocyte) equal to or greater than 10%
   - Lactate dehydrogenase (LDH) greater than 1.5 upper limit of normal (ULN)

   AND

   b. At least one of the following clinical features:

   - Has experienced a thrombotic or embolic event which required the institution of therapeutic anticoagulant therapy.
   - Has a minimum transfusion requirement of 4 units of red blood cells in the previous 12 months.
   - Has chronic or recurrent anemia where causes other than hemolysis have been excluded and demonstrated by more than one measure of hemoglobin less than or equal to 70 g/L OR more than one measure of hemoglobin less than or equal to 100 g/L with concurrent symptoms of anemia.
   - Has pulmonary insufficiency: Debilitating shortness of breath and/or chest pain resulting in limitation of normal activity (New York Heart Association Class III) and/or established diagnosis of pulmonary arterial hypertension, where causes other than PNH have been excluded.
   - Has renal insufficiency: History of renal insufficiency, demonstrated by an eGFR less than or equal to 60 mL/min/1.73 m^2, where causes other than PNH have been excluded.
   - Has smooth muscle spasm: Recurrent episodes of severe pain requiring hospitalization and/or narcotic analgesia, where causes other than PNH have been excluded.

3. Ravulizumab is prescribed by or in consultation with a hematologist or a pediatric hematologist.

Ravulizumab

Brand(s): Ultomiris

DOSAGE FORM/ STRENGTH: 300 mg/30mL, 300 mg/3 mL, 1100 mg/11 mL vial

Notes:

1. Prescribers should submit relevant bloodwork to support the diagnosis including CBC, transfusion records, bone marrow report, flow cytometry/FLAER exam report, LDH levels, and as possible, recent consult notes.
2. Prescribers should comply with the most current National Advisory Committee on Immunization (NACI) recommendations for meningococcal vaccination in patients with complement deficiencies to reduce the risk of serious infection. Appropriate vaccination for meningococcal disease should be administered atleast 2 weeks prior to receiving the first dose of ravulizumab and if this is not possible, refer to the product monograph for mitigating instructions.
3. Funding will not be considered if the patient or treating physician fails to comply adequately with treatment or measures, including monitoring requirements, required to evaluate the effectiveness of the therapy with ravulizumab.
4. Patients stabilized on eculizumab who wish to switch to ravulizumab must meet the initiation and renewal criteria (as applicable) of ravulizumab and will be considered on a case-by-case basis.

Renewal criteria:

Renewals will be considered in patients who demonstrate clinical improvement or disease stabilization of PNH compared to baseline clinical results and symptoms.

As part of the renewal of funding, confirmation of clone size (by flow cytometry) should be submitted with the request. Granulocyte and monocyte clone size should be included to compare against the baseline results.

Exclusion criteria (applies to both initial and renewals)

Patients meeting one of more of the following are not approved for funding under the Ontario drug benefit program.

1. Previously experienced treatment failure with eculizumab administered for the treatment of PNH.
2. Previously experienced treatment failure with ravulizumab administered for the treatment of PNH.
3. Ravulizumab will not be funded in combination with eculizumab.
4. Small granulocyte clone size - the treatment of patients with a granulocyte clone size below 10% will not be eligible for treatment.
5. Aplastic anemia with two or more of the following: neutrophil count below 0.5 x 10^9/L, platelet count below 20 x 10^9/L, reticulocytes below 25 x 10^9/L, or severe bone marrow hypocellularity.

Ravulizumab
Brand(s): Ultomiris
DOSAGE FORM/ STRENGTH: 300 mg/30mL, 300 mg/3 mL, 1100 mg/11 mL vial

6. Patients diagnosed with another life threatening or severe disease where the long term prognosis is unlikely to be influenced by therapy (for example acute myeloid leukemia or high-risk myelodysplastic syndrome).
7. The presence of another medical condition that might reasonably be expected to compromise a response to therapy.

Approved doses (loading and maintenance):

Weight-based dosing per the Ultomiris product monograph with maintenance doses administered up to every for weeks for patients under 20 kg and every 8 weeks for those above or equal to 20 kg.

Maintenance dosing in those above or equal to 20 kg that is administered more frequent than every 8 weeks require approval by the EAP on a case-by-case.

Approval duration of initials: 6 months

Approved dosing of renewals: 1 year

Ravulizumab
Brand(s): Ultomiris
DOSAGE FORM/ STRENGTH: 300 mg/30mL, 300 mg/3 mL, 1100 mg/11 mL vial

Atypical hemolytic uremic syndrome (aHUS)

Initiation Criteria:

For the treatment of atypical hemolytic uremic syndrome (aHUS) in patients meeting all the following criteria:

1. Age one month or older; AND

2. Has a confirmed diagnosis of aHUS at initial presentation as defined by meeting all of the following;

    a. Presence of an unexplained non- disseminated intravascular coagulation thrombotic microangiopathy (TMA) (i.e. not a secondary TMA); AND

    b. Baseline ADAMTS-13 activity greater than or equal to 10% on blood samples taken prior to plasma exchange (PE) or plasma infusion (PI);

    Note: If the sample for ADAMTS-13 was not collected prior to plasma exchange or plasma infusion, platelet counts greater than 30 x 10^9/L and eGFR less than 50 mL/min/1.73m^2 at TMA presentation will be accepted as predictive of ADAMTS-13 greater than or equal to 10% in TMA patients. In this case, measurement of ADAMTS-13 can be taken one to two weeks following the last PE. The ADAMTS-13 result must be provided within 30 days of commencement of ravulizumab and at least 1 week after the last PE; AND

    c. STEC-negative test in patients with a history of bloody diarrhea in the preceding two weeks; AND

    d. Other diagnoses and causes of TMA must be ruled out

3. Patient must have evidence of ongoing active TMA and progressing, defined by laboratory test abnormalities despite plasmapheresis, if appropriate. This is demonstrated by:

    a. Thrombocytopenia (platelet count less than 150 × 10^9 /L) that is not explained by another cause including secondary TMA and hemolysis as indicated by the documentation of two of the following: red blood cell (RBC) fragmentation (schistocytes) on the blood film; low or absent haptoglobin; or lactate dehydrogenase LDH above normal; OR

    b. Tissue biopsy confirms TMA in patients who do not have evidence of platelet consumption and hemolysis.

Ravulizumab
Brand(s): Ultomiris
DOSAGE FORM/ STRENGTH: 300 mg/30mL, 300 mg/3 mL, 1100 mg/11 mL vial

4. Patient must have documented evidence of at least one of the following clinical features of active organ damage or impairment:

    a. Kidney impairment, as demonstrated by one or more of the following:

    - A decline in estimated glomerular filtration rate (eGFR) or a rise in serum creatinine (SCr) of greater than 20% in a patient with pre-existing renal impairment;
    - SCr greater than upper limit of normal (ULN) for age or eGFR less than 60 mL/min and renal function deteriorating in spite of PE/PI in patients who have no history of preexisting renal impairment (i.e., who have no baseline eGFR measurement);
    - SCr greater than the age-appropriate ULN in pediatric patients (as determined by or in consultation with a pediatric nephrologist)
    - Renal biopsy

    b. The onset of neurological impairment related to TMA e.g., visual field defect, hemiparesis, sensory loss, asymmetric limb weakness, confusion, loss of consciousness/coma, new onset seizure).

    c. Other extra-renal TMA-related manifestations, such as TMA-related cardiac impairment, TMA-related gastrointestinal impairment (e.g. bowel ischemia, pancreatitis); TMA-related pulmonary impairment, and retinal vein occlusion.

5. Ravulizumab is prescribed by or in consultation with a pediatric nephrologist, a nephrologist, a pediatric hematologist or a hematologist.

Notes:

1. Transplant patients with a documented history of aHUS (i.e., history of TMA [not a secondary TMA only] with ADAMTS 13 greater than 10%) would be eligible for ravulizumab if they:

    a. Develop TMA immediately (within hours to 1 month) following a kidney transplant; OR
    b. Previously lost a native or transplanted kidney due to the development of TMA; OR
    c. Have a history of proven aHUS and require prophylaxis with ravulizumab at the time of a kidney transplant [if the genotype of the aHUS is tissue related (i.e., not present in the transplant), then ravulizumab the prescriber may consider ravulizumab to be given pre-transplant and for at least 1-month post-transplant with monitoring closely after discontinuation for recurrence.]

Ravulizumab
Brand(s): Ultomiris
DOSAGE FORM/ STRENGTH: 300 mg/30mL, 300 mg/3 mL, 1100 mg/11 mL vial

2. Re-initiation criteria: A patient previously diagnosed with aHUS and who responded to treatment with ravulizumab and has not failed ravulizumab is eligible to restart ravulizumab if the patient redevelops a TMA related to aHUS and meets the following clinical conditions:

    a. Significant hemolysis as evidenced by presence of schistocytes on the blood film, or low or absent haptoglobin, or LDH above normal; AND EITHER

    b. Platelet consumption as measured by either a greater than or equal to 25% decline from patient baseline or thrombocytopenia (platelet count less than 150,000 × 10^9/L);
    OR
    TMA-related organ impairment (e.g., unexplained rise in serum creatinine with onset of urine dipstick positive for hemoglobin) including on recent biopsy.

3. Assessment of treatment response should be conducted at 6 months, at 12 months, then annually thereafter.

4. Patients stabilized on eculizumab who wish to switch to ravulizumab must meet the initiation and renewal criteria (as applicable) of ravulizumab and will be considered on a case-by-case basis.

Exclusions: Patients meeting the below will not be funded:

1. Patients who have previously experienced ravulizumab treatment failure (i.e., treated with ravulizumab with a previous aHUS recurrence).
2. Ravulizumab will not be funded in combination with eculizumab.

Renewal Criteria:

Treatment with ravulizumab can be renewed as long as the patient exhibits a response to treatment or as per physician discretion (e.g., long-term funding based on factors like limited organ reserve or high-risk genetic mutation such as Factor H deficiency) AND the patient does not experience treatment failure as defined below.

At the first renewal (i.e. the 6-month assessment) treatment response and no treatment failure is required.

At the 12-month and annual assessments, treatment response, no treatment failure, and the patient has limited organ reserve or high-risk genetic mutation are required.

Ravulizumab
Brand(s): Ultomiris
DOSAGE FORM/ STRENGTH: 300 mg/30mL, 300 mg/3 mL, 1100 mg/11 mL vial

Treatment failure is defined as:

a. Dialysis-dependent at 6 months, and failed to demonstrate resolution or stabilization of neurological or extrarenal complications if these were originally present; OR
b. On dialysis for 4 or more of the previous 6 months while receiving ravulizumab and failed to demonstrate resolution or stabilization of neurological or extrarenal complications if these were originally present; OR
c. Worsening of kidney function with a reduction in eGFR or increase in SCr greater than or equal to 25% from baseline.

Assessment of treatment response should be conducted at 6 months, at 12 months, then annually thereafter.

Treatment response is defined as, but not limited to:

a. hematological normalization (e.g., platelet count, LDH)
b. stabilization of end-organ damage (such as acute kidney injury and brain ischemia)
c. transplant graft survival in susceptible individuals
d. dialysis avoidance in patients who are pre-end-stage kidney disease.

Limited organ reserve is defined as:

a. significant cardiomyopathy, neurological, gastrointestinal, or pulmonary impairment related to TMA; OR
b. Grade 4 or 5 chronic kidney disease (eGFR less than 30mL/min) is required.

Approval duration of initials: 6 months

Approved dosing of renewals: 1 year

Approved doses (loading and maintenance): Weight-based dosing per the Ultomiris product monograph with maintenance doses administered up to every four weeks for patients under 20 kg and every 8 weeks for those above or equal to 20 kg.

Maintenance dosing in those above or equal to 20 kg that is administered more frequent than every 8 weeks require approval by the EAP on a case-by-case.

Romiplostim
Brand(s): Nplate
DOSAGE FORM/ STRENGTH: 250 mcg/0.5 mL 500 mcg/mL
Effective date: May 18, 2011

For the treatment of refractory chronic idiopathic thrombocytopenic purpura (ITP) with bleeding complications in patients who meet the following criteria;

i) Patient has undergone a splenectomy[1]

ii) Patient has tried and is unresponsive to other treatment modalities[2].

[1]Requests for romiplostin where the requesting physician has stated that the patient is not a candidate for splenectomy will be assessed on a case-by-case basis. The requesting physician must provide rationale for why a splenectomy cannot be considered, and where possible, to include a preoperative evaluation on the patient's surgical risks to splenectomy to include consideration of risks of laparoscopic and open surgical interventions if these are available.

Note:The Executive Officer (EO) may revise the criteria if the frequency of patients who are not eligible for splenectomy exceeds published estimates.

[2]Appropriate first-line treatment modalities may include;

- Corticosteroids
- IV anti-D
- Intravenous immune globulin (IVIG)

[2]Appropriate second-line treatment modalities may include;

- Azathioprine
- Cyclosporine
- Cyclophosphamide
- Mycophenolate
- Rituximab
- Danazol
- Dapsone

Patients need to have failed at least two second-line therapies prior to requesting Nplate.

Duration of Approval: 1 year

Renewal of requests will be considered in patients who have a stable platelet response and reduced symptoms of ITP-related bleeding events.

Duration of Approval: 1 year

CARDIOLOGY DRUGS

Eplerenone
Brand(s): Inspra
DOSAGE FORM/ STRENGTH: 25 mg, 50 mg tablets

For the treatment of patients who have heart failure and left ventricular systolic dysfunction due to acute myocardial infarction. Patients must have:

- An ejection fraction ≤ 40% **AND**
- Prior trial of spironolactone but experienced severe symptomatic (painful) gynecomastia

Duration of Approval: Lifetime

Icosapent Ethyl
Brand(s): Vascepa
DOSAGE FORM/ STRENGTH: 1 g capsules
Effective date: July 21, 2022

Initiation criteria

For the secondary prevention of cardiovascular events in patients with established cardiovascular disease who meet all of the following criteria:

- Aged 45 years of age or older; AND
- Has been diagnosed with established cardiovascular disease [e.g. coronary heart disease (e.g. myocardial infarction, angina, coronary procedure, abdominal aortic aneurysm), cerebrovascular disease (e.g. stroke, transient ischemic attack, carotid obstruction), or peripheral artery disease]; AND
- Has documented fasting triglyceride level greater than or equal to 1.7 mmol/L (150 mg/dL) and lower than 5.6 mmol/L (500 mg/dL) at baseline[1]; AND
- Has documented low-density lipoprotein cholesterol level greater than 1.0 mmol/L (40 mg/dL) and lower than 2.6 mmol/L (100 mg/dL) at baseline[1] and is receiving maximally tolerated statin dose for a minimum of 4 weeks.[2] [Note: Statin dose should be targeted to achieve a low-density lipoprotein cholesterol lower than 2.0 mmol/L (80 mg/dL)].

[1]Baseline levels should be measured within the preceding 3 months prior to starting treatment with icosapent ethyl.

Icosapent Ethyl
Brand(s): Vascepa
DOSAGE FORM/ STRENGTH: 1 g capsules

[2]Case-by-case consideration may be provided for patients who have been on a stable statin regimen consisting of a maximally tolerated moderate to high-intensity statin dose AND who have a baseline low-density lipoprotein cholesterol level of greater or equal to 2.6 mmol/L (100mg/dL)[1] AND/OR who have a documented contraindication/intolerance to statins. Details of the contraindication/intolerance must be provided.

Renewal criteria

Renewals will be considered in patients who continue to benefit from treatment and who do not develop unacceptable toxicities to treatment.

Approved dose: up to 2 grams orally twice daily

Initial approval duration: 2 years

Renewal approval duration: 5 years

Mavacamten

Brand(s): Camzyos
DOSAGE FORM/ STRENGTH: 2.5 mg, 5 mg, 10 mg, 15 mg Capsule
Effective date: August 26, 2024

Initial Criteria:

For the treatment of symptomatic obstructive hypertrophic cardiomyopathy (oHCM) of New York Heart Association (NYHA) class II to III in adult patients who meet ALL the following criteria:

1. 18 years of age or older; AND
2. Has a confirmed diagnosis of symptomatic obstructive hypertrophic cardiomyopathy (oHCM); AND
3. Documented left ventricular ejection fraction (LVEF) equal to or greater than 55% at rest determined by echocardiography; AND
4. Left ventricular (LV) wall thickness equal to or greater than 15 mm [or equal to or greater than 13 mm with a family history of hypertrophic cardiomyopathy (HCM)]; AND
5. Left ventricular outflow tract (LVOT) peak gradient equal to or greater than 50 mm Hg at rest, after Valsalva maneuver, or postexercise as confirmed by echocardiography; AND
6. Patient must be receiving the standard of care (SOC) treatment for oHCM with a beta-blocker (BB) and/or a non-dihydropyridine calcium channel blocker (ND-CCB) (e.g. verapamil, diltiazem) and experience clinical deterioration in symptoms or echocardiography while receiving these treatments (Note 1) ; AND
7. All initial requests must be prescribed by a cardiologist or prescriber with expertise in the diagnosis of HCM working with a specialized clinic with this expertise. (Note 2)

Discontinuation Criteria:

Funding of mavacamten will be discontinued upon meeting one or more of the following conditions:

1. LVEF less than or equal to 30% determined by echocardiography; OR
2. LVEF is less than 50% on two consecutive occasions determined by echocardiography while on at least 2.5 mg daily of mavacamten; OR
3. Receives septal reduction therapy (SRT).

Duration of Initial Approval: 6 months

Mavacamten

Brand(s): Camzyos
DOSAGE FORM/ STRENGTH: 2.5 mg, 5 mg, 10 mg, 15 mg Capsule

Renewal Criteria:

Renewal of funding will be provided for patients who do not meet the discontinuation criteria and who demonstrate benefit from treatment with mavacamten.

Additionally, patients must meet at least one of the following criteria;

1. LVEF 50-55% regardless of Valsalva LVOT gradient; OR
2. LVEF greater than 55% and Valsalva LVOT gradient less than 30 mm Hg; OR
3. LVEF greater than or equal to 55% and Valsalva LVOT gradient greater than or equal to 30 mm Hg

Duration of Approval of Renewals: 1 year

Notes:

1. Case-by-case consideration will be provided for requests for patients who have contraindications, experienced toxicities/adverse reactions to the usual SOC therapies for the treatment of oHCM. Requests must include clinical details as to why the SOC treatments could not be used or a clinical consult note.

2. Requests for renewal of funding initiated by a cardiologist may be continued by another prescriber upon meeting the renewal criteria.

Recommended dose:

Refer to the product monograph for dose titration guidance.

Maintenance dose: 2.5 mg to 15 mg daily.

Sildenafil

Brand(s): Revatio and generics, Viagra and generics
DOSAGE FORM/ STRENGTH: 20 mg (Revatio versions), 25 mg, 50 mg, 100 mg (Viagra versions)
Effective date: September 9, 2022

For the treatment of severe Raynaud's phenomenon (RP) and/or digital ulcers secondary to scleroderma (systemic sclerosis) or scleroderma-like disease:

- After failure of at least one calcium channel blocker (CCB) OR without trial of a CCB in a patient who has experienced an emergency situation such as threatened ischemic digit(s) requiring hospitalization
- Must be prescribed by a specialist (i.e., rheumatologist, general internist, vascular surgeon)

Duration of initial approval: 6 months

Renewals will be considered on a case-by-case basis for patients who demonstrate benefit from treatment (e.g. positive response in the duration, frequency and or severity of RP and/or improvement in the size or number of digital ulcers.)

Duration of renewals: 1 year

Tadalafil

Brand(s): Adcirca and generics, Cialis and generics
DOSAGE FORM/ STRENGTH: 20 mg (Adcirca versions) ; 2.5 mg, 5 mg, 10 mg, 20 mg (Cialis versions)
Effective date: September 9, 2022

For the treatment of severe Raynaud's phenomenon (RP) and/or digital ulcers secondary to scleroderma (systemic sclerosis) or scleroderma-like disease:

- After failure of at least one calcium channel blocker (CCB) OR without trial of a CCB in a patient who has experienced an emergency situation such as threatened ischemic digit(s) requiring hospitalization
- Must be prescribed by a specialist (i.e., rheumatologist, general internist, vascular surgeon)

Duration of initial approval: 6 months

Renewals will be considered on a case-by-case basis for patients who demonstrate benefit from treatment (e.g. positive response in the duration, frequency and or severity of RP and/or improvement in the size or number of digital ulcers.)

Duration of renewals: 1 year

CENTRAL NERVOUS SYSTEM DRUGS

Amifampridine

Brand(s): Ruzurgi
DOSAGE FORM/ STRENGTH: 10 mg tab
Effective Date: April 18, 2023

For the symptomatic treatment of Lambert-Eaton Myasthenic Syndrome (LEMS) in patients who meet all the following criteria:

1. 6 years of age and older; AND
2. Confirmatory symptoms, bloodwork (as applicable), and test results that support the diagnosis of LEMS is provided. Please include the baseline Triple Timed Up and Go (3TUG) test results prior to initiation of amifampridine treatment; AND
3. Patient is under the care of a neurologist with expertise in the diagnosis and management of LEMS.

Note:

1. Provide details of other treatments (e.g. pyridostigmine, immunomodulators, steroids, or immunosuppressants) that have been or will be used with amifampridine.
2. Patients should be assessed for a response to treatment within 3 months of initiating amifampridine. A response to treatment is defined as an improvement of at least 30% on the Triple Timed Up and Go (3TUG) test.

Case-by-case consideration will be provided for patients who are non-ambulatory and therefore unable to complete the 3TUG test.

Renewal Criteria:

First renewal:

Renewals will be considered in patients who demonstrate an improvement of at least 30% on the Triple Timed Up and Go (3TUG) test from pre-treatment levels after 3 months of treatment.

Second and subsequent renewals:

Renewals will be provided for patients who continue to experience and maintain symptomatic benefit from treatment and who have not developed unacceptable toxicities.

Exclusion Criteria:

Amifampridine will not be funded in combination with another amifampridine or 3,4-diaminopyridine potassium channel blocker.

Amifampridine
Brand(s): Ruzurgi
DOSAGE FORM/ STRENGTH: 10 mg tablet

Approved doses:

Doses to be individualized to optimal effect. Up to 40 mg daily for those weighing 45 kg or less with maximum single dose of 10 mg.

Up to 80 mg daily for those weighing 45 kg or more with a maximum single dose of 20 mg.

Approval Duration: Initials: 6 months;

Initial Renewal: 6 months

Subsequent Renewals: 1 year

Amifampridine phosphate
Brand(s): Firdapse
DOSAGE FORM/ STRENGTH: 10 mg tab
Effective Date: August 2, 2023

Initiation Criteria:

For the symptomatic treatment of Lambert-Eaton Myasthenic Syndrome (LEMS) in patients who meet all the following criteria;

1. 18 years of age and older; AND

2. Confirmatory symptoms, bloodwork (as applicable), and test results that support the diagnosis of LEMS is provided. Please include the baseline Triple Timed Up and Go (3TUG) test results prior to initiation of amifampridine treatment; AND

3. Patient is under the care of a neurologist with expertise in the diagnosis and management of LEMS.

Note:

1. Provide details of other treatments (e.g. pyridostigmine, immunomodulators, steroids, or immunosuppressants) that have been or will be used with amifampridine.
2. Patients should be assessed for a response to treatment within 3 months of initiating amifampridine. A response to treatment is defined as an improvement of at least 30% on the Triple Timed Up and Go (3TUG) test.
3. Case-by-case consideration will be provided for patients who are non-ambulatory and therefore unable to complete the 3TUG test.

Amifampridine
Brand(s): Firdapse
DOSAGE FORM/ STRENGTH: 10 mg tablet

Renewal Criteria:

First renewal:

Renewals will be considered in patients who demonstrate an improvement of at least 30% on the Triple Timed Up and Go (3TUG) test from pre-treatment levels after 3 months of treatment.

Second and subsequent renewals:

Renewals will be provided for patients who continue to experience and maintain symptomatic benefit from treatment and who have not developed unacceptable toxicities.

Exclusion Criteria:

1. Amifampridine will not be funded in combination with another amifampridine or 3,4-diaminopyridine potassium channel blocker.

Approved doses:

Doses to be individualized to optimal effect.

Up to a maximum recommended total daily dose of 80 mg.

The maximum single dose is 20mg.

Approval Duration of initials: 6 months

Initial Renewal: 6 months

Subsequent Renewals: 1 year

Edaravone

Brand(s): Radicava
DOSAGE FORM/ STRENGTH: 30mg/100mL IV solution, 105 mg/5mL oral suspension
Effective date: May 11, 2020 (IV solution); July 19, 2023 (Oral suspension)

Initiation Criteria:

For the treatment of amyotrophic lateral sclerosis (ALS) in patients meeting ALL the following criteria:

1. Diagnosis of definite ALS or probable ALS; AND
2. ALS symptom onset occurred within the past two years or less; AND
3. Has a score greater than or the same as two (2) points on each of the 12 items of the ALS Functional Rating Scale – Revised (ALSFRS-R); AND
4. Forced vital capacity (FVC) is greater than or equal to 80% of predicted; AND
5. Does not require permanent non-invasive or invasive ventilation; AND
6. Is under the care of a specialist with experience in the diagnosis and management of ALS

Discontinuation Criteria:

Reimbursement will be discontinued in patients who meet any one of the following criteria:

- patient becomes non-ambulatory (ALSFRS-R score ≤ 1 for item 8) AND is unable to cut food and feed themselves without assistance, irrespective of whether a gastrostomy is in place (ALSFRS-R score < 1 for item 5a or 5b); or
- patient requires permanent non-invasive or invasive ventilation.

Renewal Criteria:
Renewals will be considered in patients who do not meet the discontinuation criteria.

Recommended dose:

60 mg administered as an intravenous infusion according to the following schedule:

- An initial treatment cycle with daily doses for 14 days, followed by a 14-day drug-free period
- Subsequent treatment cycles with daily doses for 10 days out of 14-day periods, followed by 14-day drug-free periods.

105 mg (5 mL) administered orally or via a feeding tube according to the following schedule:

- an initial treatment cycle with daily doses for 14 days, followed by a 14-day drug-free period, and
- subsequent treatment cycles with daily doses for 10 days out of 14-day periods, followed by 14-day drug-free periods.

Approval duration of initials and renewals: 1 year

Modafinil
Brand(s): Alertec
DOSAGE FORM/ STRENGTH: 100 mg tablet

For the symptomatic treatment of excessive daytime sleepiness in patients with narcolepsy who have demonstrated a lack of response to or an inability to tolerate dextroamphetamine AND methylphenidate.

Note: See also Multiple Sclerosis Drugs

Duration of Approval: 2 years (Initials and Renewals)

Riluzole
Brand(s): Rilutek
DOSAGE FORM/ STRENGTH: 50 mg tablet

Approvals will be provided for:

Patients who have probable or definite amyotrophic lateral sclerosis (ALS) as defined by World Federation of Neurology (WFN) criteria with onset within 5 years, who have a vital capacity of >60% predicted and do not have a tracheostomy.

Discontinuation Criteria:

Reimbursement will be discontinued if the patient progresses to require permanent assisted ventilation. This is defined as assisted ventilation required for 23 out of 24 hours for greater than or equal to 14 consecutive days.

Renewal Criteria:

Renewals will be considered in patients who do not meet the discontinuation criteria.

Approval period of initials and renewals: 12 months

Sodium phenylbutyrate and Ursodoxicoltaurine

Brand(s): Albrioza
DOSAGE FORM/ STRENGTH: 3g/1g Sachet
Effective Date: June 22, 2023

For the treatment of amyotrophic lateral sclerosis (ALS) in patients meeting all the following criteria:

1. Diagnosis of definite ALS; AND
2. ALS symptom onset occurred within the past 18 months or less; AND
3. Forced vital capacity (FVC) is greater than or equal to 60% of predicted; AND
4. Does not require permanent non-invasive or invasive ventilation; AND
5. Is under the care of a specialist with experience in the diagnosis and management of ALS

Discontinuation Criteria:

Reimbursement will be discontinued in patients who meet any one of the following criteria:

1. Patient becomes non-ambulatory AND is unable to cut food and feed themselves without assistance, irrespective of whether a gastrostomy is in place.
2. Patient requires permanent non-invasive or invasive ventilation

Renewal Criteria:

Renewals will be considered in patients who do not meet the discontinuation criteria.

Recommended dose:

For the first 3 weeks of treatment, take 1 sachet (3 g sodium phenylbutyrate, 1 g ursodoxicoltaurine) daily.

After 3 weeks, dosing should be increased to 1 sachet twice a day.

Approval duration of initials and renewals: 1 year

Tetrabenazine
Brand(s): Nitoman
DOSAGE FORM/ STRENGTH: 25 mg tablet

For the treatment of Hungtington's chorea, tic and Gille's de la Toureet syndrome and tardive dyskinesia in patients meeting the following criteria:

i) is prescribed by (or in consultation with) physicians who are experienced in the treatment of hyperkinetic movement disorders (e.g. specialists practicing in a Movement Disorder Clinic, neurologists, psychiatrists, physiatrists, geriatricians, pediatricians); **AND**

ii) have disabling Huntington's chorea OR tic and Gille's de la Tourette syndrome and have documented evidence of failure to respond, intolerable side effects or contraindication to at least one agent presently available on the Formulary.

**Note that for patients with disabling tardive dyskinesia, a trial of a Formulary *agent is NOT required (i.e. tetrabenazine can be considered for use as a first-line agent)*

Duration of Approval: 1 year

Renewals will be considered for patients whose request is prescribed by (or in consultation with) physicians who are experienced in the treatment of hyperkinetic movement disorders (e.g. specialists practicing in a Movement Disorder Clinic, neurologists, psychiatrists, physiatrists, geriatricians, pediatricians); AND who provide written confirmation that movements and functional status are stabilized on tetrabenazine therapy.

Duration of Approval: 5 years

For the treatment of Hemiballismus, senile chorea, or other disabling hyperkinetic movement disorders (HKMD) will be considered on a case-by-case basis in patients meeting the following criteria**:**

- is prescribed by (or in consultation with) physicians who are experienced in the treatment of hyperkinetic movement disorders (e.g. specialists practicing in a Movement Disorder Clinic, neurologists, psychiatrists, physiatrists, geriatricians, pediatricians); **AND**

- have documented evidence of failure to respond, intolerable side effects or contraindication to at least one agent presently available on the Formulary.

Duration of Approval: 1 year

Renewals will be considered for patients whose request is prescribed by (or in consultation with) physicians who are experienced in the treatment of hyperkinetic movement disorders (e.g. specialists practicing in a Movement Disorder Clinic, neurologists, psychiatrists, physiatrists, geriatricians, pediatricians); AND

Tetrabenazine
Brand(s): Nitoman
DOSAGE FORM/ STRENGTH: 25 mg tablet

who provide written confirmation that movements and functional status are stabilized on tetrabenazine therapy.

Duration of Approval: 5 years

Please note that information MUST BE provided about why a patient has not tried or cannot try a formulary alternative.

Requests not meeting the above criteria for HKMD will be considered through a case-by-case review and the physician must provide adequate clinical information to enable this assessment.

DERMATOLOGY DRUGS

Abrocitinib
Brand(s): Cibinqo
DOSAGE FORM/ STRENGTH: 50 mg, 100 mg, 200 mg tablets
Effective date: October 3, 2023

Initiation Criteria

For the treatment of moderate to severe atopic dermatitis in patients meeting the all the following criteria;

1. 12 years of age or older; AND
2. Diagnosed with moderate-to-severe atopic dermatitis (AD) by the Eczema Area and Severity Index (EASI) score equal to or greater than 16 points and the Investigators (Physician) Global Assessment score of 3 to 4; AND
3. Failure to maintain adequate control of their dermatitis with maximally tolerated medical topical therapies for AD combined with phototherapy (where available);[1,2] AND
4. Failure to maintain adequate control of their dermatitis with maximally tolerated medical topical therapies for AD combined with at least 1 of the 4 systemic immunomodulators (methotrexate, cyclosporine, mycophenolate mofetil, or azathioprine).[1,2]
5. Abrocitinib is prescribed by a dermatologist, allergist, pediatrician or clinical immunologist, or in consultation with one of these specialists. (Please include the consult note with the EAP application.)

Exclusion Criteria:

1. Abrocitinib will not be funded if it is used in combination with phototherapy or any immunomodulatory drugs (including biologics[3] or a Janus kinase [JAK] inhibitor treatment) for treatment of AD.

Notes:

[1]For each treatment used, provide documentation of refractory disease and/or intolerance (including a description of the adverse effect and severity of reaction). If a patient is deemed to be ineligible or contraindicated to receive the treatment, provide the reason(s) for their ineligibility.

[2]An adequate trial for patients with AD who undergo therapy with phototherapy, methotrexate, cyclosporine, mycophenolate mofetil, and azathioprine is defined as follows:

- For phototherapy: the typical duration would be considered 12 weeks (3 times per week).
- For methotrexate: an adequate trial would be 10 mg to 20 mg per week for 12 weeks.
- For cyclosporine: an adequate trial would be 2.5 mg/kg to 5 mg/kg per day for 12 weeks.

Abrocitinib
Brand(s): Cibinqo
DOSAGE FORM/ STRENGTH: 50 mg, 100 mg, 200 mg tablets

- For mycophenolate mofetil: an adequate trial would be 1 g twice daily for 12 weeks.
- For azathioprine: an adequate trial would be 1.5 to 2.5 mg/kg/day for 12 weeks

[3] The concurrent use of abrocitinib used in combination with other biologics used for other conditions will be considered on a case-by-case basis.

[4]Funding of patients who meet the above criteria and who are experiencing inadequate response using another systemic treatment (e.g. biologics, steroids) for AD will be considered on a case-by-case basis.

Renewal Criteria:

First renewal:

Renewal of funding will be considered in patients with documentation of benefit from treatment. Benefit from treatment is defined as a 75% or greater improvement from baseline in the Eczema Area and Severity Index (EASI) score (EASI-75) in the first 20 weeks of treatment initiation with abrocitinib.

Subsequent renewals:

Subsequent renewal of funding will be considered in patient who maintain the 75% or greater improvement in EASI score response from baseline.

Duration of Approval for initial requests: 6 months

Duration of Approval for first and second renewal: 6 months

Duration of Approval for 3rd and subsequent renewals: 1 year

Approved dose: Up to 200 mg orally once daily.

Please refer to the product monograph for dose adjustment recommendations.

Adalimumab – See Formulary for funded biosimilars

Brand(s): Humira and formulary listed biosimilars
DOSAGE FORM/ STRENGTH: 40 mg/0.8 mL prefilled syringe, 40mg/0.8mL and 20 mg/0.2 mL prefilled pens for subcutaneous injection

For the treatment of adult patients with active moderate to severe hidradenitis suppurativa who have not responded to conventional therapy (including systemic antibiotics) and who meet all of the following:

1. A total abscess and nodule count of 3 or greater
2. Lesions in at least two distinct anatomic areas, one of which must be Hurley Stage II or III
3. An inadequate response to a 90-day trial of oral antibiotics
4. Prescribed by a practitioner with expertise in the management of patients with HS
5. Note: Treatment with adalimumab should be discontinued if there is no improvement after 12 weeks of treatment

First renewal:

- Requests for renewal should provide objective evidence of a treatment response, defined as at least a 50% reduction in abscesses and inflammatory nodule count with no increase in abscess count or draining fistula count relative to baseline at week 12.

Subsequent renewal:

- For renewals beyond the second year, objective evidence of the preservation of treatment effect should be provided (i.e. the current AN (abscess and inflammatory nodule) count and draining fistula count should be compared to the count prior to initiating treatment with adalimumab).

Approval duration:

- Initial approval: 3 months
- First renewals: 1 year
- Subsequent renewals: 2 years

Recommended dose:

- The recommended dose is 160 mg initially (week 0), followed by 80 mg at week 2, then 40 mg at week 4, and 40 mg weekly thereafter

Dupilumab

Brand(s): Dupixent
DOSAGE FORM/ STRENGTH: 200mg/1.14mL, 300mg/2ml (Prefilled syringe and prefilled pen)
Effective date: May 6, 2021
Updated: December 3, 2021 and December 1, 2022
Updated: April 28, 2023

Initiation Criteria

For the treatment of **moderate to severe atopic dermatitis** in patients meeting the all the following criteria;

1. 12 years of age or older; AND

2. Diagnosed with moderate-to-severe atopic dermatitis (AD) by the Eczema Area and Severity Index (EASI) score equal to or greater than 16 points and the Investigators (Physician) Global Assessment score of 3 to 4; AND

3. Failure to maintain adequate control of their dermatitis with maximally tolerated medical topical therapies for AD combined with phototherapy (where available); (Note 1 and 2) AND

4. Failure to maintain adequate control of their dermatitis with maximally tolerated medical topical therapies for AD combined with at least 1 of the 4 systemic immunomodulators (methotrexate, cyclosporine, mycophenolate mofetil, or azathioprine). (Note 1 and 2).

5. Dupilumab is prescribed by a dermatologist, allergist, pediatrician or clinical immunologist, or in consultation with one of these specialists. (Please include the consult note with the EAP application.)

Exclusion Criteria:

1. Dupilumab will not be funded if it is used in combination with phototherapy or any immunomodulatory drugs (including biologics (Note 3) or a Janus kinase [JAK] inhibitor treatment) for treatment of AD.

Notes:

1. For each treatment used, provide documentation of refractory disease and/or intolerance (including a description of the adverse effect and severity of reaction). If a patient is deemed to be ineligible or contraindicated to receive the treatment, provide the reason(s) for their ineligibility.

Dupilumab
Brand(s): Dupixent
DOSAGE FORM/ STRENGTH: 200mg/1.14mL, 300mg/2ml Injection solution

2. An adequate trial for patients with AD who undergo therapy with phototherapy, methotrexate, cyclosporine, mycophenolate mofetil, and azathioprine is defined as follows:
    - For phototherapy: the typical duration would be considered 12 weeks (3 times per week).
    - For methotrexate: an adequate trial would be 10 mg to 20 mg per week for 12 weeks.
    - For cyclosporine: an adequate trial would be 2.5 mg/kg to 5 mg/kg per day for 12 weeks.
    - For mycophenolate mofetil: an adequate trial would be 1 g twice daily for 12 weeks.
    - For azathioprine: an adequate trial would be 1.5 to 2.5 mg/kg/day for 12 weeks.

3. The concurrent use of dupilumab used in combination with other biologics used for other conditions will be considered on a case-by-case basis.

Renewal Criteria:

First renewal:

Renewal of funding will be considered in patients with documentation of benefit from treatment. Benefit from treatment is defined as a 75% or greater improvement from baseline in the Eczema Area and Severity Index (EASI) score (EASI-75) within six months of treatment initiation.

Subsequent renewals:

Subsequent renewal of funding will be considered in patient who maintain the 75% or greater improvement in EASI-75 score response from baseline.

Duration of Approval for initial requests: 6 months

Duration of Approval for first and second renewal: 6 months

Duration of Approval for 3rd and subsequent renewals: 1 year

Recommended dose:

Adults: An initial dose of 600 mg followed by 300 mg every other week.

Refer to the product monograph for dosing in adolescents 17 year of age and younger.

Omalizumab
Brand(s): Xolair
DOSAGE FORM/ STRENGTH: 150 mg Injection and 150 mg/mL prefilled syringe
Effective date: December 28, 2011 (Asthma); Updated: April 27, 2017 (CIU)

Initial Criteria:

For the treatment of moderate to severe chronic idiopathic urticaria (CIU) when prescribed by a specialist (i.e. an allergist, an immunologist, a dermatologist) in patients who meet ALL the following criteria;

i) Patient must be 12 years of age or older; AND
ii) Patient must remain symptomatic despite optimum management with available oral therapies.

Approved regimen: Up to 300 mg every 4 weeks

Duration of Approval: 24 weeks

Renewals will be considered for patients who demonstrate one of the following responses to treatment;

i) Patient has had a trial of stopping omalizumab treatment after having achieved symptom control for at least 12 weeks while on therapy but who experience symptom relapse during the stoppage period; OR
ii) Patient has demonstrated improvement but has not been able to achieve complete symptom control for more than 12 consecutive weeks; OR
iii) Patient has demonstrated a partial response to treatment defined as at least a greater than or equal to 9.5 point reduction in the baseline urticaria activity score over 7 days (UAS7).

Approved regimen: Up to 300 mg every 4 weeks

Duration of Approval of Renewals: 24 week

Propranolol
Brand(s): Hemangiol
DOSAGE FORM/ STRENGTH: 3.75mg/mL oral solution
Effective date: October 29, 2018

Initial Criteria:

For the treatment of infants and children with any of the following proliferating infantile hemangiomas;

- Life or function-threatening hemangioma OR
- Ulcerated hemangioma in those experiencing pain and/or lack of response to simple wound care measures; OR
- Hemangiomas deemed to put the patient at risk of permanent scarring or disfigurement.

Requests must be from a dermatologist or a physician experienced in the care of infantile hemangiomas.

Duration of approval: up to 12 months[1]

[1] Note that the treatment duration is typically 6 months and consideration should be made to discontinue the product in the absence of improvement within the first 2 months.

Renewals: Renewals will be considered on a case-by-case basis. If wounds are not healing, please provide clinical information as to why ongoing reimbursement is required.

Rituximab – see Formulary for funded biosimilars
Brand(s): Riximyo, Ruxience, Truxima (Biosimilars); Rituxan (Originator)
DOSAGE FORM/ STRENGTH: 10 mg/mL intravenous injection

Refer to the Executive Officer Communications on the Ministry website for the Ministry's Biosimilar Policy including frequently asked questions and updates for the biosimilar policy updates. http://www.health.gov.on.ca/en/pro/programs/drugs/opdp_eo/eo_communiq.aspx

Effective March 31, 2023, the ODB program will start transitioning coverage for Copaxone®, Enbrel®, Humalog®, Humira®, Lantus®, NovoRapid®, Remicade®, and Rituxan® to their biosimilar versions.

Effective December 29, 2023, coverage for these originator biologic drugs through the ODB program will not be available for patients and the ODB program will only provide coverage for the biosimilar version of these drugs for all ODB program recipients, with limited exemptions. In general, for ODB program recipients who are already on these biologic drugs, there is up to a 9-month transition period (see the biosimilar switch policy described on page 6 to 8 of this document).

It should be noted that after the date when a biosimilar becomes publicly funded for an approved indication, patients initiated on an originator biologic for this same provincially funded indication through support from a manufacturer's patient support program, will be expected to be provided ongoing access of the originator biologic through the patient's original payer mechanism (e.g. manufacturer's patient support program) or to switch to an ODB funded biosimilar version upon meeting specified criteria. The Ministry will no longer consider funding of originator biologics that are part of the biosimilar policy with limited exemptions on or after December 29, 2023.

For the treatment of severe pemphigus vulgaris in patients who meet the following criteria.

- Patient has failed combination therapy with high-dose systemic steroids[1] and a steroid-sparing immunosuppressant[2] trialed in combination for a minimum of 3 months.
- The request must be made by a dermatologist/specialist familiar with the management of pemphigus vulgaris and with the use of rituximab in this condition.

Rituximab
(See funded biosimilar versions on the ODB formulary)
Brand(s): Riximyo, Ruxience, Truxima, Rituxan (Approved EAP exemptions only)
DOSAGE FORM/ STRENGTH: 10 mg/mL Intravenous injection

[1]Patients must have used a steroid dose equivalent to a 1 mg/kg prednisone dose equivalent (or a minimum of 60 mg/day for patients > 60 kg) for at least 4 to 6 weeks before attempting to taper to a lower dose.

[2]Patients must try at least one of the following at therapeutic doses: azathioprine, mycophenolate, cyclophosphamide, or methotrexate (in combination with a steroid).

Dose: ONE course of treatment with rituximab is considered

375 mg/m^2 administered weekly for 4 weeks (for a total of 4 doses) OR

1000 mg of rituximab administered at week 0 and week 2 (for a total of 2 doses)

Re-treatment may be provided if the patient responded to rituximab therapy then experiences disease flare, as long as the request is made no less than 6 months after the last dose of the patient's last treatment course/cycle with rituximab.

Rejection Criteria:

- Other dermatology diagnoses, such as pemphigus foliaceus and bullous pemphigoid
- Maintenance infusions (i.e. regular maintenance doses to keep disease in remission)

Duration of Approval: 1 year

Maintenance Treatment is not funded.

First Renewal: 1 year

Subsequent Renewals after first renewal: 2 years

(Rituximab is funded for course of therapy to be given at an interval of at least 6 months only upon flare of the condition.)

Upadacitinib
Brand(s): Rinvoq
DOSAGE FORM/ STRENGTH: 15 mg, 30 mg Extended Release tablet
Effective date: October 31, 2023 (AD)

Upadacitinib for Atopic Dermatitis

Initiation Criteria:

For the treatment of moderate to severe atopic dermatitis in patients meeting all the following criteria;

1. 12 years of age or older; AND
2. Diagnosed with moderate-to-severe atopic dermatitis (AD) by the Eczema Area and Severity Index (EASI) score equal to or greater than 16 points and the Investigators (Physician) Global Assessment score of 3 to 4; AND
3. Failure to maintain adequate control of their dermatitis with maximally tolerated medical topical therapies for AD combined with phototherapy (where available);[1,2] AND
4. Failure to maintain adequate control of their dermatitis with maximally tolerated medical topical therapies for AD combined with at least 1 of the 4 systemic immunomodulators (methotrexate, cyclosporine, mycophenolate mofetil, or azathioprine).[1,2]
5. Upadacitinib is prescribed by a dermatologist, allergist, pediatrician or clinical immunologist, or in consultation with one of these specialists. (Please include the consult note with the EAP application.)

Exclusion Criteria:

Upadacitinib will not be funded if it is used in combination with phototherapy or any immunomodulatory drugs (including biologics[3] or a Janus kinase [JAK] inhibitor treatment) for treatment of AD.

Notes:

[1]For each treatment used, provide documentation of refractory disease and/or intolerance (including a description of the adverse effect and severity of reaction). If a patient is deemed to be ineligible or contraindicated to receive the treatment, provide the reason(s) for their ineligibility.

[2]An adequate trial for patients with AD who undergo therapy with phototherapy, methotrexate, cyclosporine, mycophenolate mofetil, and azathioprine is defined as follows:

- For phototherapy: the typical duration would be considered 12 weeks (3 times per week).
- For methotrexate: an adequate trial would be 10 mg to 20 mg per week for 12 weeks.
- For cyclosporine: an adequate trial would be 2.5 mg/kg to 5 mg/kg per day for 12 weeks.

Upadacitinib
Brand(s): Rinvoq
DOSAGE FORM/ STRENGTH: 15 mg, 30mg ER Tablet

- For mycophenolate mofetil: an adequate trial would be 1 g twice daily for 12 weeks.
- For azathioprine: an adequate trial would be 1.5 to 2.5 mg/kg/day for 12 weeks

[3] The concurrent use of upadacitinib used in combination with other biologics used for other conditions will be considered on a case-by-case basis.

[4]Funding of patients who meet the above criteria and who are experiencing inadequate response using another systemic treatment (e.g. biologics, steroids) for AD will be considered on a case-by-case basis.

Renewal Criteria:

First renewal:

Renewal of funding will be considered in patients with documentation of benefit from treatment. Benefit from treatment is defined as a 75% or greater improvement from baseline in the Eczema Area and Severity Index (EASI) score (EASI-75) in the first 20 weeks of treatment initiation with upadacitinib.

Subsequent renewals:

Subsequent renewal of funding will be considered in patient who maintain the 75% or greater improvement in EASI score response from baseline.

Duration of Approval for initial requests: 6 months

Duration of Approval for first and second renewal: 6 months

Duration of Approval for 3rd and subsequent renewals: 1 year

Approved dose: Up to 30 mg orally once daily.

Please refer to the product monograph for dose recommendations.

EAR, NOSE AND THROAT (ENT) TREATMENTS

Mepolizumab

Brand(s): Nucala
DOSAGE FORM/ STRENGTH: 100 mg/mL Inj. (Prefilled autoinjector, Prefilled safety syringe (PFSS))
Effective date: June 11, 2024

Severe chronic rhinosinusitis with nasal polyps

Initiation Criteria:

For the treatment of severe chronic rhinosinusitis with nasal polyps (CRSwNP) in adult patients meeting the following criteria:

1. 18 years of age or older; AND
2. Has documented endoscopically or CT-confirmed bilateral nasal polyps (Note 1); AND
3. Confirmation that the patient has undergone at least 1 prior surgical intervention for nasal polyps or has a contraindication to surgery (please include a description of the contraindication); AND
4. Mepolizumab is being used as add-on maintenance therapy with intranasal corticosteroids (INCS); AND
5. CRSwNP is inadequately controlled with refractory symptoms despite use of inhaled nasal corticosteroids at maximally tolerated doses for 3 months; AND
6. Provides a completed copy of the baseline assessment of CRSwNP prior to initiation of mepolizumab using the Sino-nasal Outcome Test-22 (SNOT-22) or the endoscopic nasal polyp score (NPS) (Note 2); AND
7. Request is submitted by an otolaryngologist, allergist, respirologist, or by a physician with expertise in the treatment of severe CRSwnP.

Notes:

1. The endoscopic or CT report must be submitted with all initial requests. Patients who do not have bilateral disease should undergo a biopsy.
2. A baseline assessment of CRSwNP using the SNOT-22 or endoscopic NPS must be completed prior to initiation of mepolizumab treatment as this will be used to confirm severe CRSwNP and to evaluate the patient's response to treatment if renewal of reimbursement is requested.

Exclusion Criteria: Patients with chronic rhinosinusitis without nasal polyps will not be funded.

Mepolizumab
Brand(s): Nucala
DOSAGE FORM/ STRENGTH: 100 mg/mL Inj. (Prefilled safety syringe, Prefilled Autoinjector)

First Renewal:

Renewal of funding will be considered in patients who demonstrate a clinically meaningful response compared to baseline defined as one of the following:

i) A decline in the SNOT 22 score by at least 8.9 points compared to baseline; OR
ii) A 1-point or greater decrease in the endoscopic NPS compared with baseline NPS score.

Second and subsequent renewal:

Ongoing renewal of funding will be considered in patients who continue to demonstrate and maintain a clinically meaningful response compared with baseline results

Recommended dose: 100 mg administered subcutaneously once every 4 weeks

Approval duration of initial and renewals: 1 year

GOUT

Febuxostat

Brand(s): Generics of Uloric (see formulary OFIs)
DOSAGE FORM/ STRENGTH: 80 mg
Effective date: February 22, 2012, Criteria Updated: September 29, 2022

To lower serum uric acid levels, where recommended according to clinical guidelines, in patients with gout or hyperuricemia meeting at least one of the following:

i. Patient has experienced an inadequate response to maximum tolerated doses of allopurinol; OR
ii. Patient has experienced a hypersensitivity reaction to allopurinol; OR
iii. Patient has documentation of an absolute contraindication to allopurinol.

Patients who have experienced severe intolerances to allopurinol not meeting the above criteria will be considered on a case-by-case basis.

Duration of approval: 1 year

Renewal of funding will be considered for patients where there is objective evidence of clinical benefit from the use of febuxostat.

Renewal approval period: 5 years

GRANULOMATOSIS WITH POLYANGIITIS OR MICROSCOPIC POLYANGIITIS

Rituximab -See Formulary for funded biosimilars

Brand(s): Riximyo, Ruxience, Truxima (biosimilars); Rituxan (Originator)
DOSAGE FORM/ STRENGTH: 10 mg/mL intravenous injection

Refer to the Executive Officer Communications on the Ministry website for the Ministry's Biosimilar Policy including frequently asked questions and updates for the biosimilar policy updates. http://www.health.gov.on.ca/en/pro/programs/drugs/opdp_eo/eo_communiq.aspx

Effective March 31, 2023, the ODB program will start transitioning coverage for Copaxone®, Enbrel®, Humalog®, Humira®, Lantus®, NovoRapid®, Remicade®, and Rituxan® to their biosimilar versions.

Effective December 29, 2023, coverage for these originator biologic drugs through the ODB program will not be available for patients and the ODB program will only provide coverage for the biosimilar version of these drugs for all ODB program recipients, with limited exemptions. In general, for ODB program recipients who are already on these biologic drugs, there is up to a 9-month transition period (see the biosimilar switch policy described on page 6 to 8 of this document).

It should be noted that after the date when a biosimilar becomes publicly funded for an approved indication, patients initiated on an originator biologic for this same provincially funded indication through support from a manufacturer's patient support program, will be expected to be provided ongoing access of the originator biologic through the patient's original payer mechanism (e.g. manufacturer's patient support program) or to switch to an ODB funded biosimilar version upon meeting specified criteria. The Ministry will no longer consider funding of originator biologics that are part of the biosimilar policy with limited exemptions on or after December 29, 2023.

Rituximab
(See funded biosimilar versions on the ODB formulary)
Brand(s): Riximyo, Ruxience, Truxima, Rituxan (Approved EAP exemptions only)
DOSAGE FORM/ STRENGTH: 10 mg/mL Intravenous injection

For the induction of remission of severely active Granulomatosis with Polyangiitis (GPA) OR microscopic polyangiitis (MPA) as combination treatment with glucocorticoids, in patients who meet all of the following criteria:

1. The patient must have severe active disease that is life- or organ-threatening. At least one supporting laboratory and/or imaging report must be provided. The organ(s) and how the organ(s) is (are) threatened must be specified.

2. There is a positive serum assays for either proteinase 3-ANCA (anti-neutrophil cytoplasmic autoantibodies) or myeloperoxidase-ANCA. A copy of the laboratory report must be provided.

3. Cyclophosphamide cannot be used for the patient for at least ONE of the following reasons:

   i) The patient has failed a minimum of six IV pulses of cyclophosphamide; OR
   ii) The patient has failed three months of oral cyclophosphamide therapy; OR
   iii) The patient has a severe intolerance or an allergy to cyclophosphamide; OR
   iv) Cyclophosphamide is contraindicated; OR
   v) The patient has received a cumulative lifetime dose of at least 25 g of cyclophosphamide; OR
   vi) The patient wishes to preserve ovarian/testicular function for fertility.

The initial treatment would be a once weekly infusion dosed at 375 mg/m^2 x 4 weeks. The physician must confirm that the treatment would not be a maintenance infusion as maintenance infusions will not be funded.

Renewals will be considered provided that, the patient meets the same criteria for initial approval and the request for retreatment is made no less than 6 months after the last dose of the patient's last treatment cycle with rituximab.

First Renewal:1year

Subsequent Renewals after first renewal: 2 years

(Rituximab is funded for course of therapy to be given at an interval of at least 6 months only upon flare of the condition.)

Rituximab

Brand(s): Riximyo, Ruxience, Truxima (Biosimilars; Rituxan (Originator)
DOSAGE FORM/ STRENGTH: 10 mg/mL intravenous injection

Rituximab will be funded as maintenance therapy for patients with severely active Granulomatosis with Polyangiitis [(GPA), also known as Wegener's Granulomatosis (WG)] OR microscopic polyangiitis (MPA). Patient must meet all of the following criteria:

a) The patient must have severe active disease that is life- or organ-threatening. At least one supporting laboratory and/or imaging report must be provided. The organ(s) and how the organ(s). is(are) threatened must be specified.
b) There is a positive serum assay for either proteinase 3-ANCA (anti-neutrophil cytoplasmic autoantibodies) or myeloperoxidase-ANCA. A copy of the laboratory report must be provided.
c) Stabilization of the condition with induction doses of cyclophosphamide (IV or PO doses) and a glucocorticoid as combination over 4 to 6 months until disease remission followed by rituximab at 500mg doses every 6 months. Cyclophosphamide dosing to align with MAINRITSAN studies[1].

After remission (typically within a month of remission), rituximab will be administered as one of the following:

- A fixed dose regimen of Rituximab consisting of 500 mg dosed at days 0 and 14 followed by fixed doses of 500 mg at 6, 12, and 18 months, used in combination with low-dose prednisone of another glucocorticoid; x 18 months duration of funding OR
- A tailored dose regimen of Rituximab based on CD19 and ANCA monitoring. Dose of Rituximab funded is 500 mg on day 0 followed by a dose as early as every 3 months if CD19 exceeds 0/mm^3 or if ANCA reappears or if there is a titre increase x 18 months duration of funding.

[1]Remission-induction therapy included prednisone (starting at 1 mg per kilogram of body weight per day, followed by gradual tapering), preceded in some patients by methylprednisolone "pulses" (500 to 1000 mg daily for 1 to 3 consecutive days), and

"pulse" cyclophosphamide (0.6 g per square meter of body-surface area on days 0, 14, and 28, then 0.7 g per square meter every 3 weeks for three to six additional pulses) until remission was attained, after 4 to 6 months. At that time, and within a maximum of 1 month after the last cyclophosphamide pulse, we have also accepted oral dosing (an example of oral cyclophosphamide dosing that has been used by clinicians is 150 mg daily).

Approval duration: 18 months

Renewals:

Renewals will be considered case-by-case. Requests should include information pertaining to the number of disease flares during the period of funding and a description of symptoms during flares. The dosing interval of use must be maintained as every 6 months and should be specified.

HEPATOLOGY DRUGS

HEPATITIS C DRUGS

The following drugs are reimbursed on the Ontario drug benefit formulary as limited use benefits for patients with Chronic Hepatitis C Infection upon meeting the LU criteria:

i) Epclusa (sofosbuvir / velpatasvir) 400mg/100mg Tab

ii) Harvoni (ledipasvir / sofosbuvir) 90mg/400mg Tab (GIL)

iii) Ibavyr (ribavirin) 200mg, 400mg, 600mg Tab

iv) Maviret (glecaprevir/pibrentasvir) 100 mg/40 mg Tab

v) Sovaldi (sofosbuvir) 400mg Tab

vi) Vosevi (sofosbuvir/velpatasvir/voxilaprevir) 400 mg/100 mg/100 mg Tab

vii) Zepatier (elbasvir / grazoprevir) 50mg/100mg Tab

The Ministry only considers funding of patient with Chronic Hepatitis C infection.

Please refer to the Limited Use Criteria in the Ontario Drug Benefit Formulary for provincial reimbursement criteria for these products which are part of Ontario's hepatitis C framework.

Patients not meeting limited use criteria may be considered on a case-by-case basis through the Exceptional Access Program.

Adefovir
Brand(s): Hepsera
DOSAGE FORM/ STRENGTH: 10 mg tablet

For the treatment of chronic hepatitis B in patients with objective evidence of lamivudine virologic* breakthrough where failure is not due to poor adherence to therapy; AND

- Liver biopsy showing Metavir stage 3 fibrosis or greater; OR
- Documented evidence of cirrhosis

OR

- Patients with the presence of a lamivudine resistance mutation*****; AND
- Liver Biopsy showing Metavir stage 3 fibrosis or greater; OR

Documented evidence of cirrhosis

Duration of Approval: 1 year (If Cirrhotic: Lifetime)

Duration of Approval for Renewal: 5 years

Note: Effective February 28, 2018, Entecavir. Lamivudine, and Tenofovir became a Limited Use Benefit on the Ontario Drug Benefit Formulary – Please refer to the formulary for the Limited Use Criteria.

Obeticholic Acid
Brand(s): Ocaliva
DOSAGE FORM/ STRENGTH: 5 mg, 10 mg tablet
Effective date: September 13, 2018

Obeticholic Acid (Ocaliva) will be funded for the treatment of primary biliary cholangitis (PBC) in adult patients who meet the following criteria:

i) Diagnosis of PBC is demonstrated by antimitochondrial antibodies or a liver biopsy; AND

ii) Used in combination therapy with ursodeoxycholic acid (UDCA) in patients who have experienced an inadequate response[1] to a minimum of twelve months of treatment with UDCA OR as monotherapy in patients who have experienced unmanageable intolerance to UDCA; AND

iii) The request is prescribed by or in consultation with a prescriber who is a gastroenterologist, hepatologist or internist with experience in the treatment of PBC. (If you are a prescriber who is not one of the specialists identified above, please submit the consultation note with the request.)

Obeticholic Acid
Brand(s): Ocaliva
DOSAGE FORM/ STRENGTH: 5 mg, 10 mg tablet

[1]Note that an inadequate response is defined as a patient who has used UDCA to treat PBC for a minimum of twelve (12) months and demonstrates ANY ONE or more of the following;

a) alkaline phosphatase ≥ 1.67 x upper limit of normal

b) total bilirubin > 1 x upper limit of normal and < 2 x upper limit of normal

c) abnormal bilirubin with progressing and/or compensated cirrhosis

(Documentation of lab work to be submitted with the request application.)

Renewals will be considered in patients who continue to benefit from treatment as evidenced by any one of the following;

a) a reduction in the alkaline phosphatase level to less than 1.67 x upper limit of normal; and/or

b) a 15% reduction in the alkaline phosphatase level compared with baseline values prior to initiation of treatment with obeticholic acid; and/or

c) a normal bilirubin level.

and the patient has not developed unacceptable toxicity from treatment with obeticholic acid.

Patients not meeting the above renewal criteria may be considered on a case-by-case basis.

Exclusion Criteria (applies to both initial and renewal requests):

Pre-liver transplant patients and/or patients who have complete biliary obstruction will not be funded.

Duration of funding approval for initials: 1 year

Duration of funding approval for renewals: 1 year

Trientine

Brand(s): Mar-trientine ; Waymade-Trientine
DOSAGE FORM/ STRENGTH: 250 mg cap
Effective date: March 28, 2022 (Mar-trientine); August 19, 2022(Waymade-trientine)
Note that these two products are not interchangeable, however they have the same clinical funding criteria.

Initiation criteria:

For the treatment of patients diagnosed with Wilson's Disease (WD) who have experienced unacceptable intolerance(s) from treatment with d-penicillamine OR who have contraindication(s) to d-penicillamine.

Renewal criteria:

Renewal of funding will be provided for patients who continue to respond to treatment with trientine and who do not develop unacceptable intolerances.

Notes:

1. In adult patients, trientine therapy must be initiated by a clinician with expertise in the management of WD and in pediatric patients initiation and renewal of treatment must be overseen by a clinician experienced in the management of WD. Consult notes from an expert in WD may be provided to support the request from prescribers.

2. Please include a description of the d-penicillamine intolerances and/or contraindications with your initial application.

3. At renewal, please include clinical parameters/results used to determine that the patient is responding to treatment.

Approval duration of initials and renewals: 1 year

INFLAMMATORY BOWEL DISEASES

Adalimumab – See Formulary for funded biosimilars

Brand(s): Humira and formulary listed biosimilars
DOSAGE FORM/ STRENGTH: 40 mg/0.8 mL prefilled syringe, 40mg/0.8mL and 20 mg/0.2 mL prefilled pens for subcutaneous injection

Refer to the Executive Officer Communications on the Ministry website for the Ministry's Biosimilar Policy including frequently asked questions and updates for the biosimilar policy updates.
http://www.health.gov.on.ca/en/pro/programs/drugs/opdp_eo/eo_communiq.aspx

Effective March 31, 2023, the ODB program will start transitioning coverage for Copaxone®, Enbrel®, Humalog®, Humira®, Lantus®, NovoRapid®, Remicade®, and Rituxan® to their biosimilar versions.

Effective December 29, 2023, coverage for these originator biologic drugs through the ODB program will not be available for patients and the ODB program will only provide coverage for the biosimilar version of these drugs for all ODB program recipients, with limited exemptions. In general, for ODB program recipients who are already on these biologic drugs, there is up to a 9-month transition period (see the biosimilar switch policy described on page 6 to 8 of this document).

It should be noted that after the date when a biosimilar becomes publicly funded for an approved indication, patients initiated on an originator biologic for this same provincially funded indication through support from a manufacturer's patient support program, will be expected to be provided ongoing access of the originator biologic through the patient's original payer mechanism (e.g. manufacturer's patient support program) or to switch to an ODB funded biosimilar version upon meeting specified criteria. The Ministry will no longer consider funding of originator biologics that are part of the biosimilar policy with limited exemptions on or after December 29, 2023.

The below criteria are for Adalimumab as Humira. Refer to the ODB formulary for the Limited Use Criteria for Adalimumab biosimilars which was updated with the January 2023 ODB Formulary Update.

For the treatment of fistulising Crohn's disease with concomitant luminal disease in patients who meet the following criteria;

- Patient with actively draining perianal or enterocutaneous fistula(e) that have recurred or persist despite a course of appropriate antibiotic therapy (e.g. ciprofloxacin and/or metronidazole) AND immunosuppressive therapy (e.g. azathioprine or 6-mercaptopurine) AND
- Harvey Bradshaw Index (HBI) score ≥ 7

The dose that will be considered is Adalimumab 160 mg at week zero, 80 mg at week two, followed by 40 mg every two weeks.

Duration of Approval: 3 months

Renewal will be considered based on the response to therapy.

The dose that will be considered on renewals is Adalimumab 40 mg every two weeks. All requests for higher doses will not be approved.

Duration of Approval: 3 months to 1 year pending fistula(e) resolution

Second Renewal:

2 years for 2nd renewal of requests with complete resolution

Case-by-case duration for renewal of requests with partial resolution

Pediatric patients will be considered case-by-case.

Adalimumab – See Formulary for funded biosimilars

Brand(s): Humira and formulary listed biosimilars
DOSAGE FORM/ STRENGTH: 40 mg/0.8 mL prefilled syringe, 40mg/0.8mL and 20 mg/0.2 mL prefilled pens for subcutaneous injection

The below criteria are for Adalimumab as Humira. Refer to the ODB formulary for the Limited Use Criteria for Adalimumab biosimilars which was updated with the January 2023 ODB Formulary Update.

Treatment of moderate to severe (luminal) Crohn's Disease in patients who have:

- HBI (Harvey Bradshaw Index) score ≥7*; and
- Failed to respond to conventional treatment with glucocorticoids (prednisone 40mg/day or equivalent for at least 2 weeks or dose cannot be tapered to below prednisone 20 mg/day or equivalent); and
- Failed to respond to an immunosuppressive agent (azathioprine, 6-mercaptopurine, methotrexate, or cyclosporine) tried for at least 3 months.

Note: Any intolerance(s) or contraindication(s) to treatment with required alternative(s) must be described in detail.

*If the patient has HBI <7, the request will be reviewed by external medical experts when the following information is provided: bloodwork (with hematocrit, hemoglobin, C reactive protein, ESR, platelets, and ferritin levels); supporting endoscopy; details of weight loss; and a list of narcotic analgesics being used.

Pediatric patients will be considered case-by-case.

Adalimumab – See Formulary for funded biosimilars

Brand(s): Humira and formulary listed biosimilars
DOSAGE FORM/ STRENGTH: 40 mg/0.8 mL prefilled syringe, 40mg/0.8mL and 20 mg/0.2 mL prefilled pens for subcutaneous injection

Duration of Approval: 6 months

Renewal will be considered for patients with 50% reduction in HBI from pre-treatment as well as improvement of symptoms (e.g., absence of bloody diarrhea and weight stabilization or increase) and no longer using steroids. Biochemical improvements may also be required.

The planned dosing regimen for the requested biologic should be provided.

The recommended: Adalimumab: 160mg at week 0; 80mg at week 2; followed by 40mg every two weeks

Duration of Approval: First renewal: 1 year

Second and subsequent renewals: 2 years

The below criteria are for Adalimumab as Humira. Refer to the ODB formulary for the Limited Use Criteria for Adalimumab biosimilars since January 2023.

For the treatment of ulcerative colitis disease in adult patients[1] who meet the following criteria: **Induction Criteria**

Mild disease
a. Mayo score <6 AND
b. Patients with mild disease will be considered on a case-by-case basis BUT submission must include the rationale for coverage

Moderate disease
a. Mayo score between 6 and 10 (inclusive); AND
b. Endoscopic* subscore of 2; AND
c. Failed 2 weeks of oral prednisone at daily doses ≥40mg (or a 1 week course of IV equivalent) AND 3 months of azathioprine (AZA)/ 6-mercaptopurine (6MP) (or where the use of immunosuppressants is contraindicated); OR
Stabilized with 2 weeks of oral prednisone at daily dose ≥ 40mg (or a 1 week course of IV equivalent) but the prednisone dose cannot be tapered despite 3 months of AZA/ 6MP (or where the use of immunosuppressants is contraindicated)

Severe disease
a. Mayo score >10 AND
b. Endoscopic* subscore of ≥2 AND
c. Failed 2 weeks of oral prednisone at daily dose ≥ 40mg (or 1 week IV equivalent); OR

Adalimumab – See Formulary for funded biosimilars

Brand(s): Humira and formulary listed biosimilars
DOSAGE FORM/ STRENGTH: 40 mg/0.8 mL prefilled syringe, 40mg/0.8mL and 20 mg/0.2 mL prefilled pens for subcutaneous injection

Stabilized with 2 weeks oral prednisone ≥ 40 mg (or 1 week of IV equivalent) but the prednisone dose cannot be tapered despite 3 months of AZA/6MP (or where the use of immunosuppressants is contraindicated)

Initial Approval: 6 months at 160 mg initially administered at week 0, followed by 80mg at week 2, then 40 mg every other week thereafter.

*The endoscopy procedure must be done within the 12 months prior to initiation of treatment.

Maintenance Criteria

After 8 weeks of adalimumab therapy:

a. Mayo score <6 AND
b. 50% reduction in prednisone from the starting dose

Approval: 6 months at 40mg every other week.
If patient is completely off steroids,

Approval: 12 months at 40 mg every other week.

Subsequent renewals:

a. Mayo score <6; AND
b. Must be completely off steroids

Approval: 2 years at 40mg every other week.
(Patients who remain on steroids will be considered on a case-by-case basis)

Pediatric patients will be considered case-by-case.

Infliximab-See formulary for funded biosimilars
Brand(s): Avsola, Inflectra, Renflexis (Biosimilars); Remicade (Originator)
DOSAGE FORM/ STRENGTH: 100mg/vial Injection for Infusion

Refer to the Executive Officer Communications on the Ministry website for the Ministry's Biosimilar Policy including frequently asked questions and updates for the biosimilar policy updates.
http://www.health.gov.on.ca/en/pro/programs/drugs/opdp_eo/eo_communiq.aspx

Effective March 31, 2023, the ODB program will start transitioning coverage for Copaxone®, Enbrel®, Humalog®, Humira®, Lantus®, NovoRapid®, Remicade®, and Rituxan® to their biosimilar versions.

Effective December 29, 2023, coverage for these originator biologic drugs through the ODB program will not be available for patients and the ODB program will only provide coverage for the biosimilar version of these drugs for all ODB program recipients, with limited exemptions. In general, for ODB program recipients who are already on these biologic drugs, there is up to a 9-month transition period (see the biosimilar switch policy described on page 6 to 8 of this document).

It should be noted that after the date when a biosimilar becomes publicly funded for an approved indication, patients initiated on an originator biologic for this same provincially funded indication through support from a manufacturer's patient support program, will be expected to be provided ongoing access of the originator biologic through the patient's original payer mechanism (e.g. manufacturer's patient support program) or to switch to an ODB funded biosimilar version upon meeting specified criteria. The Ministry will no longer consider funding of originator biologics that are part of the biosimilar policy with limited exemptions on or after December 29, 2023.

Infliximab-See formulary for funded biosimilars

Brand(s): Avsola, Inflectra, Renflexis (Biosimilars); Remicade (Only for those approved for biosimilar exemption)
DOSAGE FORM/ STRENGTH: 100mg/vial Injection for Infusion

The below criteria are for Infliximab as Remicade. Refer to the ODB formulary for the Limited Use Criteria for Infliximab biosimilars which was updated with the January 2023 ODB Formulary Update.

Treatment of moderate to severe (luminal) Crohn's Disease in patients who have:

- HBI (Harvey Bradshaw Index) score ≥7*; and
- Failed to respond to conventional treatment with glucocorticoids (prednisone 40mg/day or equivalent for at least 2 weeks or dose cannot be tapered to below prednisone 20 mg/day or equivalent); and
- Failed to respond to an immunosuppressive agent (azathioprine, 6-mercaptopurine, methotrexate, or cyclosporine) tried for at least 3 months.

Note: Any intolerance(s) or contraindication(s) to treatment with required alternative(s) must be described in detail.

*If the patient has HBI <7, the request will be reviewed by external medical experts when the following information is provided: bloodwork (with hematocrit, hemoglobin, C reactive protein, ESR, platelets, and ferritin levels); supporting endoscopy; details of weight loss; and a list of narcotic analgesics being used.

Pediatric patients will be considered case-by-case.

Duration of Approval: 6 months

Renewal will be considered for patients with 50% reduction in HBI from pre-treatment as well as improvement of symptoms (e.g., absence of bloody diarrhea and weight stabilization or increase) and no longer using steroids. Biochemical improvements may also be required.

The planned dosing regimen for the requested biologic should be provided.

Infliximab – See Formulary funded biosimilars
Brand(s): Avsola, Inflectra, Renflexis (Biosimilars); Remicade (Originator)
DOSAGE FORM/ STRENGTH: 100mg/vial Injection for infusion

Recommended dose: Infliximab 5 mg/kg/dose at 0, 2 and 6 weeks followed by 5mg/kg/dose every 8 weeks

Requests for higher doses of infliximab must provide a description of symptoms and HBI score on standard dosing and may include laboratory support of infliximab levels for consideration of case-by-case consideration.

Duration of Approval: First renewal: 1 year

Second and subsequent renewals: 2 years

The below criteria are for Infliximab as Remicade. Refer to the ODB formulary for the Limited Use Criteria for Infliximab biosimilars which was updated with the January 2023 ODB Formulary Update.

Remicade for fistulizing Crohn's disease:

Actively draining perianal or enterocutaneous fistula(e) that have recurred or persist despite a course of:

- appropriate antibiotic therapy (e.g., ciprofloxacin and/or metronidazole); AND
- immunosuppressive therapy (azathioprine or 6-mercaptopurine therapy).

Duration of approval: Infliximab 3 doses of **5mg**/kg/dose, administered at 0, 2 and 6 weeks.

Duration of Approval: 6 months

If the patient has been using a higher dosing regimen over the past year, the requesting MD must provide the rationale for this dose by comparing the patient's symptoms on standard dosing and the current dosing. Then the request should be sent for external review.

Renewal of funding of patients using Remicade for the treatment of fistulizing Crohn's Disease will be considered for patients with resolution of fistulae.

The planned dosing regimen for the requested biologic should be provided. The recommended dose for the treatment of Crohn's Disease is 5 mg/kg/dose at 0, 2 and 6 weeks followed by 5mg/kg/dose every 8 weeks with up to 10 mg/kg/dose every 8 weeks being considered on a case-by-case basis.

Approval duration of first renewal: 6 months to 1 year pending fistula(e) resolution

Approval duration of second and subsequent renewals: 2 years with complete resolution; case-by-case duration with partial resolution

Infliximab – See Formulary funded biosimilars
Brand(s): Avsola, Inflectra, Renflexis (Biosimilars); Remicade (Originator)
DOSAGE FORM/ STRENGTH: 100mg/vial Injection for infusion

Initial induction requests for infliximab for patients with mild Ulcerative Colitis (Mayo score < 6) may be considered for Infliximab as Inflectra on a case-by-case basis through EAP but the submission must include the rationale for coverage.

Patients treatment experienced to Remicade and transitioning to public funding must meet the initiation (induction) criteria before consideration of funding of maintenance under renewal criteria will be applied.

Induction (Initiation) Criteria

For the treatment of ulcerative colitis disease in patients who meet the following criteria:

1. **Moderate disease**
   - Mayo score between 6 and 10 (inclusive); AND
   - *Endoscopic subscore of 2; AND
   - Failed 2 weeks of oral prednisone ≥ 40mg (or IV equivalent for at least 1 week) **AND** 3 months of azathioprine(AZA)/ 6-mercaptopurine (6-MP) (or where the use of immunosuppressants is contraindicated**)
     OR
     Stabilized with 2 weeks of oral prednisone ≥40mg (or a 1 week course of IV equivalent) but the prednisone dose cannot be tapered despite 3 months of AZA/6MP (or where the use of immunosuppressants is contraindicated**)

*The endoscopy procedure must be done within the last year but does not have to be full endoscopy.

**Contraindication to Aza/6MP includes pancreatitis, allergic reaction [fever and/or rash and arthritis], malaise, diarrhea and hepatitis

Approved Dose: Infliximab 5mg/kg/dose at 0, 2 and 6 weeks followed by 5mg/kg/dose every 8 weeks.

Approval duration: 6 months

2. **Severe disease**
   - Mayo score >10; AND
   - *Endoscopy subscore of 2 or more; AND
   - Failed 2 weeks of oral prednisone ≥40mg (or 1 week IV equivalent)
     OR
     Stabilized with 2 weeks of oral prednisone ≥40mg (or 1 week of IV equivalent) but the prednisone dose cannot be tapered despite 3 months of Aza/6MP (or where the use of immunosuppressants is contraindicated**)

Infliximab – See Formulary funded biosimilars
Brand(s): Avsola, Inflectra, Renflexis (Biosimilars); Remicade (Originator)
DOSAGE FORM/ STRENGTH: 100mg/vial Injection for infusion

*The endoscopy procedure must be done within the last year but does not have to be full endoscopy.

**Contraindication to Aza/6MP includes pancreatitis, allergic reaction [fever and/or rash and arthritis], malaise, diarrhea and hepatitis

Approval duration: 6 months
Dose: Remicade 5mg/kg/dose at 0, 2 and 6 weeks followed by 5mg/kg/dose every 8 weeks.

Maintenance (Renewal) Criteria for first renewal

After **3 loading doses** of Remicade if Mayo score <6 AND 50% reduction in prednisone from the starting dose

Approval duration: 6 months

If After **3 loading doses** of Remicade if Mayo score <6 AND patient is no longer on prednisone

Approval duration: 12 months

Approved Dose: Infliximab 5mg/kg/dose up to every 6 weeks

Maintenance (Renewal) Criteria for second and subsequent renewals

a. Mayo score <6* AND
b. Must be off steroids

Patients who remain on steroids will be considered on a case-by-case basis.

Approval duration: 12 months to up to 2 years for those off steroids

Approved Dose: 5 mg/kg/dose up to every 6 weeks

[1]Note that the endoscopy procedure must be done within the last year but does not have to be full endoscopy.

Pediatric patients will be considered case-by-case.

Golimumab

Brand(s): Simponi

DOSAGE FORM/ STRENGTH: 50 mg/0.5mL Pre-Filled Syringe Or Auto-Injector, 100 mg/ mL Pre-filled Syringe or Auto-Injector

For the treatment of ulcerative colitis disease in patients who meet the following criteria:

Induction Criteria

Mild disease

a. Mayo score <6 AND
b. Patients with mild disease will be considered on a case-by-case basis BUT submission must include the rationale for coverage

Moderate disease

a. Mayo score between 6 and 10 (inclusive) AND
b. Endoscopic subscore of 2 AND
c. Failed 2 weeks of oral prednisone ≥40mg (or a 1 week course of IV equivalent) but the prednisone dose cannot be tapered despite 3 months azathioprine(AZA)/6-mercaptopurine(6MP) (or where the use of immunosuppressants is contraindicated)

   OR

   Stabilized with 2 weeks of oral prednisone ≥ 40mg (or a 1 week course of IV equivalent) but the prednisone dose cannot be tapered despite 3 months of AZA/6MP (or where the use of immunosuppressants is contraindicated)

Severe disease

a. Mayo score >10 AND
b. Endoscopy subscore of ≥2 AND
c. Failed 2 weeks of oral prednisone ≥ 40mg (or 1 week IV equivalent)

   OR

   Stabilized with 2 weeks oral prednisone ≥ 40mg (or 1 week of IV equivalent) but the prednisone dose cannot be tapered despite 3 months of AZA/6MP (or where the use of immunosuppressants is contraindicated)

Golimumab

Brand(s): Simponi
DOSAGE FORM/ STRENGTH: 50 mg/0.5mL Pre-Filled Syringe Or Auto-Injector, 100 mg/ mL Pre-filled Syringe or Auto-Injector

Initial Approval: 6 months at 200 mg initially administered at week 0, followed by 100mg at week 2, and then 50 mg every 4 weeks thereafter. The maintenance dose of 100mg every 4 weeks can be considered at the discretion of the treating physician

Maintenance Criteria

After 4 loading doses of Simponi:

a. Mayo score <6 AND

b. 50% reduction in prednisone from the starting dose

Approval: 6 months at 50 mg or 100 mg every 4 weeks

If patient is completely off steroids.

Approval: 12 months at 50 mg or 100 mg every 4 weeks.

Subsequent renewals:

a. Mayo score <6; AND

b. Must be off steroids

(Patients who remain on steroids will be considered on a case-by-case basis)

Approval: 2 years at 50 mg or 100 mg every 4 weeks.

Duration of Approval:

Renewal duration: 6 months to 1 year (Pending if patient continues on steroids.)

Second and subsequent renewal duration: 2 years for those off steroids.

Mirikizumab

Brand(s): Omvoh
DOSAGE FORM/ STRENGTH: 300 mg/15 mL Vial; 100 mg/mL Pre-Filled Syringe or Prefilled pen
Effective date: November 4, 2024

Initiation Criteria

For the treatment of moderate to severe ulcerative colitis in patients who meet ALL the following criteria:

1. Has a Mayo score greater than or equal to 6 with an endoscopic subscore* of at least 2 (or other validated disease activity score confirming moderate to severe disease); AND
2. Has failed conventional treatment with a corticosteroid (prednisone 40–60 mg/day [or equivalent]) for a minimum of 14 days (or intravenous corticosteroid for 1 week);
   OR
   Has responded to or has been stabilized on conventional treatment with a corticosteroid, with or without an immunosuppressant (e.g., azathioprine, 6-mercaptopurine) and is switching to or adding mirikizumab to the treatment regimen;
   OR
   Is unable to use a corticosteroid (e.g. has a contraindication to or experienced intolerable adverse reactions) but patient has experienced an inadequate response to an immunosuppressant (e.g., azathioprine, 6-mercaptopurine), OR another funded biologic (e.g. adalimumab, infliximab, golimumab), OR a funded Janus kinase inhibitor (e.g. tofacitinib, upadacitinib) for the treatment of their ulcerative colitis;

   AND
3. Mirikizumab is being used to induce remission or as a steroid-sparing maintenance therapy.

*The endoscopy procedure must be done within the 12 months prior to initiation of treatment.

Notes:

1. Patients with mild ulcerative colitis disease (e.g., Mayo score less than 6) may be considered on a case-by-case basis. Application must include the rationale for coverage and other relevant details.

Approved dose in first 24 weeks:

Induction Dose:

The recommended induction dosage regimen is 300 mg infused intravenously at Week 0, Week 4, and Week 8

Mirikizumab
Brand(s): Omvoh
DOSAGE FORM/ STRENGTH: 300 mg/15 mL Vial; 100 mg/mL PFS or PF pen

Evaluate patients at 12 weeks induction dosing, and if there is an inadequate therapeutic response at week 12 consider extended induction dosing by administering 300 mg at Weeks 12, 16, and 20

Discontinue Omvoh in patients who do not show evidence of therapeutic benefit to extended induction therapy by Week 24.

Maintenance dose:

200 mg subcutaneous every 4 weeks.

Renewal Criteria:

Maintenance therapy is funded for patients who met the initiation criteria and have demonstrated a treatment response or are in remission.

Examples of treatment response include clinically meaningful reductions in disease activity scores (e.g., Mayo score less than 6), along with improvements in endoscopic findings and reduction of corticosteroid doses by 50% in the first 6 months of treatment with mirikizumab with discontinuation of corticosteroids by 12 months.

Patients who remain on corticosteroids following the first year of treatment will be considered on a case-by-case basis.

Prescribers may wish to consider other funded alternatives for patients unable to discontinue corticosteroid therapy.

Approved dose for renewals:

Maintenance dose: 200 mg subcutaneous every 4 weeks

Exclusion criteria (for Initials and Renewals):
Combination therapy with another biologic* used to treat inflammatory bowel disease will not be funded.

*Note: This includes Jak-2 inhibitors

Approval funding durations:

Initial approval: 7 months

First renewal: 6 months to 1 year depending on whether the patient is able to reduce and/or discontinue corticosteroid treatment.

Second and subsequent renewals: 2 years with complete discontinuation of corticosteroid treatment

Ozanimod
Brand(s): Zeposia
DOSAGE FORM/ STRENGTH: Starter pack of 0.23 mg and 0.46 mg capsules, 0.92 mg capsules
Effective date: April 10, 2024

Induction (initiation) criteria:

1. Has a Mayo score greater than or equal to 6 with an endoscopic subscore* of at least 2 (or other validated disease activity score confirming moderate to severe disease); AND
2. Has failed conventional treatment with a corticosteroid (prednisone 40 to 60 mg/day [or equivalent]) for a minimum of 14 days (or intravenous corticosteroid for 1 week);

   OR

   Has responded to or has been stabilized on conventional treatment with a corticosteroid, with or without an immunosuppressant (e.g., azathioprine, 6-mercaptopurine);

   OR

   Has a contraindication to corticosteroids which prevents the use of initial conventional treatment with corticosteroids;

AND

3. Ozanimod is being used to induce remission or as a steroid-sparing maintenance therapy.

*The endoscopy procedure must be done within the 12 months prior to initiation of treatment.

Notes:

1. Patients with mild ulcerative colitis disease (e.g., Mayo score less than 6) may be considered on a case-by-case basis. Application must include the rationale for coverage and other relevant details.

Approved Dose:

0.23 mg once daily on days 1 to 4, then 0.49 mg once daily on days 5 to 7, then 0.92 mg once daily on day 8 and thereafter.

Approved Duration of Initials: 6 months

Ozanimod

Brand(s):Zeposia
DOSAGE FORM/ STRENGTH: Starter pack 0.23 mg and 0.46 mg capsules, 0.92 mg capsules

Renewal (Maintenance) criteria:

Maintenance therapy is funded for patients who met the initiation criteria and have demonstrated a treatment response or are in remission.

Maintenance therapy is funded for patients who meet the Ministry initiation criteria, AND whose disease activity scores have been reduced (e.g. Mayo score less than 6) along with improvements in endoscopic findings (as possible), and at least a 50% reduction in the dose of corticosteroid compared with the baseline dose prior to initiation of ozanimod following the first 6 months of treatment with ozanimod, and with discontinuation of corticosteroids after the first year of treatment of ozanimod.

Patients who remain on corticosteroids following the first year of treatment will be considered on a case-by-case basis.

Prescribers may wish to consider other funded alternatives for patients unable to discontinue corticosteroid therapy.

Approved Dose: 0.92 mg once daily

Exclusion Criteria for both Initials and Renewals: Ozanimod will not be funded if it is used in combination with other Janus kinase (JAK) inhibitors or other biologic DMARDs to treat the patient's UC.

Approved Duration of first renewal: 6 months to 1 year depending on whether the patient is able to reduce and/or discontinue corticosteroid treatment.

Approved duration of second and subsequent renewals: 12 months

Risankizumab
Brand(s): Skyrizi
DOSAGE FORM/ STRENGTH: 600 mg/10 mL, 360 mg/2.4 mL Injection
Effective date: April 12, 2024

Moderate to severe luminal Crohn's disease

Initiation Criteria:

For the treatment of moderate to severe luminal Crohn's disease in adult patients who meet ALL of the following criteria:

1. Has a Harvey Bradshaw Index (HBI) score greater than or equal to 7 (or other validated disease activity score confirming moderate to severe luminal Crohn's disease); AND
2. Has failed conventional treatment with a corticosteroid (prednisone 40–60 mg/day [or equivalent]) for a minimum of 14 days (or an intravenous corticosteroid for 1 week);
   OR
   Has responded to or has stabilized on conventional treatment with a corticosteroid, with or without an immunosuppressant (e.g., azathioprine, 6-mercaptopurine, methotrexate) and is requiring maintenance using a corticosteroid-free treatment;
   OR
   Has a contraindication to corticosteroids which prevents the use of initial conventional treatment with corticosteroids;
   AND
3. Risankizumab is being used to induce remission or as a steroid-sparing maintenance therapy.

Note:
1. Patients with mild Crohn's disease (e.g., HBI less than 7) may be considered on a case-by-case basis but the application must include the rationale for coverage and other relevant details.

Renewal Criteria:

Maintenance therapy is funded for patients who met the initiation criteria and have demonstrated a treatment response or are in remission. Examples of treatment response include clinically meaningful reductions in disease activity scores (e.g., HBI score decrease greater than or equal to 50% from pre-treatment measurement), along with improvements in endoscopic findings and reduction or discontinuation of corticosteroids.

Prescribers may wish to consider other funded alternatives for patients unable to discontinue corticosteroid therapy.

Risankizumab
Brand(s): Skyrizi
DOSAGE FORM/ STRENGTH: 600 mg/10 mL 360 mg/2.4 mL injection

Exclusion criteria (for Initials and Renewals):

1. Combination therapy with another biologic used to treat inflammatory bowel disease will not be funded.

Approved Initial and Maintenance dose:

The recommended dose is 600 mg administered by intravenous infusion at Week 0, Week 4, and Week 8, followed by 360 mg administered by subcutaneous injection at Week 12, and every 8 weeks thereafter as maintenance.

Approval Durations:

Initial approval: 6 months

First EAP renewal: 1 year

Second and subsequent EAP renewals: 2 years

<u>Fistulising Crohn's Disease with Concomitant Luminal Disease</u>

Initiation Criteria:

For the treatment of fistulising Crohn's disease with concomitant luminal disease in patients who meet ALL the following criteria:

1. Patient has actively draining perianal or enterocutaneous fistula(e) that have recurred or persist despite a course of
   - appropriate antibiotic therapy (e.g. ciprofloxacin and/or metronidazole) and immunosuppressive therapy (e.g. azathioprine or 6-mercaptopurine) (Note 1) OR
   - appropriate antibiotic therapy (e.g. ciprofloxacin and/or metronidazole) and adalimumab or infliximab with or without an immunosuppressive therapy

AND

2. Harvey Bradshaw Index (HBI) score greater than or the same as 7 (or other validated disease activity score confirming moderate to severe disease)

Note:

1. Patients should have received a trial of an anti-tumour necrosis factor (anti-TNF) therapy (e.g. infliximab or adalimumab) for their fistulizing Crohn's disease.

Risankizumab
Brand(s): Skyrizi
DOSAGE FORM/ STRENGTH: 600 mg/10 mL 360 mg/2.4 mL injection

Renewal Criteria

Maintenance therapy is funded for patients who met the initiation criteria and who achieve and maintain response to therapy (e.g., partial or complete resolution of fistulae and symptom improvement). Please include information describing the patient's fistula(e) resolution (e.g., partial or complete resolution) and HBI score.

Exclusion criteria (for Initials and Renewals):

1. Combination therapy with another biologic used to treat inflammatory bowel disease will not be funded.

Approved Initial and Maintenance dose:

The recommended dose is 600 mg administered by intravenous infusion at Week 0, Week 4, and Week 8, followed by 360 mg administered by subcutaneous injection at Week 12, and every 8 weeks thereafter as maintenance.

Approval durations:

Initial approval: 6 months

First renewal: 6 months to 1 year pending fistula(e) resolution

Second and subsequent renewals: 2 years with complete resolution

The duration of approval for patients with partial resolution will be provided on a case-by-case basis.

Teduglutide
Brand(s): Revestive
DOSAGE FORM/ STRENGTH: 5 mg vials for Injection
Updated April 6, 2021

Applications for reimbursement should be accompanied by a copy of the parenteral support weekly usage volumes at baseline prior to start of teduglutide and must include the parenteral support usage volumes for the 4 weeks of use prior to the date that the Ministry funding for initial or renewal is requested.

Adults (age ≥ 18 years) - Initial Criteria:

For the ongoing funding of patients who have turned 18 years of age who were previously funded upon meeting EAP funding criteria and who continue to meet the adult renewal criteria; OR

For the ongoing treatment of new patients requesting public funding who are at least 18 years of age with Short Bowel Syndrome (SBS) who meet the following criteria:

Prior to starting teduglutide (Revestive), the patient meets the following;

- Has short bowel syndrome (SBS) as a result of major intestinal resection due to injury, volvulus, vascular disease, cancer, or Crohn's Disease[1]; AND
- Patient's intestinal resection has resulted in dependency on parenteral nutrition for at least 12 months; AND
- Patient requires parenteral nutrition required at least three times weekly to meet caloric, fluid or electrolyte needs due to ongoing malabsorption; AND
- Patient's frequency and volume of parenteral nutrition has been stable for at least one month;

Those who are initiated on teduglutide upon meeting the above criteria will be reimbursed for ongoing access of teduglutide through the Exceptional Access Program (EAP) upon meeting the below criteria;

- The patient has achieved at least a 20% reduction in Parenteral Support volume while on teduglutide in the 4 weeks prior to the application for funding to EAP compared to their baseline measures in the 4 weeks prior to start of teduglutide.[2] [3]

[1] Case-by-case consideration will be provided for requests for patients with short bowel syndrome not due to the reasons provided.
[2] Parenteral Support volumes measurements are to compare the 4 weeks of use prior to start of teduglutide with the 4 weeks of use prior to the date that EAP request for funding is provided.
[3] For adult patients (i.e. at least 18 years of age) requesting EAP funding for ongoing teduglutide therapy who initiated on teduglutide between 1 and 17 years of age that was

not publicly funded, ongoing response to teduglutide will be evaluated through comparing the patient's *current* (i.e. while on teduglutide in the 4 weeks prior to the application for funding to EAP) Parenteral Support volume to the patient's *adjusted initial* Parenteral Support volume; for clarity, *adjusted initial* Parenteral Support volume is defined as the patient's last available weight as a pediatric multiplied by the patient's baseline Parenteral

Support volume and divided by the patient's baseline weight at initiation (i.e. in the 4 weeks prior to start of teduglutide as a pediatric) of teduglutide.

Duration of approval: 12 months

Exclusion Criteria:

- Patients with active gastrointestinal malignancy or history of gastrointestinal malignancy in the past 5 years before start of treatment

Renewal Criteria:

Renewals will be considered in those who are able to demonstrate a reduction in their Parenteral Support volume requirements by at least 20% compared to baseline measures prior to commencing therapy with teduglutide. [3]
Applications for renewal of reimbursement should be accompanied by a copy of the Parenteral Support weekly usage volumes for the 4 weeks of use prior to the date that the Ministry funding is requested.
Duration of approval: 12 months

Discontinuation/Stopping Criteria:
Patients will not be approved for funding by the EAP if a 20% reduction in the usual average weekly volume of Parenteral Support solutions prior to starting therapy with teduglutide has not been achieved/maintained by 52 weeks of treatment with teduglutide

Teduglutide
Brand(s): Revestive
DOSAGE FORM/ STRENGTH: 5 mg vials for Injection

Pediatrics (age between 1 and 17 years) - Initial Criteria:

For the ongoing treatment of patients between 1 and 17 years of age with Short Bowel Syndrome (SBS) who are dependent on Parenteral Support who meet the following criteria:

Prior to starting teduglutide (Revestive), the patient meets the following criteria:

- Has short bowel syndrome (SBS) as a result of major intestinal resection; AND
- Parenteral Support requirements must be stable or there must have been no improvement in enteral feeding for at least the preceding three months; AND
- The cumulative lifetime duration of Parenteral Support therapy must be at least 12 months; AND
- Patient requires parenteral support to provide more than 30% of caloric, and/or fluid/electrolyte needs due to ongoing malabsorption; AND
- Request is from a physician or nurse practitioner working within a specialized multi-disciplinary intestinal rehabilitation program.

Those who are initiated on teduglutide upon meeting the above criteria will be reimbursed for ongoing access of teduglutide through the Exceptional Access Program (EAP) upon meeting the below criteria:

- Initial treatment response is assessed 6 months or more after initiating treatment with teduglutide.
- The patient has achieved at least a 20% reduction in weight-adjusted Parenteral Support volume while on teduglutide in the 4 weeks prior to the application of funding to EAP compared to their baseline weight-adjusted Parenteral Support volume measures in the 4 weeks prior to start of teduglutide.[1] [2]

[1] Weight-adjusted Parenteral Support volume is defined as the patient's Parenteral Support volume divided by the Patient's weight.

[2] Parenteral Support volumes measurements are to compare the 4 weeks of use prior to start of teduglutide with the 4 weeks of use prior to the date that EAP request for funding is provided.

Teduglutide
Brand(s): Revestive
DOSAGE FORM/ STRENGTH: 5 mg vials for Injection

Notes:

a. Parenteral Support volume and percentage of total consumption should be documented at each clinic visit.

b. Assessments for subsequent renewals should be carried out at 6 months intervals.

Duration of first EAP approval: 7 months

Exclusion Criteria:

- Patients with active gastrointestinal malignancy or history of gastrointestinal malignancy in the past 5 years before start of treatment

Renewal Criteria:

Renewals will be considered in patients who are able to demonstrate a reduction in their weight-adjusted Parenteral Support volume requirements by at least 20% compared to baseline weight-adjusted Parenteral Support volume measures prior to commencing therapy with teduglutide.[1]

Applications for renewal of reimbursement should be accompanied by a copy of the weight-adjusted Parenteral Support weekly usage volumes for the 4 weeks of use prior to the date that the Ministry funding is requested.

Duration of approval: 12 months

Discontinuation/Stopping Criteria

Patients meeting initial funding criteria will not be approved for ongoing funding by the EAP if a 20% reduction in the usual average weekly volume of weight-adjusted Parenteral Support solutions prior to starting therapy with teduglutide has not been achieved/maintained at the time of renewal.

Upadacitinib
Brand(s): Rinvoq
DOSAGE FORM/ STRENGTH: 15 mg, 30 mg, 40 mg Extended Release tablet
Effective date: August 8, 2024 (CD)

Upadacitinib for Luminal Crohn's disease

Initiation Criteria:

For the treatment of moderate to severe luminal Crohn's disease in patients who meet ALL of the following criteria:

1. Has a Harvey Bradshaw Index (HBI) score greater than or equal to 7 (or other validated disease activity score confirming moderate to severe luminal Crohn's disease); AND

2. Has failed conventional treatment with a corticosteroid (prednisone 40–60 mg/day [or equivalent]) for a minimum of 14 days (or an intravenous corticosteroid for 1 week);
   OR
   Has responded to or has stabilized on conventional treatment with a corticosteroid, with or without an immunosuppressant (e.g., azathioprine, 6-mercaptopurine, methotrexate)

   AND
3. Upadacitinib is being used to induce remission or as a steroid-sparing maintenance therapy.

Notes:

1. Patients with mild Crohn's disease (e.g., HBI less than 7) may be considered on a case-by-case basis but the application must include the rationale for coverage and other relevant details.
2. Patients who have not demonstrated prior treatment failure, (i.e., an inadequate response to, loss of response to, or intolerance to at least one of conventional and/or biologic therapy) will be considered on a case-by-case basis.

Renewal Criteria:

Maintenance therapy is funded for patients who met the initiation criteria and have demonstrated a treatment response or are in remission. Examples of treatment response include clinically meaningful reductions in disease activity scores (e.g., HBI score decrease greater than or equal to 50% from pre-treatment measurement), along with improvements in endoscopic findings and reduction or discontinuation of corticosteroids. Prescribers may wish to consider other funded alternatives for patients unable to discontinue corticosteroid therapy.

Upadacitinib
Brand(s): Rinvoq
DOSAGE FORM/ STRENGTH: 15 mg, 30mg, 40 mg ER Tablet

Approved doses:

Induction dose: Up to 45 mg once daily for 12 weeks

Maintenance dose:15 mg or 30 mg* once daily.

For patient 65 years of age or older: 15 mg once daily

*Depending on therapeutic response, 30 mg once daily may also be used for maintenance in some patients younger than 65 years of age. However, the lowest effective dose possible should be used for maintenance therapy to minimize adverse effects.

Exclusion criteria (for Initials and Renewals):

1. Combination therapy with another biologic or JAK inhibitor treatment used to treat inflammatory bowel disease will not be funded.

Approved doses:

Induction dose: 45 mg once daily for 12 weeks

Maintenance dose:15 mg or 30 mg once daily
For patient 65 years of age or older: 15 mg once daily

Approval Durations:

Initial approval: 6 months

First EAP renewal: 1 year

Second and subsequent EAP renewals: 2 years

Upadacitinib
Brand(s): Rinvoq
DOSAGE FORM/ STRENGTH: 15 mg, 30mg, 40 mg ER Tablet

Upadacitinib for Fistulising Crohn's disease with concomitant luminal disease

Initiation Criteria:

For the treatment of fistulising Crohn's disease with concomitant luminal disease inpatients who meet ALL the following criteria;

1. Patient has actively draining perianal or enterocutaneous fistula(e) that have recurred or persist despite a course of
    a. appropriate antibiotic therapy (e.g. ciprofloxacin and/or metronidazole) and immunosuppressive therapy (e.g. azathioprine or 6-mercaptopurine) OR
    b. appropriate antibiotic therapy (e.g. ciprofloxacin and/or metronidazole) and a biologic (e.g. adalimumab, infliximab, ustekinumab) with or without an immunosuppressive therapy

    AND

2. Harvey Bradshaw Index (HBI) score greater than or the same as 7 (or other validated disease activity score confirming moderate to severe disease)

Initial approved dose:

Doses exceeding the standard recommended doses will be considered on a case-by-case basis. Please provide clinical rationale to support the request for higher doses.

Renewal Criteria

Maintenance therapy is funded for patients who met the initiation criteria and who achieve and maintain response to therapy (e.g., partial or complete resolution of fistulae and symptom improvement). Please include information describing the patient's fistula(e) resolution (e.g., partial or complete resolution) and HBI score.

Exclusion criteria (for Initials and Renewals):

1. Combination therapy with another biologic or other JAK inhibitor treatments used to treat inflammatory bowel disease will not be funded.

Upadacitinib
Brand(s): Rinvoq
DOSAGE FORM/ STRENGTH: 15 mg, 30mg, 40 mg ER Tablet

Approved doses:

Induction dose: Up to 45 mg once daily for 12 weeks

Maintenance dose:15 mg or 30 mg* once daily.

For patient 65 years of age or older: 15 mg once daily

*Depending on therapeutic response, 30 mg once daily may also be used for maintenance in some patients younger than 65 years of age. However, the lowest effective dose possible should be used for maintenance therapy to minimize adverse effects

Approval durations:

Initial approval: 6 months

First renewal: 6 months to 1 year pending fistula(e) resolution

Second and subsequent renewals: 2 years with complete resolution

The duration of approval for patients with partial resolution will be provided on a case-by-case basis.

Vedolizumab

Brand(s): Entyvio
DOSAGE FORM/ STRENGTH: 300 mg Injection, 108 mg/0.68mL prefilled syringe and prefilled pen
Updated: October 18, 2022

Vedolizumab for Fistulising Crohn's disease with concomitant luminal disease

For the treatment of fistulising Crohn's disease with concomitant luminal disease inpatients who meet ALL the following criteria;

1. Patient has actively draining perianal or enterocutaneous fistula(e) that have recurred or persist despite a course of
   - appropriate antibiotic therapy (e.g. ciprofloxacin and/or metronidazole) and immunosuppressive therapy (e.g. azathioprine or 6-mercaptopurine) OR
   - appropriate antibiotic therapy (e.g. ciprofloxacin and/or metronidazole) and adalimumab or infliximab with or without an immunosuppressive therapy

AND

2. Harvey Bradshaw Index (HBI) score greater than or the same as 7 (or other validated disease activity score confirming moderate to severe disease)

Initial approved dose: 300 mg initially Intravenously (IV) administered at week 0, followed by 300mg at week 2, 300mg at week 6, then 300 mg every 8 weeks thereafter.

Note: Entyvio subcutaneous (SC) doses is to be used as a maintenance treatment, following at least two intravenous infusions, 108 mg administered by subcutaneous injection once every 2 weeks, with the first subcutaneous dose administered in place of the next scheduled intravenous dose and every 2 weeks thereafter.

Doses exceeding the standard recommended doses will be considered on a case-by-case basis. Please provide clinical rationale to support the request for higher doses.

Renewal Criteria

Maintenance therapy is funded for patients who met the initiation criteria and who achieve and maintain response to therapy (e.g., partial or complete resolution of fistulae and symptom improvement). Please include information describing the patient's fistula(e) resolution (e.g., partial or complete resolution) and HBI score.

Approved Renewal/Maintenance dose: 300 mg every eight weeks or 108 mg SC every 2 weeks

Exclusion criteria (for Initials and Renewals):

1. Combination therapy with another biologic used to treat inflammatory bowel disease will not be funded.

Vedolizumab
Brand(s): Entyvio
DOSAGE FORM/ STRENGTH: 300 mg Injection, 108 mg/0.68mL prefilled syringe and prefilled pen

Approval durations:

Initial approval: 6 months
First renewal: 6 months to 1 year pending fistula(e) resolution
Second and subsequent renewals: 2 years with complete resolution

The duration of approval for patients with partial resolution will be provided on a case-by-case basis.

Vedolizumab for Luminal Crohn's disease

Initial Criteria:

For the treatment of moderate to severe luminal Crohn's disease in patients who meet ALL of the following criteria:

1. Has a Harvey Bradshaw Index (HBI) score greater than or equal to 7 (or other validated disease activity score confirming moderate to severe luminal Crohn's disease); AND
2. Has failed conventional treatment with a corticosteroid (prednisone 40–60 mg/day [or equivalent]) for a minimum of 14 days (or an intravenous corticosteroid for 1 week);
   OR
   Has responded to or has stabilized on conventional treatment with a corticosteroid, with or without an immunosuppressant (e.g., azathioprine, 6-mercaptopurine, methotrexate);
   OR
   Has a contraindication to corticosteroids which prevents the use of initial conventional treatment with corticosteroids;
   AND
3. Vedolizumab is being used to induce remission or as a steroid-sparing maintenance therapy.

Notes:

1. Patients with mild Crohn's disease (e.g., HBI less than 7) may be considered on a case-by-case basis but the application must include the rationale for coverage and other relevant details.

Vedolizumab

Brand(s): Entyvio
DOSAGE FORM/ STRENGTH: 300 mg Injection, 108 mg/0.68mL prefilled syringe and prefilled pen

Initial approved dose: 300 mg initially Intravenously (IV) administered at week 0, followed by 300mg at week 2, 300mg at week 6, then 300 mg every 8 weeks thereafter.

Note: Entyvio subcutaneous (SC) doses is to be used as a maintenance treatment, following at least two intravenous infusions, 108 mg administered by subcutaneous injection once every 2 weeks, with the first subcutaneous dose administered in place of the next scheduled intravenous dose and every 2 weeks thereafter.

Doses exceeding the standard recommended doses will be considered on a case-by-case basis. Please provide clinical rationale to support the request for higher doses.

Renewal Criteria:

Maintenance therapy is funded for patients who met the initiation criteria and have demonstrated a treatment response or are in remission. Examples of treatment response include clinically meaningful reductions in disease activity scores (e.g., HBI score decrease greater than or equal to 50% from pre-treatment measurement), along with improvements in endoscopic findings and reduction or discontinuation of corticosteroids.
Prescribers may wish to consider other funded alternatives for patients unable to discontinue corticosteroid therapy.

Approved Renewal/Maintenance doses: 300mg IV every 8 weeks or 108 mg SC every 2 weeks.

Note: Entyvio subcutaneous (SC) doses is to be used as a maintenance treatment, following at least two intravenous infusions, 108 mg administered by subcutaneous injection once every 2 weeks, with the first subcutaneous dose administered in place of the next scheduled intravenous dose and every 2 weeks thereafter.

Doses exceeding the standard recommended doses will be considered on a case-by-case basis. Please provide clinical rationale to support the request for higher doses.

Exclusion criteria (for Initials and Renewals):

1. Combination therapy with another biologic used to treat inflammatory bowel disease will not be funded.

Approval Durations:
Initial approval: 6 months
First EAP renewal: 1 year
Second and subsequent EAP renewals: 2 years

Vedolizumab
Brand(s): Entyvio
DOSAGE FORM/ STRENGTH: 300 mg Injection, 108 mg/0.68mL prefilled syringe and prefilled pen

Vedolizumab for Ulcerative Colitis

For the treatment of moderate to severe ulcerative colitis in patients who meet ALL the following criteria:

1. Has a Mayo score greater than or equal to 6 with an endoscopic subscore* of at least 2 (or other validated disease activity score confirming moderate to severe disease); AND
2. Has failed conventional treatment with a corticosteroid (prednisone 40–60 mg/day [or equivalent]) for a minimum of 14 days (or intravenous corticosteroid for 1 week);
   OR
   Has responded to or has been stabilized on conventional treatment with a corticosteroid, with or without an immunosuppressant (e.g., azathioprine, 6-mercaptopurine);
   OR
   Has a contraindication to corticosteroids which prevents the use of initial conventional treatment with corticosteroids;
   AND
3. Vedolizumab is being used to induce remission or as a steroid-sparing maintenance therapy.

*The endoscopy procedure must be done within the 12 months prior to initiation of treatment.

Notes:
1. Patients with mild ulcerative colitis disease (e.g., Mayo score less than 6) may be considered on a case-by-case basis. Application must include the rationale for coverage and other relevant details.

Initial approved dose: 300 mg initially Intravenously (IV) administered at week 0, followed by 300mg at week 2, 300mg at week 6, then 300 mg every 8 weeks thereafter.

Note: Entyvio subcutaneous (SC) doses is to be used as a maintenance treatment, following at least two intravenous infusions, 108 mg administered by subcutaneous injection once every 2 weeks, with the first subcutaneous dose administered in place of the next scheduled intravenous dose and every 2 weeks thereafter.

Doses exceeding the standard recommended doses will be considered on a case-by-case basis. Please provide clinical rationale to support the request for higher doses.

Vedolizumab

Brand(s): Entyvio
DOSAGE FORM/ STRENGTH: 300 mg Injection, 108 mg/0.68mL prefilled syringe and prefilled pen

Renewal Criteria:

Maintenance therapy is funded for patients who met the initiation criteria and have demonstrated a treatment response or are in remission. Examples of treatment response include clinically meaningful reductions in disease activity scores (e.g., Mayo score less than 6), along with improvements in endoscopic findings and reduction of corticosteroid doses by 50% in the first 6 months of treatment with vedolizumab with discontinuation of corticosteroids by 12 months. Patients who remain on corticosteroids following the first year of treatment will be considered on a case-by-case basis.

Prescribers may wish to consider other funded alternatives for patients unable to discontinue corticosteroid therapy.

Approved Renewal/Maintenance dose: 300 mg every eight weeks or 108 mg SC every 2 weeks

Exclusion criteria (for Initials and Renewals):

1. Combination therapy with another biologic used to treat inflammatory bowel disease will not be funded.

Approval durations:

Initial approval: 6 months
First renewal: 6 months to 1 year depending on whether the patient is able to reduce and/or discontinue corticosteroid treatment
Second and subsequent renewals: 2 years with complete discontinuation of corticosteroid treatment

MISCELLANEOUS TREATMENTS

Zopiclone
Brand(s): Imovane + generic brands
DOSAGE FORM/ STRENGTH: 5 mg, 7.5 mg tablet

For the treatment of insomnia as a single hypnotic agent in patients who meet the following criteria;

- Have failed at least two benzodiazepines; OR
- Have failed or experienced intolerance to at least one benzodiazepine and one other hypnotic (i.e., amitriptyline, trazodone, etc)

Duration of Approval: 2 Years

For the treatment of insomnia if patient has an identified psychiatric diagnosis. **Renewals** will be considered in patients who are responding to therapy AND who continues to require therapy AND who are using zopiclone as a single agent.

Duration of Approval: 2 Years

METABOLIC/GENETIC MODIFIERS

Asfotase alfa
Brand(s): Strensiq
DOSAGE FORM/ STRENGTH: 18mg/0.45mL, 28mg/0.7mL, 40mg/1mL, 80mg/0.8mL

Initiation Criteria:

For the treatment of perinatal/infantile, childhood, or juvenile-onset hypophosphatasia (HPP) in patients who meet the following criteria:

- Diagnosis is confirmed by genetic testing (i.e. documented tissue-nonspecific alkaline phosphatase gene mutations); AND
- Serum alkaline phosphatase (ALP) level is below the age-adjusted normal range[1] using age and gender adjusted norms; AND
- Plasma pyridoxal-5-phosphate (PLP) above the upper limit of normal; AND
- Radiologically confirmed HPP-related skeletal abnormalities; AND
- Diagnosis occurred before the patient's 12th birthday with documented onset of signs/symptoms[2] of HPP prior to their 12th birthday; AND
- Patient is younger than 18 years of age at the time the treatment is initiated; AND
- Patient does not have odonto- or pseudo- HPP (i.e. craniosynostosis alone, premature loss of deciduous teeth alone and vitamin D deficiency to be ruled out); AND
- The patient's treatment plan and goals of therapy is provided prior to the initiation of therapy; AND
- Patient is under the care of a metabolic specialist with expertise in the diagnosis and management of HPP.

Approval duration for initial requests: 6 months

Renewal Criteria:

Renewals of reimbursement will be considered in patients meeting the following criteria:
- Patient continues to be under the care of a metabolic specialist; AND
- Patient has demonstrated compliance to the treatment and monitoring schedule: AND
- Pre-specified goals[3] based on the patient's clinical status at initiation of treatment are met and the patient is deemed to continue to benefit from treatment. (Note: The request must include information about the treatment responses and milestones)

First renewal: 6 months

Subsequent renewals: 1 year

Asfotase alfa
Brand(s): Strensiq
DOSAGE FORM/ STRENGTH: 18mg/0.45mL, 28mg/0.7mL, 40mg/1mL, 80mg/0.8mL

Stopping Criteria:

- Discontinuation to be considered after growth is completed based on objective measure of height, weight and closure of bone growth plates as confirmed radiologically.
- Babies with perinatal/infantile HPP who fail treatment trials of 6 months
- If pre-specified goals are not met at reassessment, the treatment should not be continued.

Notes:

[1]Normal range as informed by the Canadian Laboratory Initiative on Paediatric Reference Intervals (CALIPER) can be used as a reference for this information. Below upper limit of normal refers to 2 or lower standard deviations above the mean.

[2]Incoming Requests should address the following;

- baseline skeletal symptoms including age and dates of for those assessments
- abnormalities of skeletal mineralization
- fracture history
- growth plate irregularities and bone and skeletal growth
- description of growth and developmental milestones
- Signs, symptoms, and history of seizures
- respiratory function including need for ventilator support
- Activity and mobility
- Laboratory markers that include vitamin D levels, calcium levels

Assessments such as the Radiographic Global Impressive of Change (RGIC) score and/or the Thacher score for evaluating rickets may be provided at baseline and at the time of renewal of coverage (as applicable) as a measure of response and benefit from therapy.

[3]Specific patient treatment goals should be developed on a case-by-case basis and may include some of the following; Healing of rickets, improved bone mineralization, fewer fractures, reduced pain, improved growth, mobility, improvement in respiratory status, attainment of age-appropriate growth milestones, improvement in gait or deformities, improved quality of life measures.

Documentation of improvement from baseline is to be provided at the time of renewal.

Please note that effective April 8, 2021, foreign labelled Strensiq (generic name: asfotase alfa) has been added as a temporary Exceptional Access Program benefit due to drug shortage.

PIN	MA (EU) Number	Brand Name	Generic Name	Strength	Dosage Form & Package Size
9857647	EU/1/15/1015/006	Strensiq	Asfotase alfa	18mg/0.45mL	Single Use Vial
9857648	EU/1/15/1015/008	Strensiq	Asfotase alfa	28mg/0.7mL	Single Use Vial
9857649	EU/1/15/1015/010	Strensiq	Asfotase alfa	40mg/1mL	Single Use Vial
9857650	EU/1/15/1015/004	Strensiq	Asfotase alfa	80mg/0.8mL	Single Use Vial

Burosumab
Brand(s): Crysvita
DOSAGE FORM/ STRENGTH: 10 mg/mL, 20 mg/mL, 30 mg/mL Vial
Effective date: December 21, 2021

Initiation Criteria:

For the treatment of X-linked hypophosphatemia (XLH) in patients who meet all of the following criteria:

1. Treatment is initiated in a pediatric patient who is at least 1 year of age and in whom the epiphyseal closure has not occurred yet; **AND**
2. XLH diagnosis is confirmed by genetic documentation of phosphate-regulating endopeptidase homolog, X-linked (PHEX) gene variant in either the patient or in a directly related family member with appropriate X-linked inheritance; **AND**
3. Clinical presentation consistent with XLH diagnosis, including fasting hypophosphatemia[1] and normal renal function (defined as fasting serum creatinine level below the age-adjusted upper limit of normal); **AND**
4. Radiographic evidence of rickets with a baseline[2] rickets severity score (RSS) total score of 2 or greater at the time Crysvita treatment is initiated; **AND**
5. Patient is under the care of a specialist with expertise in the diagnosis and management of XLH.

[1]Normal range based on age and gender as informed by the Canadian Laboratory Initiative on Pediatric Reference Intervals (CALIPER; https://caliperproject.ca/) can be used as a reference of this information.

[2]Baseline RSS total score is defined as the RSS total score measured immediately prior to initiation of Crysvita therapy.

Renewal Criteria:

Renewals of reimbursement will be considered in patients meeting the following criteria:

- Patient continues to be under the care of a specialist with expertise in the diagnosis and management of XLH; **AND**
- The patient does not meet any of the discontinuation criteria while on therapy.

Patients should be assessed on an annual basis. In pediatric patients in whom epiphyseal closure has not occurred, documentation demonstrating improvement from baseline RSS total score in the first 12 months and/or maintenance of RSS total score improvement achieved in the first 12 months is to be provided at the time of renewal.

Burosumab
Brand(s): Crysvita
DOSAGE FORM/ STRENGTH: 10 mg/mL, 20 mg/mL, 30 mg/mL vial

Discontinuation Criteria:

- In pediatric[a] patients in whom epiphyseal closure has not yet occurred and who met the above initiation criteria, treatment should be discontinued upon meeting any of the following circumstances:
  - There is no demonstrated improvement in the 12-month RSS total score from baseline[2] RSS total score; OR
  - The patient's RSS total score achieved after the first 12 months of burosumab therapy has not been maintained subsequently.

- In adolescent[b] patients in whom epiphyseal closure has occurred and who met the above initiation criteria and initiated treatment as a pediatric patient, treatment should be discontinued upon development of any of the following clinical circumstances:
  - Hyperparathyroidism; OR
  - Nephrocalcinosis; OR
  - Evidence of fracture or pseudo-fracture based on radiographic assessment.

- In adult[c] patients who met the above initiation criteria and initiated treatment as a pediatric patient, treatment should be discontinued upon development of any of the following clinical circumstances:
  - Hyperparathyroidism; OR
  - Nephrocalcinosis; OR
  - Evidence of fracture or pseudo-fracture based on radiographic assessment.

[2]Baseline RSS total score is defined as the RSS total score measured immediately prior to initiation of Crysvita therapy.

[a]Pediatric refers to a patient who is aged 17 years or younger.

[b]Adolescent refers to a pediatric patient who is aged 13 to 17 years.

[c]Adult refers to a patient who is 18 years of age and older.

Approval duration for initial requests: 1 year

Burosumab
Brand(s): Crysvita
DOSAGE FORM/ STRENGTH: 10 mg/mL, 20 mg/mL, 30 mg/mL vial

Approved dosage for initial and renewal:

Funding will be provided at a minimum dose of 10 mg up to a maximum dose of 90 mg.

- Children (1-17 years of age): 0.8mg/kg of body weight (rounded to the nearest 10 mg) subcutaneously every 2 weeks.
- Adults (18 years of age and older): 1mg/kg of body weight subcutaneously (rounded to the nearest 10 mg) every 4 weeks.

Dose to be adjusted based on serum phosphorus levels.

Canakinumab
Brand(s): Ilaris
DOSAGE FORM/ STRENGTH: 150 mg/vial injection

Muckle-Wells Syndrome:

The patient has a diagnosis of Muckle-Wells Syndrome (MWS) based on meeting each of the following confirmatory results:

1. Clinical diagnosis of MWS;
2. NLRP3 mutation (mutational analysis required);
3. SAA levels ≥ 10 mg/L; and
4. Assessment score of patient's disease activity determined by the following 4 parameters: skin disease, arthralgia, conjunctivitis, and fatigue/malaise ≥ mild, moderate, or severe.

If a patient is without NLRP3 mutation, a request will be considered on a case-by-case basis if the other confirmatory criteria are met and if the exclusion criteria are not met. However, the initial approval would be for 6 months; if the patient demonstrated a sustained SAA level < 10 mg/L, a renewal of funding for a 1 year approval period would be considered.

Initial Approval Period: 1 year

NOMID Syndrome:

The patient has a Diagnosis of Neonatal-Onset Multisystem Inflammatory Disease (NOMID) based on meeting each of the following confirmatory results:
1. Clinical diagnosis of NOMID.
2. Presentation of symptoms of NOMID made in a patient < 6 months of age.
3. NLRP3 mutation (mutational analysis required).
4. A score of patient's disease activity determined by the following 4 parameters: skin disease, arthralgia, conjunctivitis, and fatigue/malaise ≥ mild, moderate, or severe.

If a patient is without NLRP3 mutation, a request will be considered on a case-by-case basis if the other confirmatory criteria are met and if the exclusion criteria are not met. However, the initial approval would be for 6 months; if the patient demonstrated a sustained SAA level < 10 mg/L, a renewal of funding for a 1 year approval period would be considered.

Initial Approval Period: 6 months

For Both Indications

For all patients, the treatment is supervised by medical specialists with knowledge in the management of CAPS (Cryopyrin-Associated Periodic Syndromes).

Canakinumab
Brand(s): Ilaris
DOSAGE FORM/ STRENGTH: 150 mg/vial injection

The approved dosage will be:

- Bodyweight > 40 kg: 150 mg subcutaneously every 8 weeks
- Bodyweight = 15 kg – 40 kg: 2 mg/kg subcutaneously every 8 weeks. (For children 15 kg – 40 kg with an inadequate response, the dose can be increased to 3 mg/kg.)

For all patients, funding requests will be denied if any of the <u>exclusion criteria</u> is met:

i) The patient is bedridden where any physical activity brings on discomfort and symptoms which occur at rest <u>AND</u> not amenable to surgical/medical intervention;

ii) The patient has another life-threatening disease where prognosis is unlikely to be influenced by Ilaris® (canakinumab) therapy (e.g. neuroblastoma, leukemia etc.);

iii) The patient has a life-expectancy of six months or less, regardless of the cause; or

iv) The patient has Familial Cold Auto-Inflammatory Syndrome (FCAS).

<u>Renewal Criteria</u>:

Confirmation from the Patient's physician that the patient has benefited or continues to benefit from therapy with Ilaris, is expected to continue to do so and that each of the following is met:

1. The patient has SAA levels < 10 mg/L. If SAA levels 10 mg/L or higher over a 6 month interval and that is sustained over two consecutive 6 month intervals, approval for funding may be withdrawn.

2. An assessment score of patient's skin disease, arthralgia, conjunctivitis, and fatigue/malaise shows no or minimal disease activity

3. The patient:

    a) is not bedridden where any physical activity brings on discomfort and symptoms which occur at rest <u>AND</u> not amenable to surgical/medical intervention;

    b) has no other life-threatening disease where prognosis is unlikely to be influenced by Ilaris® (canakinumab) therapy (e.g. neuroblastoma, leukemia etc.); or

Canakinumab
Brand(s): Ilaris
DOSAGE FORM/ STRENGTH: 150 mg/vial injection

c) has not developed a life-threatening complication or a severe injection reaction to Ilaris® (canakinumab) not treatable by other therapeutic measures.

4. The patient has adhered with prescribed injection schedule for optimal management of the disease

5. The patient has adhered to all safety and effectiveness monitoring of the treatment

6. Treatment will be supervised by medical specialists with knowledge in the management of CAPS

The approved dosage for Subsequent Approvals is the same as Initial Approvals.

Cerliponase alfa
Brand(s): Brineura
DOSAGE FORM/ STRENGTH: 150mg/5mL (30mg/mL) Injection
Updated December 2, 2020

Initiation Criteria:
For the treatment of Neuronal Ceroid Lipofuscinosis Type 2 (CLN2) disease/ tripeptidyl peptidase 1 (TPP1) deficiency, in patients who meet the following criteria at the time of treatment initiation:

- Diagnosis of CLN2 disease is confirmed by TTP1 enzyme activity and CLN2 genotype analysis; AND

- CLN2 Rating Scale demonstrates the following requirements:
  - A minimum score greater than or the same as 1 in each of the motor and the language domains; AND
  - A minimum score greater than or the same as 3 for the aggregate motor-language score

- AND Patient is under the care of a prescriber/specialist with expertise in the diagnosis and management of CLN2 disease.

Approval duration of initials: 24 weeks

Renewal Criteria:

Renewal of funding will be considered for patients who do not meet any of the exclusion criteria and who have not demonstrated any of the stopping/discontinuation criteria while on therapy.

Cerliponase alfa

Brand(s): Brineura
DOSAGE FORM/ STRENGTH: 150mg/5mL (30mg/mL) Injection

Exclusion Criteria (Applies to both initiation and renewal criteria):

Patients meeting any of the following criteria will not be funded:

- Requires ventilation support (except for non-invasive support at night);
- Presence of contraindications to intracerebroventricular (ICV) drug administration;
- Presence of acute ICV device complications;
- Presence of ventriculoperitoneal (VPS) shunts

Stopping/Discontinuation Criteria for Brineura:

Treatment with Brineura will be discontinued if:

- There is reduction of 2 or more points in the aggregate motor-language score of the CLN2 Clinical Rating Scale that is maintained over any 2 consecutive 24-week assessments; OR
- The aggregate motor-language score of the CLN2 Clinical Rating Scale reaches 0 (zero) at 2 consecutive 24-week assessments; OR
- The patient has developed contraindication to ICV drug administrations

Recommended dose:

300 mg (10 mL solution) administered by intracerebroventricular (ICV) infusion once every 2 weeks.

Approval duration of renewals: 12 months

Elosulfase Alfa

Brand(s): Vimizim
DOSAGE FORM/ STRENGTH: 1 mg/mL Injection
Effective date: May 13, 2019

Initiation Criteria:

For the treatment of mucopolysaccharidosis type IVA (MPS IVA) in patients meeting all the following criteria;

i) Diagnosis is confirmed by enzymatic assay for N-acetylgalactosamine-6-sulfate sulfatase (GALNS) activity in peripheral blood leukocytes or fibroblasts (excluding multiple sulfatase deficiency) AND mutational analysis of GALNS[1] ; AND
ii) Patient is under the care of a specialist with experience in the diagnosis and management of MPS IVA; AND
iii) The following baseline evaluations prior to initiation of Vimizim (elosulfase alfa) must be provided with the request for coverage:
iv) Detailed medical history documenting surgeries, medical admissions, subspecialty assessments
v) Orthopedic evaluation including spinal and cranial MRI, skeletal x-rays, pain symptoms from bone and joints as appropriate to age and clinical disease.
vi) Mobility measure: 6MWT and stair climb (if appropriate for age and disease status)
vii) Respiratory function testing including sleep study testing (if appropriate for age)
viii) Age appropriate quality of life measure (such as HAQ, PODCI, EQ5D5L or SF36)[2]
ix) documentation of mobility aide requirement, such as a walker or cane
x) documentation of requirement for respiratory aides, including ventilation status and changes in respiratory support requirements;
xi) Ophthalmologic and ear, nose and throat (ENT) assessment (if appropriate)
xii) Urine keratin sulfate (KS) determination: specific KS determination is preferred over total glycosaminoglycans (GAGs)
xiii) Cardiac echocardiogram

[1]Note: not all MPS IVA patients will have 2 known pathogenic alleles identified and parental mutation analysis to establish the phase of mutations should be performed.
[2]Note that academic goals (e.g. attendance or participation in school) may be considered case-by-case in pediatric patients.

Exclusion Criteria (Patient will not be started on Vimizim if any of the following are met/apply):

i) The patient is diagnosed with an additional progressive life limiting condition where treatment would not provide long term benefit (such as cancer or multiple sclerosis)
ii) The patient has a forced vital capacity (FVC) of less than 0.3 liters and requires continuous ventilator assistance.
iii) The patient/family is unwilling to comply with the associated monitoring criteria
iv) The patient/family is unwilling to attend clinics for assessment and treatment purposes

Elosulfase alfa
Brand(s): Vimizim
DOSAGE FORM/ STRENGTH: 1 mg/mL

Approval duration of initials: 1 year

Recommended dose: 2mg/kg IV infusion once a week.

Renewal criteria:

Patients must demonstrate at least 3 of the 5 following treatment effects for continuation of coverage of treatment with elosulfase alfa:

- 6 MWT or Stair Climb test stabilized at or improved by at least 5% of baseline measure
- Forced Vital Capacity (FVC) or Forced Expiratory Volume in one second (FEV-1) stabilized at or improved by at least 5% of baseline measure or remaining within 2 standard deviations of normal for the patient's age
- Improvement or no change (if minimal effect) in age appropriate quality of life measure[3]
- Reduction of urine KSs of 20%
- Stability of cardiac ejection fraction reduction (within 5% of baseline)

[3]Note that academic goals (e.g. attendance or participation in school) may be considered case-by-case in pediatric patients.

Discontinuation criteria

Patients will not be eligible for coverage of treatment if they:
- Fail to meet 3 of the 5 continuation criteria
- Are unable to tolerate infusions due to infusion related adverse events that cannot be resolved
- Require permanent invasive ventilation
- Miss more than 6 infusions in a 12-month interval, unless for medically related issues.
- Meets any one of the Exclusion Criteria

Approval duration of renewals: 1 year

Recommended dose: 2mg/kg IV infusion once a week.

Givosiran

Brand(s): Givlaari
DOSAGE FORM/ STRENGTH: 189 mg/mL injection
Effective date: September 7, 2023

Initiation Criteria:

As **treatment for the prevention of acute hepatic porphyria (AHP) attacks** in patients meeting all the following criteria:

1. 18 years of age or older; AND
2. A confirmed diagnosis of acute hepatic porphyria (see note 1); AND
3. Has experienced four (4) or more porphyria attacks in the year prior to initiation of givosiran with each attack resulting in either hospitalization, an urgent healthcare visit, or treatment with intravenous hemin ; AND
4. Patient is under the care of a clinician experienced in the management of AHP.

Exclusion Criteria:

Givosiran will not be funded if it is used in combination with prophylactic IV hemin.

Renewal Criteria:

Renewals will be considered in those demonstrating a reduction in the annualized porphyria attack rate that required hospitalization, an urgent care visit, or acute treatment with IV hemin compared to the baseline period prior to start of givosarin AND who have not developed any unacceptable toxicities from treatment with givosiran.

Renewal requests must include the total number of porphyria attacks during the 12 month period of givosiran administration, including the dates of any attacks requiring hospitalization, urgent care visits, or acute IV hemin treatment.

Additionally, reconfirm that the patient does not meet exclusion criteria.

Notes:

1. The EAP request application must include at least one of or both (if available) of the following:
   i) documented biochemical test results, including one of, or both if they are available, urinary delta-aminolevulinic acid (ALA) and urinary porphobilinogen (PBG) tests, confirming the diagnosis of AHP, including the specified subtype, if it is known;
   ii) genetic test results confirming the diagnosis of AHP.

Givosiran
Brand(s): Givlaari
DOSAGE FORM/ STRENGTH: 189 mg/mL injection

2. The baseline number of attacks before initiation of givosiran will be annualized. Requests should include the number of porphyria attacks over the specific period of time within the year before the initiation of givosiran and should include the approximate dates and the management of each attack (i.e. hospitalization, urgent care visit, dose of IV hemin used to treat the attack) for at least 4 of the attacks that occurred in the 12 month period before treatment initiation with givosiran. For patients who have already initiated givosiran therapy, this information for at least 4 attacks from the year prior to treatment initiation will also be required. The baseline attack history will also be required to administer renewal criteria.
3. If a patient experiences an acute attack while on givosiran, IV hemin as treatment for the acute attack may be administered as appropriate.
4. Patients with stable disease who transition to menopause may consider a trial of treatment discontinuation.
5. Retreatment will be considered in patients who experience a relapse of attacks following treatment discontinuation of givosarin.

Recommended Dose:

2.5 mg/kg SC injection monthly.

(Refer to the product monograph for dosing information)

Approval duration of initials and renewals: 1 year

Glycerol phenylbutyrate
Brand(s): Ravicti
DOSAGE FORM/ STRENGTH: 1.1g/mL-25mL bottle

For the management of patients with chronic urea cycle disorders(UCD) who meet all the following criteria:

- Glycerol phenylbutyrate is being used as a nitrogen binding agent; AND
- Patient has demonstrated that they cannot be managed by dietary protein restriction and/or amino acid supplementation alone[1]; AND
- Patient is under the care of a physician with expertise in the treatment of patients with UCD or in consultation with a physician with this expertise.

[1]The initial request should include levels for blood ammonia and glutamine levels demonstrating inadequate effects of protein restriction or amino acid supplementation.

Exclusion Criteria:

- Is not used in combination with other forms of phenylbutyrate
- Will not be funded for patients who are not using a low protein diet while on treatment
- Not funded for the management of acute hyperammonemia
- Not funded for patients under 2 months of age

Recommended dose: 5 g/m^2 to 12.4 g/m^2 per day

Approval duration: 1 year

Renewal Criteria:

Renewals will be considered in patients who demonstrate benefit from treatment[2] and who have not developed unacceptable toxicities requiring discontinuation.

[2]At the time of renewal, please provide recent (within 3 months) blood ammonia and glutamine levels while on treatment and address the number and severity of hyperammonemic events experienced while on treatment in the previous 12 months and any treatment emergent events requiring urgent care or hospitalization.

First renewal: 1 year

Subsequent renewals: 2 years

Lumasiran

Brand(s): Oxlumo
DOSAGE FORM/ STRENGTH: 94.5 mg/0.5 mL Injection
Effective date: July 29, 2024

Initiation Criteria:

For the treatment of primary hyperoxaluria type 1 (PH1) to reduce the production of endogenous oxalate production in patients who meet all the following criteria:

1. Patients must have a genetically confirmed diagnosis of PH1 as determined by a mutation in the alanine-glyoxylate aminotransferase (AGXT) gene; AND

2. Patient has been compliant with Standard of Care (SOC) therapy for PH1 (Note 1) for a duration of 3 to 6 months and meets at least one of the following requirements;

a) Patient with preserved kidney function where urinary oxalate can be measured but patient has demonstrated that they are unable to normalize 24-hour urine oxalate excretion (Note 2).
b) Pediatric patient aged 6 years and younger who is noncontinent and who has a high spot oxalate to creatinine (oxalate:creatinine) ratio compared with normal age-based reference ranges
c) the Patient has end-stage kidney disease and either:

   i) has an estimated glomerular filtration rate (eGFR) less than 30 mL/min/1.73m^2 and has an increased plasma oxalate level compared with normal laboratory reference ranges, which must be submitted with the request; OR

   ii) is on dialysis and has an increased pre-dialysis plasma oxalate level compared with normal laboratory reference ranges, which must be submitted with the request;

All requests must include a recent eGFR that is measured at the time of the measurement of urine oxalate levels and/or plasma oxalate levels to ensure an accurate evaluation of the laboratory findings.

3. Initial requests must be provided by a nephrologist or metabolic diseases specialist with experience in the diagnosis and management of PH1.

Include the following clinical details with your request:

- Kidney function and most recent eGFR
- Confirm if patient is on dialysis
- pre-treatment kidney stone history and/or frequency per year. A nil result can be provided.
- Description of systemic oxalosis in organs and tissues, including nephrocalcinosis or confirmation of no systemic deposition.

Lumasiran
Brand(s): Oxlumo
DOSAGE FORM/ STRENGTH: 94.5 mg/0.5 mL injection

Discontinuation Criteria

1. Treatment with lumasiran should be discontinued if there is evidence of no response or loss of response.

Response is defined as the below:

a) For patients in whom urinary oxalate can be measured: Lowering of 24-hour urine oxalate to less than 1.5 times the Upper Limit of Normal (ULN) (Note 2, 3 and 4)

b) For patients 6 years of age or younger who are noncontinent: Demonstrating a 30% reduction in spot oxalate:creatinine ratio (Note 5 and 6)

c) For patients with end-stage kidney disease or who are on dialysis: Demonstrating a 15% reduction in plasma oxalate level. (Note 3)

2. Treatment with lumasiran should be discontinued if the patient has received a liver transplant with or without a kidney transplant.

Notes:

1. Standard of Care therapy means therapy that includes vitamin B6 (pyridoxine), oral hyperhydration, and crystallization inhibitors, such as citrate supplementation or bicarbonate salts that lower urine acidity, including potassium or sodium citrate and potassium or sodium bicarbonate, and an oxalate-controlled diet used at adequate doses.
2. 24 hour urine oxalate results should be corrected for creatinine or body surface area. Additionally, due to the possibility of individual day-to-day variations in the results, repeated measurement may be provided to ensure appropriate evaluation of baseline values compared with the required response to therapy parameters.
3. Patients with end-stage kidney disease (ESKD) or those who are on dialysis should have pre-dialysis plasma oxalate levels measured instead of urine oxalate. Please submit the plasma oxalate.
4. Evaluate if patient is adherent to standard of care treatment, oxalate controlled dietary restrictions, and determine if eGFR has declined.
5. In patients who are less than 18 years of age, oxalate excretion results should be corrected to a mg per body surface area (BSA) of 1.73 m^2 to be properly interpreted.
6. Measurement of oxalate:creatinine ratio should be taken at least twice a year to monitor for response to treatment.

Lumasiran

Brand(s): Oxlumo
DOSAGE FORM/ STRENGTH: 94.5 mg/0.5 mL injection

Exclusion Criteria for both initial and renewal criteria.

1. Patients with Primary hyperoxaluria type 2 (PH2) are not funded.
2. Patients with Primary hyperoxaluria type 3 (PH3) are not funded.
3. Patients who have received a liver transplant for PH1 are not funded.

Renewal Criteria

Renewals will be considered in patients **who do not meet the discontinuation criteria** and who continue to demonstrate a response to treatment.

At the time of renewal please submit a recent eGFR along with the biochemical results. Please include clinical details of improvements to kidney function, kidney stone frequency in the past year, and symptoms of systemic oxalosis, as applicable, to demonstrate a response to treatment. You may include consult notes.

Subsequent renewals following the initial prescription can be requested by a pediatrician instead of a nephrologist or metabolic diseases physician.

Approval duration: 12 months

Approved doses:

Loading dose for less than 20 kg patients - up to 6 mg/kg once monthly for 3 doses

Maintenance doses

Patients less than 10 kg - 3 mg/kg once a month

Patients 10 kg to less than 20 kg - up to 6 mg/kg once every 3 months.

Loading dose for patient greater than 20 kg – 3 mg/kg once monthly for 3 doses followed by maintenance doses of up to 3 mg/kg once every 3 months.

Inotersen

Brand(s): Tegsedi
DOSAGE FORM/ STRENGTH: 284 mg/ 1.5 mL prefilled syringes
Effective date: July 20, 2020

Initiation criteria

For the treatment of polyneuropathy in patients with hereditary transthyretin-mediated amyloidosis (hATTR), meeting all the following criteria:

1. Age 18 years of age or older; AND
2. Has a confirmed genetic diagnosis of hereditary transthyretin-mediated amyloidosis: AND
3. Symptomatic with Polyneuropathy disability stage I to ≤ IIIB or with Familial amyloidotic polyneuropathy stage I or II.
4. Under the care of a specialist with experience in the diagnosis and management of hATTR

Exclusion Criteria:

- Pre-symptomatic patients
- Patients diagnosed with severe heart failure symptoms (defined as New York Heart Association class III or IV).
- Patients who are recipients of a liver transplant
- Patients with platelet count < 100 x 10^9/L before initiation of treatment
- Patients who will be using Inotersen in combination with other interfering ribonucleic acid drugs or transthyretin stabilizers used to treat hATTR.

Discontinuation criteria:

Treatment with inotersen will be discontinued for patients who are:

- Permanently bedridden and dependent on assistance for basic activities of daily living, or
- Receiving end-of-life/palliative care where survival of less than one year is expected.

Renewal Criteria:
Renewal of funding will be considered if patients do not meet the discontinuation criteria.

Dosage: 300 mg of inotersen sodium (284mg of inotersen) sc injection once a week. (Patients should be assessed after 9 months of treatment and then every six months thereafter.)

Duration of Approval of initiation requests: 10 months
Duration of Approval of first renewal: 6 months
Duration of Approval of 2nd and subsequent renewals: 1 year

Inotersen
Brand(s): Tegsedi
DOSAGE FORM/ STRENGTH: 284 mg/ 1.5 mL prefilled syringes

Notes to Prescribers:

- Laboratory documentation for the genetic mutation for hATTR must be included with the application.
- Signs and symptoms of polyneuropathy should be listed.
- In your application please list all drugs that the patient is using including whether he/she is using any of the following: Diflunisal, Patisiran, Tafamidis
- Confirmation that the patient does not meet each of the listed exclusions must be provided on the request.

Definitions:

Familial Amyloid Polyneuropathy (FAP) stage: Clinical staging system for the neuropathy symptoms of hATTR (formerly termed familial amyloid neuropathy).

- FAP Stage 1: Walking without assistance, mild neuropathy (sensory, autonomic, and motor) in lower limbs
- FAP Stage 2: Walking with assistance, moderate impairment in lower limbs, trunk, and upper limbs
- FAP Stage 3: wheelchair or bed-ridden, severe neuropathy

Polyneuropathy disability score (PND): A five-stage measure of neuropathy impairment ranging from 0 (no impairment) to 4 (confined to a wheelchair or bedridden).

- Stage 0: no impairment
- Stage I: sensory disturbances but preserved walking capability
- Stage II: impaired walking capability but ability to walk without a stick or crutches
- Stage IIIA: walking only with the help of one stick or crutch
- Stage IIIB: walking with the help of two sticks or crutches
- Stage IV: confined to a wheelchair or bedridden

Mecasermin
Brand(s): Increlex
DOSAGE FORM/STRENGTH: 40 mg/mL Injection
Effective date: May 26, 2023

Initiation Criteria:

For the treatment of growth failure in patients with confirmed severe primary insulin-like growth factor deficiency (SPIGFD) who meet ALL the following criteria;

1. Patient is 2 to 18 years of age; AND
2. Patient is at least 2 years of age at the time of treatment initiation; AND
3. Epiphyseal growth plates have not closed; AND
4. SPIGFD diagnosis is confirmed as defined by
    a. having a known genetic mutation that causes SPIGFD (e.g. mutations in the GH receptor (GHR) gene/Laron's syndrome, post-GHR signaling pathway, and IGF-1 gene defects) (See Note 1) and/or

    b. having clinical and biochemical features of SPIGFD:
        i. height standard deviation score ≤ –3.0 and;
        ii. basal IGF-1 levels below the 2.5th percentile for age and gender and;
        iii. GH sufficiency (i.e. patient is not GH deficient; random or stimulated GH level of > 10 ng/mL and failure to increase IGF-1 by 50 ng/mL in response to exogenous GH during an IGF-1 generation test)
        iv. exclusion of secondary forms of IGF-1 deficiency, such as malnutrition, hypopituitarism, hypothyroidism, or chronic treatment with pharmacologic doses of anti-inflammatory steroids.

    AND
5. Patient is under the care of, or in consultation with a pediatric endocrinologist; AND
6. Mecasermin is not being used in combination with recombinant growth hormone (GH) treatment.

Notes:
1. Not all cases of SPIGFD have an identifiable genetic variant and case-by-case consideration may be provided if the clinical and biochemical criteria are not supported by a genetic diagnosis or by the presence of GH antibodies.

Mecasermin
Brand(s): Increlex
DOSAGE FORM/ STRENGTH: 40 mg/mL Injection

Discontinuation Criteria:
Treatment with mecasermin must be discontinued upon the occurrence of any ONE or more of the following:

1. height velocity is less than 1 cm per 6 months or less than 2 cm per year, or
2. bone age is more than 16 years in boys and 14 years in girls.
3. Patient is 19 years of age or older
4. Epiphyseal plates have closed

Renewal Criteria:

Renewal of funding of Mecasermin will be considered in patients who do not meet any of the discontinuation criteria and who do not develop unacceptable toxicities.

Recommended dose: The recommended starting dose is 0.04 to 0.08 mg/kg (40 to 80 mcg/kg) twice daily by subcutaneous injection up to a maximum dose of 0.12 mg/kg (120 mcg/kg) sc twice daily.

Approval duration for initial and renewal requests: 1 year

Migalastat
Brand(s): Galafold
DOSAGE FORM/ STRENGTH: 123 mg capsule
Effective date: May 13, 2019

EAP Initiation criteria:

For the treatment of Fabry disease (FD) in adult patients who meet ALL the following criteria;

1. Has a confirmed diagnosis of Fabry disease (deficiency of α-galactosidase A [α-Gal A]) and must be otherwise eligible for enzyme replacement therapy (ERT) for the treatment of FD as determined by a panel of Fabry disease experts consistent with criteria for diagnosis from the Canadian Fabry Disease Initiative (CFDI)[1]
2. Has an α-galactosidase A mutation that is determined to be amenable to migalastat by an in vitro assay[2]
3. Migalastat is not being used concomitantly with ERT[3].
4. Patient is considered to be compliant/adherent to treatment
5. Prescriber must be an expert in genetic disorders or a clinician experienced in the diagnosis and management of Fabry disease.

[1]Refer to Canadian Fabry Disease treatment guidelines 2017 at

http://www.garrod.ca/wp-content/uploads/Canadian-FD-Treatment-Guidelines-2017.pdf

Information submitted with requests to support the diagnosis of FD should include:

i) Clinical features associated with FD
ii) Biochemical markers (e.g. alpha-galactosidase activity in plasma or leukocytes, elevated plasma and/or urine biomarkers)
iii) Molecular changes
iv) Pathologic findings (e.g. biopsy results from involved tissues)

[2]Definition of an amenable mutation: mutation that increases activity of alpha galactosidase A in an *in vitro* cell culture system (human embryonic kidney or HEK cells) by 1.2 times the baseline activity with an absolute value for enzyme activity of 3% or greater when compared with wildtype values. You may refer to the following website http://canada.galafoldamenabilitytable.com/?validated=1&redirect=en&hcp=1&licensed=1 or other appropriate supplementary tables to determine amenable α-Gal A mutations to migalastat.

[3]Enzyme replacement therapies (ERT) for Fabry disease (e.g. agalsidase alfa [Replagal, agalsidase beta [Fabrazyme])

Exclusion criteria:

- Individuals who do not have an amenable mutation to miglalastat
- If used concomitantly with an enzyme replacement therapy for FD
- Individuals with severe renal insufficiency (GFR <30 mL/min/1.73m^2)
- Individuals who are pregnant or nursing
- Individuals with poor adherence/compliance to treatment

Migalastat
Brand(s): Galafold
DOSAGE FORM/ STRENGTH: 123 mg capsule

Note: Patients should be monitored every 6 months or more frequently during the first 3 to 5 years of treatment.

Recommended dose: 123 mg every other day

Approval duration: 6 months

Renewal criteria:

Renewals will be considered on a case-by-case basis in individuals who;
- are adherent with treatment; and
- who demonstrate a response while on therapy as compared to baseline results; and
- who have not developed unacceptable toxicities to migalastat; and
- who continue not meet any of the exclusion criteria (see above)

Requests for ongoing reimbursement should include information related to the patient's renal and cardiac function, cerebrovascular events, hospitalizations or emergency room visits for FD-related issues, health related quality of life measures as evaluated through a valid HRQL test (SF-36), gastrointestinal symptoms, pain measures, and other relevant clinical outcomes from treatment. Please address the patient's adherence/compliance with treatment and any adverse effects / toxicities from treatment with migalastat. The Fabry disease expert panel may be consulted for renewal recommendations.

Approval duration of renewals: 1 year

Nusinersen
Brand(s): Spinraza
DOSAGE FORM/ STRENGTH: 2.4 mg/mL – 5mL vial Pk
Effective date: November 20, 2018 and Updated June 12, 2019

For the treatment of spinal muscular atrophy (SMA) in patients meeting all the following criteria:

a) Provides genetic documentation of 5q SMA homozygous gene deletion, homozygous mutation, or compound heterozygote.
b) Patient meets one (1) of the following clinical scenarios:
   - Pre-symptomatic with 2 or 3 copies of the survival motor neuron 2 (SMN2) gene; OR
   - Have had disease duration of less than 6 months, 2 copies of the SMN2 gene, and symptom onset after the first week after birth and on or before 7 months of age; OR
   - Are under the age of 18 with symptom onset after 6 months of age, and never achieved the ability to walk independently.
c) Patient does not require permanent invasive ventilation.
d) Patient is under the care of a specialist experienced in the diagnosis and management of SMA.

In addition, symptomatic Type 2 and 3 patients under the age of 18 regardless of ever achieving the ability to walk independently will be considered on a case by case basis.

Other patients who do not meet the expanded funding criteria may be considered in exceptional cases.

Renewal Criteria:
Renewal of funding will be considered for patients who have not demonstrated any of the Stopping/discontinuation criteria while on therapy.

Stopping/Discontinuation Criteria for Spinraza

These criteria are applicable to patients funded upon meeting either initial or renewal criteria.)

An assessment of the response to therapy should be made prior to the fifth dose or every subsequent dose of Spinraza. Treatment should be discontinued upon meeting any of the following circumstances;

- Patient is not demonstrating/achieving response in motor milestones as assessed using the Hammersmith Infant Neurological Examination (HINE) Section 2, Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP INTEND), or Hammersmith Functional Motor Scale-Expanded (HFMSE), as follows:

Nusinersen
Brand(s): Spinraza
DOSAGE FORM/ STRENGTH: 2.4mg/mL – 5mL Vial Pk

- there is no demonstrated improvement in motor milestone function above pre-treatment scores (as assessed using the HINE Section 2, CHOP INTEND or HFMSE); OR
- there is no demonstrated maintenance of motor milestone function (as assessed using HINE Section 2, CHOP INTEND or HFMSE);

OR

- Patient requires Permanent Invasive Ventilation (PIV)[1]

Exclusion criteria:

a) Patient has SMA type 4
b) Patient has more than four (4) SMN2 gene copies
c) Patient with permanent invasive ventilation (PIV)[1]

[1]Permanent Invasive Ventilation (PIV) is defined as the use of tracheostomy and a ventilator due to progression of SMA that is not due to an identifiable and reversible cause.

Recommended dose:

Loading doses:

12 mg administered intrathecally on days 0, 14, 28 and 58 (Note: 4th loading dose is administered approximately 30 days after the 3rd loading dose)

Maintenance dose:

12 mg administered intrathecally every 4 months starting 4 months after the 4th loading dose.

Approval duration for initial request: 8 months

Approval duration of Renewals: 1 year

Onasemnogene abeparvovec

Brand(s): Zolgensma
DOSAGE FORM/ STRENGTH: 2 x 10^{13} vector genomes (VG)/mL solution for infusion
Effective date: October 29, 2021

For the treatment of spinal muscular atrophy (SMA) in individuals meeting all the following criteria:

1. Diagnosis of SMA is confirmed by genetic documentation of 5q spinal muscular atrophy with biallelic mutations in the survival motor neuron 1 (SMN1) gene; AND
2. Patient is 180 days of age or younger at the time that the treatment is administered; AND
3. Patient is pre-symptomatic or symptomatic with one to three copies of the survival motor neuron 2 (SMN2) gene; AND
4. Patient does not require permanent ventilatory support (invasive or non-invasive)* or a permanent feeding tube; AND
5. Patient must be under the care of a specialist with experience in the diagnosis and management of spinal muscular atrophy.

*Permanent ventilatory support is defined as the need for a tracheostomy or requirement of 16 hours or more of respiratory assistance per day (via non-invasive ventilatory support) for 14 or more consecutive days in the absence of an acute reversible illness excluding perioperative ventilation.

Exclusion Criteria:

1. Reimbursement is limited to one lifetime administration of onasemnogene abeparvovec. Patients who have received a prior dose of onasemnogene abeparvovec accessed by any mechanism (e.g. private insurance plan, clinical trial, compassionate access) will not be funded.
2. Patients with 4 (four) or more copies of SMN2 gene will not be funded.

Notes:

1. Patients must test for the presence of anti-AAV9 antibodies and provide the report of antibody titers. It should be noted that patients with titers above 1:50 will not be funded. Repeat testing results will be considered for newborns suspected of having acquired interim antibodies from maternal transmission.
2. No further treatment with nusinersen or other medications indicated for the treatment of SMA will be considered after the patient has received a dose of onasemnogene abeparvovec.

Dosage recommended: A maximum single lifetime dose of 1.1 x 10^{14} vector genomes (vg)/kg

Renewal of therapy is not considered.

Risdiplam

Brand(s): Evrysdi
DOSAGE FORM/ STRENGTH: 0.75 mg/mL (60 mg/bottle) Pwd for oral or enteral Solution
Effective date: March 28, 2022

Initiation Criteria:

For the treatment of spinal muscular atrophy (SMA) in patients meeting all the following criteria:

1. Genetic documentation of 5q SMA homozygous gene deletion, homozygous mutation, or compound heterozygote; AND
2. Has genetic documentation of 2 or 3 copies of the SMN2 gene; AND
3. Patient is symptomatic; AND
4. Aged between 2 months to 7 months (inclusive) OR Is non-ambulatory and aged 8 months to 25 years (inclusive); AND
5. Patient is under the care of a specialist experienced in the diagnosis and management of SMA.

Discontinuation Criteria:

Treatment should be discontinued upon meeting any of the following circumstances;

- There is no demonstrated achievement in, or maintenance of, motor milestone function as assessed using an age-appropriate measurement after treatment initiation in patients aged between 2 months and 2 years at the time of treatment initiation.
- There is no demonstrated maintenance of motor function (as assessed using an age-appropriate measurement) after treatment initiation in patients aged between 2 years and 25 years at the time of treatment initiation.
- Permanent invasive ventilation is required.

It should be noted that the decision to discontinue reimbursement should be based on 2 assessments separated by no longer than a 12-week interval, with the first evaluation taken close to (i.e. within 3 months) of the date of renewal of funding. The second assessment is only required for patients who demonstrated a decline in motor milestones/motor function at the time of the first evaluation.

Risdiplam

Brand(s): Evrysdi
DOSAGE FORM/ STRENGTH: 0.75 mg/mL (60 mg/bottle) powder for oral or enteral solution

Notes:

1. Patients who meet all the initiation criteria but who are ambulatory may be considered on a case-by-case basis.
2. Patients who are pre-symptomatic or asymptomatic may be considered on a case-by-case basis.
3. Age-appropriate measurements include the Hammersmith Infant Neurological Examination (HINE) Section 2, Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP INTEND), Hammersmith Functional Motor Scale-Expanded (HFMSE), and the Revised Upper Limb Module (RULM) Scores. You may submit the evaluations from more than one age-appropriate test to support your renewal request.
4. Requests to switch from nusinersen to risdiplam and vice versa will be considered on a case-by-case basis for patients who meet inclusion criteria and who have not met discontinuation criteria on their current SMA treatment.

Exclusion criteria:

- Patient with SMA type 4 will not be funded.
- Patient with more than four (4) SMN2 gene copies will not be funded.
- Patient with permanent invasive ventilation (PIV) will not be funded.
- Risdiplam is not funded in patients as combination therapy with nusinersen.
- Risdiplam is not funded in patients who have received onasemnogene abeparvovec.

Renewal criteria:

Renewal of funding will be considered for patients who do not meet any of the exclusion criteria AND who have not demonstrated any of the stopping/discontinuation criteria while on therapy.

Funded Dose: Age and weight appropriate doses of 0.2 mg/kg to 0.25 mg/kg up to a maximum dose of 5 mg daily.

Approval Duration of Initials and Renewals: 12 months

Patisiran

Brand(s): Onpattro
DOSAGE FORM/ STRENGTH: 2 mg/mL injection
Effective date: April 8, 2021

Initiation criteria

For the treatment of polyneuropathy in patients with hereditary transthyretin-mediated amyloidosis (hATTR), meeting all the following criteria:

1. Age 18 years of age or older; AND
2. Has a confirmed genetic diagnosis of hereditary transthyretin-mediated amyloidosis: AND
3. Symptomatic with Polyneuropathy disability stage I to ≤ IIIB or with Familial amyloidotic polyneuropathy stage I or II.
4. Under the care of a specialist with experience in the diagnosis and management of hATTR

Exclusion Criteria:

- Pre-symptomatic patients
- Patients diagnosed with severe heart failure symptoms (defined as New York Heart Association class III or IV).
- Patients who are recipients of a liver transplant
- Patients who will be using patisiran in combination with other interfering ribonucleic acid drugs or transthyretin stabilizers used to treat hATTR.

Discontinuation criteria:

Treatment with patisiran will be discontinued for patients who are:

- Permanently bedridden and dependent on assistance for basic activities of daily living, or
- Receiving end-of-life/palliative care where survival of less than one year is expected.

Renewal Criteria:
Renewal of funding will be considered if patients do not meet the discontinuation criteria.

Dosage: 0.3 mg/kg IV once every three weeks, with a maximum dose of 30 mg for patients who weigh 100 kg or greater.

Patients should be assessed after **9** months of treatment and then every six months thereafter.

Duration of Approval of initiation requests: 10 months
Duration of Approval of first renewal: 6 months
Duration of Approval of 2nd and subsequent renewals: 1 year

Notes to Prescribers:

- Laboratory documentation for the genetic mutation for hATTR must be included with the application.
- Signs and symptoms of polyneuropathy should be listed.
- In your application please list all drugs that the patient is using including whether he/she is using any of the following: Diflunisal, Inotersen, Tafamidis
- Confirmation that the patient does not meet each of the listed exclusions must be provided on the request.

Patisiran
Brand(s): Onpattro
DOSAGE FORM/ STRENGTH: 2 mg/mL Injection

Definitions:

Familial Amyloid Polyneuropathy (FAP) stage: Clinical staging system for the neuropathy symptoms of hATTR (formerly termed familial amyloid neuropathy).

- FAP Stage 1: Walking without assistance, mild neuropathy (sensory, autonomic, and motor) in lower limbs
- FAP Stage 2: Walking with assistance, moderate impairment in lower limbs, trunk, and upper limbs
- FAP Stage 3: wheelchair or bed-ridden, severe neuropathy

Polyneuropathy disability score (PND): A five-stage measure of neuropathy impairment ranging from 0 (no impairment) to 4 (confined to a wheelchair or bedridden).

- Stage 0: no impairment
- Stage I: sensory disturbances but preserved walking capability
- Stage II: impaired walking capability but ability to walk without a stick or crutches
- Stage IIIA: walking only with the help of one stick or crutch
- Stage IIIB: walking with the help of two sticks or crutches
- Stage IV: confined to a wheelchair or bedridden

Pegvisomant
Brand(s): Somavert
DOSAGE FORM/ STRENGTH: 10 mg, 15 mg, 20 mg, 25 mg, 30 mg for sc Injection

Initiation Criteria:

For the treatment of patients with proven acromegaly who meet the following criteria;

1. Active disease as indicated by GH concentration following an oral glucose tolerance test of >1 ug/L;AND

2. Failed pituitary surgery or pituitary surgery is not possible[1]; AND

3. After a failed 6 month trial of a somatostatin analogue[2] (Failure is defined as IGF-1 levels more than 25% above upper limits of age-adjusted normal range.)

4. Treatment should be supervised by an endocrinologist.

Note: Maximum daily dose of 30mg of Pegvisomant will be approved.

Approval Duration: 1 year

Renewal Criteria:

Patient has been able to tolerate the medication (i.e. no significant adverse effects) and there is objective evidence of response to therapy demonstrated by:

1. Normalization of IGF-1 level; AND

2. Improvement in the patient's symptoms and/or co-morbid complications; AND

3. No progression of pituitary tumour

Note: Maximum daily dose of 30mg of Pegvisomant will be approved. The approval letter will include a note to consider once weekly dosing.

Approval Duration: 1 year

[1]Surgery may not be appropriate in some patients due to technical reasons or due to unstable co-morbid conditions. The requesting physician should provide documentation (i.e. surgical consultation notes). Patients with acromegaly due to non-pituitary tumours will also be considered for reimbursement using the above criteria.

[2]Patient must have documented intolerance to the maximal dose and/or have failed to achieve normalization of age-adjusted IGF-1 levels from treatment with maximal dose.

Sapropterin

Brand(s): Kuvan
DOSAGE FORM/ STRENGTH: 100 mg tablet
Effective date: February 20, 2013; Updated December 2, 2020

Ongoing funding of sapropterin (Kuvan) will be considered through the EAP for non-pregnant patients and patients actively planning pregnancy who have a diagnosis of Phenylketonuria(PKU) and who have demonstrated a response to the initial 6 month trial of sapropterin [generally reimbursed through the Biomarin, the manufacturer of Kuvan].

Initial Criteria for the Trial Period (First 6 months)

For the management of patients with the diagnosis of hyperphenylalaninemia (HPA) due to tetrahydrobiopterin (BH4)-responsive phenylketonuria (PKU) who meet **ALL** of the following criteria:

1. Diagnosis of PKU confirmed through an approved test.
2. Compliance with low protein diet and formulas.
3. Documented baseline blood phenylalanine (Phe) levels, which have been measured at least twice during a 3 to 6 month period, are greater than 360 µmol/L despite compliance with a low protein diet;
4. Baseline protein intake assessment by a dietitian. Ability to comply with their medication regimen
5. Managed by a prescriber specialized in metabolic/ biochemical diseases.
6. the Patient's blood Phe tolerance levels will be documented at months 1 to 2 and 4 to 6 during the Trial Period.

Modified Criteria for Pregnant Patients during the 6 month trial period:

1. Patient has a diagnosis of PKU confirmed through an approved test

2. Patient's treatment is being managed by a prescriber specialized in metabolic/biochemical diseases; and

3. Patient's baseline blood Phe level is greater than 360 µmol/L despite compliance with all recommendations for dietary intervention and monitoring or compliance with a low protein diet.

In the case of Patients who are eligible for but do not utilize the Patient support program for a 185-day or 6-month trial. Executive Officer will approve a request to reimburse claims for Kuvan at a dosage of up to 20mg/kg per day for the trial period of up to 6 months provided that the above conditions are met.

Sapropterin
Brand(s): Kuvan
DOSAGE FORM/ STRENGTH: 100 mg tablet

Approval Duration: 6 months

Funding Criteria for Kuvan in the Post Trial Period: Patients must have demonstrated the response as per the trial criteria to be funded following the 6 month trial period.

Initial Criteria Post Trial:

For the management of patients with the diagnosis of hyperphenylalaninemia (HPA) due to tetrahydrobiopterin (BH4)-responsive phenylketonuria (PKU) who meet **ALL** of the following criteria:

1. Compliance with low protein diet, formulas, and Kuvan; AND

2. During the 6 month trial period under EAP or PSP patient has achieved one of more of the following:

    i) a demonstrated response to the Kuvan responsiveness test or PKU clinical protocol, based on the following information:

    ii) the clinic's definition for response; and

    iii) all relevant laboratory results used to determine that the Patient was a responder to Kuvan

3. Patient meets one of the following:

    i) normal sustained Blood Phe levels [> 120 µmol/L and < 360 µmol/L] (At least 2 levels measured at least 1 month apart); OR
    ii) sustained blood Phe reduction of at least 30% (At least 2 levels measured at least 1 month apart)compared to baseline if the Phe baseline level is < 1200 µmol/L*;* OR
    iii) sustained blood Phe reduction of at least 50% (At least 2 levels measured at least 1 month apart) compared to baseline if the Phe baseline level is > 1200 µmol/L;

4. Demonstrated an increase in dietary protein tolerance based on targets set between the clinician and patient

5. Managed by a prescriber specialized in metabolic/ biochemical diseases.

Dosage: Up to a maximum of 20 mg/kg per day

Approval Duration: 1 year

Sapropterin
Brand(s): Kuvan
DOSAGE FORM/ STRENGTH: 100 mg tablet

Renewal Criteria:

Renewals will be considered for patients meeting the following criteria:
1. Demonstrates ongoing response to treatment; AND
2. Complies with and will continue to comply with a low protein diet, formulas, and treatment with Kuvan; AND
3. the request for extended coverage includes a recent follow-up from a prescriber specialized in metabolic/biochemical diseases.

Exclusion Criteria for both Initial (Trial and Post Trial period) and Renewal criteria: (Patients meeting any of the following criteria will not be funded)
- the Patient is not on a low protein diet or is not compliant with their low protein diet; or
- the Patient has a baseline blood PHe level less than 360 µmol/L prior to initiating therapy with Kuvan.

Dosage: Up to a maximum of 20 mg/kg per day

Approval Duration: 1 year

Sebelipase alfa
Brand(s): Kanuma
DOSAGE FORM/ STRENGTH: 2 mg/mL solution
Effective date: April 8, 2021

Initiation Criteria:

For the treatment of lysosomal acid lipase (LAL) deficiency in patients meeting ALL the following criteria:

- Has documented biochemical evidence of deficient LAL activity; AND
- Has two documented pathogenic mutations in the LIPA gene; AND
- Is under the care of a specialist with experience in the diagnosis and management of LAL deficiency; AND
- The onset of clinical manifestations of LAL deficiency occurred before six months of age;

  OR

  Patient is six months of age or older; AND
  - Presents with one or more of the following:
    - Persistently elevated transaminases (Alanine aminotransferase (ALT) > 1.5 x ULN[1] or Aspartate transaminase (AST) > 1.5 x ULN[1]) as measured by two assessments three to six months apart
    - Persistent dyslipidemia (Low-density lipoprotein cholesterol (LDL-C) and/or Triglycerides (TG) values in the top 5th percentile based on sex and age) as measured by two assessments three to six months apart
    - Any documented hepatomegaly or hepatosplenomegaly
    - Liver fibrosis confirmed by biopsy
    - Failure to thrive
    - Growth impairment[2]
    - Evidence of intestinal affection and/or malabsorption;

    AND
  - Does not present with any of the following:
    - Increased portal vein pressures, or de novo evidence of portal hypertension on ultrasound and Doppler, or new clinical presentation of portal hypertension (e.g., esophageal varices); OR
    - Severe hepatic dysfunction (Child-Pugh Class C); OR
    - End-stage liver disease.

NOTE: The requesting prescriber must provide baseline values for the following clinical components before starting sebilipase alfa; Bloodwork for ALT, AST, liver fibrosis, growth curve, spleen and liver volume/sizes, portal vein pressures, patient's age, weight, and height.

Discontinuation Criteria:

Reimbursement will be discontinued in patients who have experienced adverse events from sebelipase alfa (particularly hypersensitivity reactions, including anaphylaxis, hypotension, or fever), which cannot be managed with standard treatment, and/or which have a significant impact on the patient's quality of life, or are life-threatening.

Sebelipase alfa
Brand(s): Kanuma
DOSAGE FORM/ STRENGTH: 2 mg/mL solution

For patients with onset of clinical manifestations of LAL deficiency at six months of age and older, reimbursement will be discontinued if:

- Patient has progressed to end-stage liver failure or multi-organ failure; OR
- Patient has at least three out of the five following response components compared with baseline values after 12 months of therapy:
    1. Less than 10% improvement in ALT or AST
    2. Worsening of liver fibrosis confirmed by biopsy
    3. Persisting growth impairment[2] despite sebelipase alfa therapy and nutritional interventions
    4. At least a 15% increase in spleen volume and/or greater than 15% increase in liver volume on ultrasound
    5. Increased portal vein pressures, or de novo evidence of portal hypertension on ultrasound and Doppler, or new presentation of portal hypertension (e.g. esophageal varices)

[1] Based on age- and sex-specific normal values for ALT and AST

[2] Growth impairment is defined as decreased body weight across at least two of the major centiles on a World Health Organization (WHO) weight-for-age chart, or body weight below 10th centile and no weight gain within two weeks and/or decreased height across at least two of the major centiles on a WHO height-for-age chart (URLs: https://www.who.int/toolkits/child-growth-standards/standards/weight-for-age, https://www.who.int/toolkits/child-growth-standards/standards/length-height-for-age)

Exclusion Criteria: Patients with severe liver disease and/or those who have progressed to end stage liver disease.

Renewal Criteria: Renewals will be considered in patients who do not meet the discontinuation criteria.

Recommended dose:

For patients with onset of clinical manifestations of LAL deficiency before six months of age:

1mg/kg administered as an intravenous infusion once weekly. Based on clinical response, dose increase to 3mg/kg may be considered.

For patients with onset of clinical manifestations of LAL deficiency at six months of age or older:

1mg/kg administered as an intravenous infusion once every other week.

Approval duration of initials and renewals: 12 months initial, 6 months renewal

Somatrogon
Brand(s): Ngenla
DOSAGE FORM/ STRENGTH: 24 mg/1.2mL, 60 mg/1.2 mL (Prefilled Pens)
Effective date: May 15, 2023

Initiation Criteria:

For the treatment of pediatric patients with growth failure due to an inadequate secretion of endogenous growth hormone (i.e. growth hormone deficiency (GHD)) who meet all the following criteria;

1. Patient is pre-pubertal and aged 3 years or older; AND
2. Epiphyseal growth plates have not closed/fused; AND
3. Bone age is less than 16 years for a male and 14 years for a female; AND
4. Diagnosed with isolated growth hormone deficiency OR growth hormone insufficiency as part of multiple pituitary hormone deficiency; AND
5. Patient is under the care of a pediatric endocrinologist.

Notes:

1. Bone age assessments may be based on the Greulich Pyle Atlas, Tanner-Whitehouse, or other appropriate methods of assessments. A copy of the bone age report and other supporting documentation must be provided.
2. Case-by-case consideration will be provided for patients who are on another recombinant growth hormone therapy (i.e. somatropin) and wish to switch to somatrogon if initiation criteria are met, and discontinuation and exclusion criteria are not met. Please include the reason(s) for the switch in treatment.
3. Treatment response should be assessed every 3 to 4 months in younger children, every 6 months in elementary school-aged children, and every 4 to 6 months in pubertal aged children.
4. An inadequate response after the initiation of somatrogon in patients with GHD is often defined by one or more of the following criteria: a change in height velocity of less than 2 cm per year, a height velocity standard deviation score (SDS) of less than 0, or a change in height SDS of less than 0.3 per year during the first 6 months to 12 months of therapy.
5. Patients who are not adherent to therapy should be discontinued.

Somatragon
Brand(s): Ngenla
DOSAGE FORM/ STRENGTH: 24mg/1.2mL, 60mg/1.2 mL (Prefilled pen)

Discontinuation criteria:

Somatrogon must be discontinued upon the occurrence of any of the following;

- The change in height velocity is less than 2 cm per year on treatment and bone age is more than 16 years in males and 14 years in females
- Closure of the epiphyseal growth plates

Renewal criteria:

Renewals will be considered in patients who continues to respond to therapy, and who do not meet any of the discontinuation criteria or the exclusion criteria.

Exclusion criteria:

1. Patients with closed/fused epiphyseal growth plates.
2. Patients with active malignancy
3. Patients who do not have isolated growth hormone deficiency or growth hormone insufficiency as part of multiple pituitary hormone deficiency but have other medical or genetic conditions in which recombinant growth hormone therapies are used (e.g. chronic renal failure, Turner syndrome, idiopathic short stature, Prader-Willi syndrome, or adult-onset growth hormone deficiency).

Approved dosage: 0.66 mg per kg administered subcutaneously once weekly adjusted based on growth velocity, body weight, and serum insulin-lie growth factor 1 concentrations.

Approval duration for initial and renewal requests: 1 year

Tafamidis Meglumine / Tafamidis

Brand(s): Vyndaqel (Added May 12, 2021), Vyndamax (Added September 15, 2022)
DOSAGE FORM/ STRENGTH: 20 mg capsule (Vyndaqel), 61 mg capsule (Vyndamax)
Updated September 15, 2022

Initiation criteria

For the treatment of adult patients with cardiomyopathy due to transthyretin (TTR)-mediated amyloidosis in patients meeting the following criteria:

1. Patient has documented cardiac disease due to wild-type or hereditary TTR-mediated amyloidosis cardiomyopathy (ATTR-CM)

   i) Documented wild-type ATTR-CM consists of all of the following:
   - absence of a variant TTR genotype;
   - evidence of cardiac involvement by echocardiography with end-diastolic interventricular septal wall thickness >12 mm;
   - positive findings on technetium-99m pyrophosphate (Tc-99m-PYP) scintigraphy with single-photon emission computed tomography (SPECT) scanning
     OR
     presence of amyloid deposits in biopsy tissue[1] (fat aspirate, salivary gland, median nerve connection tissue sheath, or cardiac) and TTR precursor protein identification by immunohistochemistry, scintigraphy, or mass spectrometry.

   ii) Documented hereditary ATTR-CM consists of all of the following:
   - presence of a variant TTR genotype associated with cardiomyopathy and presenting with a cardiomyopathy phenotype;
   - evidence of cardiac involvement by echocardiography with end-diastolic interventricular septal wall thickness greater than12 mm;
   - positive findings on Tc-99m-PYP scintigraphy with SPECT scanning OR presence of amyloid deposits in biopsy tissue[1] (fat aspirate, salivary gland, median nerve connective tissue sheath, or cardiac)

2. Patient with New York heart Association (NYHA) class I to III

3. History of heart failure, defined as at least one prior hospitalization for heart failure or clinical evidence of heart failure that required treatment with a diuretic.

4. Request is from a prescriber with experience in the diagnosis and management of ATTR-CM.

[1]A biopsy is required if results from the Tc-99m-PYP scintigraphy are equivocal, unavailable or clinical suspicion remains high despite negative results.

Tafamidis

Brand(s): Vyndaqel, Vyndamax
DOSAGE FORM/ STRENGTH: 20 mg capsule (Vyndaqel), 61 mg capsule (Vyndamax)

Exclusion criteria:

Patients meeting one or more of the following will not be eligible for funding:

- Patients who have received a heart or liver transplant
- Patients with an implanted cardiac mechanical assist device (CMAD)
- Patients being treated with other disease-modifying treatments for ATTR
- Patients with NYHA Class IV

Discontinuation criteria:

Treatment with tafamidis will not be funded upon meeting one or more of the following discontinuation criteria:

- Patients who progress to NYHA Class IV
- Patients who receive a heart or liver transplant
- Patient who receive an implanted CMAD

Renewal criteria:

Renewals will be considered in patients who do not meet the discontinuation criteria.

Recommended dose:

Vyndaqel: 80 mg (administered as four 20 mg capsules) taken orally, once daily, with or without food. Dose may be adjusted to a dose of 20 mg if not tolerated.

Vyndamax: 61 mg taken orally once daily, with or without food

Note that Vyndaqel (tafamidis meglumine) capsules and Vyndamax (tafamidis) capsules are different formulations with the active moiety tafamidis and are not interchangeable. To avoid dosing errors, it is important that prescriptions of tafamidis/tafamidis meglumine specify the salt form and the prescribed dose.

Initial approval duration: 6 months

First renewal duration: 6 months

Second and subsequent renewal duration: 1 year

Triheptanoin
Brand(s): Dojolvi
DOSAGE FORM/ STRENGTH: 100% w/w oral liquid
Effective date: July 27, 2023

Initiation Criteria:

As a source of calories and fatty acids for the treatment of patients with long-chain fatty acid oxidation disorders (LC-FAOD) who meet the following criteria:

1. Patient presents with one or more acute life-threatening events consistent with LC-FAOD; AND
2. Patient meets one of the following circumstances;
   i) Triheptanoin is being used as second or subsequent line therapy in a patient who has a confirmed diagnosis of one of the types of LC-FAOD (Note 1) who is being treated with a less costly therapy with conventional even-chain MCT oil (e.g. trioctanoin) (Note 3) but is experiencing an inadequate response and requires alternative therapy to conventional even-chain medium-chain triglyceride (MCT) supplementation,

   OR

   ii) Triheptanoin is being initiated as first line therapy in a patient who has a confirmed diagnosis of one of the types of LC-FAOD (Note 1) who is presenting with acute life-threatening events of LC-FAOD,

   OR

   iii) Triheptanoin is being used as first line therapy in a patient who presents with acute life-threatening events consistent with a LC-FAOD but who does not have a confirmed diagnosis of LC-FAOD (Note 2);

   AND
3. Patient is under the care of a clinician experienced in the management of LC-FAOD

Notes:

1. Provide documentation of genetic, biochemical, molecular, and clinical findings and investigations used to support the type of LC-FAOD diagnosis and the severity of the symptoms impacting the affected organ systems.

   Request applications should include newborn testing results including genetic testing results as available and applicable (e.g. mutations in CPT1A, SLC25A20, CPT2, ACADVL, HADHA, HADHB genes) and may include the following to support the initiation criteria:

- transaminase levels
- creatine kinase
- plasma total and free carnitine

Triheptanoin
Brand(s): Dojolvi
DOSAGE FORM/ STRENGTH: 100% w/w oral liquid

- plasma acylcarnitine profile
- urine organic acids
- urine acylglycines
- glucose and ketone patterns
- ammonia levels
- organ systems impacted and severity, frequency, and duration of events
- treatments used for LC-FAOD including the name, doses, and duration of use of conventional even-chain MCT oils, carnitine (as applicable), and information related to dietary measures to manage the condition.

  Requests with a confirmed diagnosis should specify the type of LC-FAOD diagnosis and renewal requests initiated without a confirmed diagnosis should specify the type of LC-FAOD when the diagnosis is confirmed at the time of renewal:

  i) Carnitine palmitoyltransferase 1 A deficiency (CPT1A)
  ii) Carnitine palmitoyltransferase 2 deficiency (CPT 2)
  iii) Carnitine-acylcarnitine translocase (CACT) deficiency
  iv) Very long-chain acyl-coenzyme A dehydrogenase (VLCAD) deficiency
  v) Long-chain 3-hydroxyacyl-coenzyme A dehydrogenase (LCHAD) deficiency
  vi) Trifunctional protein (TFP) deficiency

2. Requests should specify the acute life-threatening events that the patient presents with that are consistent with LC-FAOD and include clinical and biochemical findings of impacted organ systems which support warranted triheptanoin initiation. Consult notes may be provided.
3. Please refer to Ontario's Inherited Metabolic diseases (IMD) program for funding of conventional MCT oil in Ontario. (https://www.health.gov.on.ca/en/pro/programs/drugs/funded_drug/fund_inherited_drug.aspx)
4. Requests for patients who were using therapy with conventional even-chain MCT oil (e.g., trioctanoin) should include information related to adherence and optimization on conventional even-chain MCT oil at the time of symptom presentation.

Triheptanoin
Brand(s): Dojolvi
DOSAGE FORM/ STRENGTH: 100% w/w oral liquid

Exclusion Criteria:

1. Triheptanoin is not funded in combination with conventional even-chain medium-chain triglyceride (MCT) oil.
2. Triheptanoin will not be funded as initial first line or subsequent line therapy after conventional even-chain MCT oil in asymptomatic patients with a confirmed diagnosis of LC-FAOD.

Approval duration for initial requests for patients with a confirmed diagnosis of LC-FAOD: 1 year

Approval duration for initial requests for patients without a confirmed diagnosis of LC-FAOD: 7 months

Renewal Criteria:

Renewals will be considered for patients meeting ALL the following criteria:

1. Patient continues to be under the care of a clinician experienced in the management of LC-FAOD
2. Patient who was initiated on triheptanoin without a confirmed diagnosis of LC-FAOD has subsequently received a confirmed diagnosis established by a specialist in metabolic diseases experienced in the treatment and management of LC-FAOD with the type of LC-FAOD specified and the genetic and other findings provided to confirm the diagnosis.
3. Patient is optimized on, and adherent to, appropriate dietary management. (Note: Please provide reasons and management plan if this criterion is not met.)
4. Patient continues to benefit from triheptanoin therapy.

   Note that patients who were started on triheptanoin as first line for acute life-threatening events based on meeting the above criteria and who did not have a prior use of a less costly even-chained MCT oil, are to be transitioned to conventional even-chain MCT oil within a year of initiating treatment with Dojolvi. If this is not considered to be appropriate, prescribers should provide rationale as to why this is not warranted for case-by-case review.

Approval duration for renewals: 1 year

Recommended dosage: Daily dosage of up to 35% of the patient's total prescribed daily caloric intake (DCI) divided into at least four doses. Treatment should be individualized based on disease presentation and other clinical findings.

Vutrisiran

Brand(s): Amvuttra
DOSAGE FORM/ STRENGTH: 25 mg/0.5 mL prefilled syringe
Effective date: December 13, 2024

Initiation criteria:

For the treatment of patients with hereditary transthyretin-mediated amyloidosis with polyneuropathy (hATTR-PN), meeting all the following criteria:

1. Age 18 years of age or older; AND
2. Has a confirmed genetic diagnosis of hereditary transthyretin-mediated amyloidosis: AND
3. Symptomatic with Polyneuropathy disability stage I to ≤ IIIB or with Familial amyloidotic polyneuropathy stage I or II.
4. Under the care of a specialist with experience in the diagnosis and management of hATTR-PN

Exclusion Criteria:

- Pre-symptomatic patients.
- Patients diagnosed with severe heart failure symptoms (defined as New York Heart Association class III or IV).
- Patients who are recipients of a liver transplant.
- Patients who will be using vutrisiran in combination with other interfering ribonucleic acid drugs or transthyretin stabilizers used to treat hATTR.

Discontinuation criteria:

Treatment with vutrisiran will be discontinued for patients who are:

- Permanently bedridden and dependent on assistance for basic activities of daily living, or
- Receiving end-of-life/palliative care where survival of less than one year is expected.

Renewal Criteria:

Renewal of funding will be considered if patients do not meet the discontinuation criteria.

Vutrisiran

Brand(s): Amvuttra
DOSAGE FORM/ STRENGTH: 25 mg/0.5 mL Prefilled Syringe

Dosage:

25 mg injected subcutaneously once every 3 months.

Patients should be assessed after **9** months of treatment and then every six months thereafter.

Duration of Approval of initiation requests: 10 months

Duration of Approval of first renewal: 6 months

Duration of Approval of 2nd and subsequent renewals: 1 year

Notes to Prescribers:

- Laboratory documentation for the genetic mutation for hATTR must be included with the application.
- Signs and symptoms of polyneuropathy should be listed.
- In your application please list all drugs that the patient is using including whether he/she is using any of the following: Diflunisal, Inotersen, Patisiran, Tafamidis
- Confirmation that the patient does not meet each of the listed exclusions must be provided on the request.

Definitions:

Familial Amyloid Polyneuropathy (FAP) stage: Clinical staging system for the neuropathy symptoms of hATTR (formerly termed familial amyloid neuropathy).

- FAP Stage 1: Walking without assistance, mild neuropathy (sensory, autonomic, and motor) in lower limbs
- FAP Stage 2: Walking with assistance, moderate impairment in lower limbs, trunk, and upper limbs
- FAP Stage 3: wheelchair or bed-ridden, severe neuropathy

Polyneuropathy disability score (PND): A five-stage measure of neuropathy impairment ranging from 0 (no impairment) to 4 (confined to a wheelchair or bedridden).

- Stage 0: no impairment
- Stage I: sensory disturbances but preserved walking capability
- Stage II: impaired walking capability but ability to walk without a stick or crutches
- Stage IIIA: walking only with the help of one stick or crutch
- Stage IIIB: walking with the help of two sticks or crutches
- Stage IV: confined to a wheelchair or bedridden

MIGRAINE DRUGS

Atogepant

Brand(s): Qulipta
DOSAGE FORM/ STRENGTH: 10 mg, 30 mg, 60 mg tablets
Effective date: December 11, 2023 (episodic migraines)
Updated; December 12, 2024 (add chronic migraine)

Initiation Criteria

For the prophylaxis of headaches in adults meeting the following criteria:

1. The patient has a diagnosis of either episodic or chronic migraine according to the International Headache Society criteria, defined as:

    a. Episodic migraine: < 15 headache days per month for more than 3 months, of which ≥ 4 days per month are with migraine
    b. Chronic migraine: ≥ 15 headache days per month for more than 3 months, of which ≥ 8 days per month are with migraine.

    AND
2. The patient has experienced an inadequate response[1], intolerance, or contraindication to 2 or more oral prophylactic migraine medications[2]; AND
3. Atogepant is not used in combination with onabotulinum toxin A or another Calcitonin gene-related peptide (CGRP) receptor antagonist; AND
4. Request must be provided by a physician or nurse practitioner with experience in the management of migraine headaches.

[1]*Inadequate response* is defined as no therapeutic or unsatisfactory effect (< 30% reduction in frequency of headache days) to an adequate dose and duration of 2 oral prophylactic medications[2] where both medications must be of different types/classes.

Contraindication or intolerable side effects necessitating discontinuation will be considered for 1 of the 2 drugs only.

[2]Oral prophylactic therapy types/classes to be considered include:

- Beta blockers
- Tricyclic antidepressants
- Verapamil or flunarizine
- Sodium valproate (or divalproex sodium)
- Topiramate
- Gabapentin

Atogepant
Brand(s): Qulipta
DOSAGE FORM/ STRENGTH: 10 mg, 30 mg, 60 mg tablets

Initial requests should contain the following information:

- Objective measures of baseline migraine headache days (e.g. headache diary) and/or baseline disability measures (i.e. Six-Item Headache Impact Test [HIT-6] score).
- List of previously trialed oral prophylactic medications, including dosing regimen, duration of treatment, treatment response and reasons for discontinuation.
- Confirmation that the patient is under the care of a physician or nurse practitioner with experience in the management of migraine headaches.

Renewal criteria

Objective evidence demonstrating that the patient has achieved or maintained an adequate treatment response, defined as:

- A reduction of at least 50% in the frequency of migraine headache days per month compared with baseline; **OR**
- A reduction of at least 30% in the frequency of migraine headache days per month compared with baseline AND an improvement of greater than or same as 5 points in the HIT-6 score compared with baseline.

Renewal requests should contain the following information:

- Outcome measures (i.e. headache diary, HIT-6 score) of the patient's response to atogepant therapy.

Approved dosage: up to a dose of 60 mg daily.

Duration of Approval of Initials and Renewals: 6 months

Eptinezumab
Brand(s): Vyepti
DOSAGE FORM/ STRENGTH: 100 mg/mL, 300 mg/3mL Vial for Injection
Effective date: August 4, 2023 Updated: October 29, 2024 (new dosage format)

Initiation Criteria

For the prophylaxis of headaches in adults meeting the following criteria:

1. The patient has a diagnosis of either episodic or chronic migraine according to the International Headache Society criteria, defined as:

    a. Episodic migraine: < 15 headache days per month for more than 3 months, of which ≥ 4 days per month are with migraine
    b. Chronic migraine: ≥ 15 headache days per month for more than 3 months, of which ≥ 8 days per month are with migraine.

    AND
2. The patient has experienced an inadequate response[1], intolerance, or contraindication to 2 or more oral prophylactic migraine medications[2]; AND
3. Eptinezumab is not used in combination with onabotulinum toxin A or another Calcitonin gene-related peptide (CGRP) receptor antagonist; AND
4. Request must be provided by a physician or nurse practitioner with experience in the management of migraine headaches.

[1]*Inadequate response* is defined as no therapeutic or unsatisfactory effect (< 30% reduction in frequency of headache days) to an adequate dose and duration of 2 oral prophylactic medications[2] where both medications must be of different types/classes.

Contraindication or intolerable side effects necessitating discontinuation will be considered for 1 of the 2 drugs only.

[2]Oral prophylactic therapy types/classes to be considered include:

- Beta blockers
- Tricyclic antidepressants
- Verapamil or flunarizine
- Sodium valproate (or divalproex sodium)
- Topiramate
- Gabapentin

Initial requests should contain the following information:

- Objective measures of baseline migraine headache days (e.g. headache diary) and/or baseline disability measures (i.e. Six-Item Headache Impact Test [HIT-6] score).

Eptinezumab
Brand(s): Vyepti
DOSAGE FORM/ STRENGTH: 100 mg/mL injection solution

- List of previously trialed oral prophylactic medications, including dosing regimen, duration of treatment, treatment response and reasons for discontinuation.
- Confirmation that the patient is under the care of a physician or nurse practitioner with experience in the management of migraine headaches

Renewal criteria

Objective evidence demonstrating that the patient has achieved or maintained an adequate treatment response, defined as:

1. A reduction of ≥ 50% in frequency of migraine headache days per month compared with baseline; **OR**
2. A reduction of ≥ 30% in frequency of migraine headache days per month compared with baseline AND an improvement of ≥ 5 points in the HIT-6 score compared with baseline.

Renewal requests should contain the following information:

- Outcome measures (i.e. headache diary, HIT-6 score) of the patient's response to epitinezumab therapy.

Approved dosage: 100 mg every 12 weeks IV up to 300 mg every 12 weeks

Duration of Approval of Initials and Renewals: 6 months

Fremanezumab
Brand(s): Ajovy
DOSAGE FORM/ STRENGTH: 225 mg/1.5 mL prefilled syringe (PFS)
Effective date: March 3, 2022

Initiation Criteria

For the **prophylaxis of headaches** in adults meeting the following criteria:

5. The patient has a diagnosis of either episodic or chronic migraine according to the International Headache Society criteria, defined as:

    a. Episodic migraine: < 15 headache days per month for more than 3 months, of which ≥ 4 days per month are with migraine
    b. Chronic migraine: ≥ 15 headache days per month for more than 3 months, of which ≥ 8 days per month are with migraine.

    AND
6. The patient has experienced an inadequate response[1], intolerance, or contraindication to 2 or more oral prophylactic migraine medications[2]; AND
7. Fremanezumab is not used in combination with onabotulinum toxin A or another Calcitonin gene-related peptide (CGRP) receptor antagonist; AND
8. Request must be provided by a physician or nurse practitioner with experience in the management of migraine headaches.

[1]*Inadequate response* is defined as no therapeutic or unsatisfactory effect (< 30% reduction in frequency of headache days) to an adequate dose and duration of 2 oral prophylactic medications[2] where both medications must be of different types/classes.

Contraindication or intolerable side effects necessitating discontinuation will be considered for 1 of the 2 drugs only.

[2]Oral prophylactic therapy types/classes to be considered include:
- Beta blockers
- Tricyclic antidepressants
- Verapamil or flunarizine
- Sodium valproate (or divalproex sodium)
- Topiramate
- Gabapentin

Initial requests should contain the following information:

- Objective measures of baseline migraine headache days (e.g. headache diary) and/or baseline disability measures (i.e. Six-Item Headache Impact Test [HIT-6] score).

Fremanezumab
Brand(s): Ajovy
DOSAGE FORM/ STRENGTH: 225 mg/1.5mL Prefilled syringe (PFS)

- List of previously trialed oral prophylactic medications, including dosing regimen, duration of treatment, treatment response and reasons for discontinuation.

- Confirmation that the patient is under the care of a physician or nurse practitioner with experience in the management of migraine headaches.

Dosing: As per product monograph

Duration of Approval: 6 months

Renewal criteria

Objective evidence demonstrating that the patient has achieved or maintained an adequate treatment response , defined as:

- A reduction of ≥ 50% in frequency of migraine headache days per month compared with baseline; **OR**
- A reduction of ≥ 30% in frequency of migraine headache days per month compared with baseline AND an improvement of ≥ 5 points in the HIT-6 score compared with baseline.

Renewal requests should contain the following information:

- Outcome measures (i.e. headache diary, HIT-6 score) of the patient's response to fremanezumab therapy.

Dosing: As per product monograph

Duration of Approval: 6 months

Galcanezumab
Brand(s): Emgality
DOSAGE FORM/ STRENGTH: 120 mg/mL Prefilled syringe (PFS) and Prefilled pen
Effective date: December 1, 2022

Initiation Criteria

For the prophylaxis of headaches in adults meeting the following criteria:

1. The patient has a diagnosis of either episodic or chronic migraine according to the International Headache Society criteria, defined as:
    a. Episodic migraine: < 15 headache days per month for more than 3 months, of which ≥ 4 days per month are with migraine
    b. Chronic migraine: ≥ 15 headache days per month for more than 3 months, of which ≥ 8 days per month are with migraine.

    AND
2. The patient has experienced an inadequate response[1], intolerance, or contraindication to 2 or more oral prophylactic migraine medications[2]; AND
3. Galcanezumab is not used in combination with onabotulinum toxin A or another Calcitonin gene-related peptide (CGRP) receptor antagonist; AND
4. Request must be provided by a physician or nurse practitioner with experience in the management of migraine headaches.

[1]*Inadequate response* is defined as no therapeutic or unsatisfactory effect (< 30% reduction in frequency of headache days) to an adequate dose and duration of 2 oral prophylactic medications[2] where both medications must be of different types/classes.

Contraindication or intolerable side effects necessitating discontinuation will be considered for 1 of the 2 drugs only.

[2]Oral prophylactic therapy types/classes to be considered include:

- Beta blockers
- Tricyclic antidepressants
- Verapamil or flunarizine
- Sodium valproate (or divalproex sodium)
- Topiramate
- Gabapentin

Initial requests should contain the following information:

- Objective measures of baseline migraine headache days (e.g. headache diary) and/or baseline disability measures (i.e. Six-Item Headache Impact Test [HIT-6] score).
- List of previously trialed oral prophylactic medications, including dosing regimen, duration of treatment, treatment response and reasons for discontinuation.
- Confirmation that the patient is under the care of a physician or nurse practitioner with experience in the management of migraine headaches.

Galcanezumab
Brand(s): Emgality
DOSAGE FORM/ STRENGTH: 120 mg/mL Prefilled syringe (PFS) and Prefilled Pen

Dosing: As per product monograph

Duration of Approval: 6 months

Renewal criteria

Objective evidence demonstrating that the patient has achieved or maintained an adequate treatment response, defined as:

- A reduction of ≥ 50% in frequency of migraine headache days per month compared with baseline; **OR**
- A reduction of ≥ 30% in frequency of migraine headache days per month compared with baseline AND an improvement of ≥ 5 points in the HIT-6 score compared with baseline.

Renewal requests should contain the following information:

- Outcome measures (i.e. headache diary, HIT-6 score) of the patient's response to Galcanezumab therapy.

Dosing: As per product monograph

Duration of Approval: 6 months

Onabotulinum Toxin A
Brand(s): Botox
DOSAGE FORM/ STRENGTH: 50 U/Vial, 100 U/Vial, 200 U/vial

For the **prophylaxis of headaches** in adults meeting the following criteria for funding:

- Patient with chronic migraine (defined as ≥15 days per month with continuous headache lasting ≥4 hours AND at least 4 distinct headache episodes each lasting ≥4 hours); AND

- Patient has failed[1] three or more prior oral prophylactic medications[2]; AND

- Request for Botox to treat migraine must be provided by a physician with specialty training in the management of headache. Administration should only be given by physicians with the appropriate qualifications and experience in the treatment, use, and proper administration of Botox for headaches.

[1]Failure is defined as no therapeutic or unsatisfactory effect

(Less than a 30% reduction in frequency of headache days) to an adequate dose and duration of 3 prophylactic therapies[2] where two treatments must be of different types/classes.

Contraindication or intolerable side effects necessitating discontinuation will be considered for 1 of the 3 drugs only.

[2]Prophylactic therapies to be considered include:

- Beta blockers
- Tricyclic antidepressants
- Verapamil or flunarizine
- Sodium valproate (or divalproex sodium)
- Topiramate
- Gabapentin

Requests should contain the following information:

- Objective measure of baseline headache days and response to other prophylactic medications (i.e. headache diary)
- List of previously tried prophylactic medications, including doses and duration as well as why they were discontinued
- Confirmation of specialty training in the management of headache.

Onabotulinum Toxin A
Brand(s): Botox
DOSAGE FORM/ STRENGTH: 50 U/Vial, 100 U/Vial, 200 U/vial

Dosing: As per product monograph
Notes regarding continued therapy with “Botox”:

i) Patients who have not obtained an adequate treatment response after 2 treatment cycles should be discontinued from further therapy.

ii) Patients who obtain an adequate response and who transition from chronic migraine to episodic migraine should be discontinued from therapy within 3 months of that transition.

An adequate treatment response is defined as a ≥ 50% reduction in frequency of headache days per month

Duration of Approval: 1 year

Renewal criteria:

- Objective evidence (i.e. headache diary) that the patient has obtained an adequate treatment response defined as a ≥ 50% reduction in frequency of headache days per month; AND

- Confirmation that the patient has not transitioned from chronic migraine to episodic migraine. Therapy will be reimbursed for a maximum of 3 months after transition from chronic migraine to episodic migraine.

- Consideration will be given for renewals in patients who had an initial adequate response to Botox, discontinued therapy and subsequently transitioned back to chronic migraine status.

Duration of Approval: 1 year

Almotriptan
Brand(s): Axert
DOSAGE FORM/ STRENGTH: 6 mg, 12.5mg tablet

Naratriptan
Brand(s): Amerge
DOSAGE FORM/ STRENGTH: 1 mg, 2.5 mg tablet

Rizatriptan
Brand(s): Maxalt, Maxalt RPD
DOSAGE FORM/ STRENGTH: 5 mg, 10 mg tablet and wafer

Sumatriptan
Brand(s): Imitrex
DOSAGE FORM/ STRENGTH: 50 mg, 100 mg tablet

For the treatment of migraines with or without aura in patients who failed adequate trials of other medications for migraines (e.g. acetaminophen, NSAIDs) and where the following information is provided:

- Details of migraine prophylactic regimens (e.g. amitriptyline, beta-blockers) tried or rationale why they are inappropriate; and
- The number of attacks, duration, and severity of migraines.

Duration of Approval: 5 years

Renewal requests may be considered for patients who continue to benefit from treatment. The physician must provide the frequency of triptan use.

Warning: The frequent use of triptans (i.e. more than three days per week for longer than three months at a time) may predispose a patient to developing triptan-induced chronic daily headaches.

Sumatriptan

Brand(s): Imitrex Injection
DOSAGE FORM/ STRENGTH: 12 mg/mL subcutaneous injection

Brand(s): Imitrex Nasal Spray
DOSAGE FORM/ STRENGTH: 5 mg/dose and 20 mg/dose nasal spray

For the treatment of migraines with or without aura in patients who failed adequate trials of other medications for migraines (e.g. acetaminophen, NSAIDs) and has documented intolerance* to an oral triptan. The following information must also be provided:

- Details of migraine prophylactic regimens (e.g. amitriptyline, beta-blockers) tried or rationale why they are inappropriate; and
- The number of attacks, duration, and severity of migraines.

* The nature of intolerance or why oral sumatriptan cannot be used must be specified.

Duration of Approval 5 years

Renewal requests for sumatriptan may be considered for patients who continue to benefit from treatment. The physician must provide the frequency of triptan use.

Warning: The frequent use of triptans (i.e. more than three days per week for longer than three months at a time) may predispose a patient to developing triptan-induced chronic daily headaches.

Zolmitriptan

Brand(s): Zomig
DOSAGE FORM/ STRENGTH: 2.5 mg tablet

Brand(s): Zomig Rapimelt
DOSAGE FORM/ STRENGTH: 2.5 mg dispersible tablet

For the treatment of migraines with or without aura in patients who have failed an adequate trial of or experienced intolerance to all other oral triptans considered under the Exceptional Access Program.

Duration of Approvals: 5 years

Renewal requests may be considered for patients who continue to benefit from treatment. The physician must provide the frequency of triptan use.

MULTIPLE SCLEROSIS DRUGS

Alemtuzumab

Brand(s): Lemtrada
DOSAGE FORM/ STRENGTH: 12 mg/ 1.2 mL Solution for IV infusion
Effective date: July 6, 2016 Updated February 17, 2022

Initiation criteria

As monotherapy for the treatment of Relapsing Remitting Multiple Sclerosis (RRMS) in adult patients with active disease at the approved dosage provide that the following criteria have been met:

1. Diagnosis of RRMS is in accordance with the McDonald 2017 criteria demonstrating dissemination of lesions in the central nervous system in space and time meeting the following:
   i) 2 or more attacks[1] and clinical evidence of 2 or more lesions[2];
   OR
   ii) 2 or more attacks and clinical evidence of 1 lesion with clear historical evidence of prior attack involving lesion in different location;

[1]If the patient has experienced only one attack, the patient must meet ONE of the additional criteria of dissemination in time in the list below:

a) Additional clinical attack
b) Simultaneous presence of both enhancing and non-enhancing, symptomatic or asymptomatic MS-typical MRI lesions; OR new T2 or enhancing MRI lesion compared to baseline scan (without regard to timing of baseline scan)
c) Presence of cerebrospinal fluid (CSF)-specific oligoclonal bands

[2]If the patient has evidence of only one lesion the patient must meet ONE of the additional criteria of dissemination in space in the list below:

a) Additional clinical attack implicating different CNS site
b) 1 or more MS-typical T2 lesions in 2 or more areas of the Central Nervous System (CNS): periventricular, cortical, juxtacortical, infratentorial or spinal cord

AND

2. The patient has either:
   i) Failed to respond to full and adequate courses of at least TWO of the following therapies*: interferon, glatiramer acetate, dimethyl fumarate, or teriflunomide, or ocrelizumab; or
   ii) has a documented intolerance or contraindication to two or more of the therapies listed above.

   AND
3. Patient has experienced a clinical relapse and/or new MS lesions in the last 2 years;
   AND
4. Patient has had a significant increase in T2 lesion load compared with that from a previous MRI scan (i.e. 3 or more new lesions) OR at least one gadolinium-enhancing lesion;

Alemtuzumab
Brand(s): Lemtrada
DOSAGE FORM/ STRENGTH: 12 mg/ 1.2 mL Solution for IV infusion

AND

5. The drug request is from a neurologist experienced in the management of RRMS from one of the MS Society recognized Ontario MS clinics[3] or includes a consult note from a neurologist from one of these clinics supporting the diagnosis.

   [3]MS Society recognized Ontario MS clinics*:

   * Hamilton MS Clinic HHS, McMaster University
   * Kingston MS Clinic, Kingston General Hospital
   * London MS Clinic, London Health Sciences Centre
   * Ottawa MS Research clinic, Ottawa Hospital General Campus
   * Ottawa Pediatric MS Clinic, CHEO
   * Toronto MS Clinic, St Michael's Hospital
   * Toronto Pediatric MS Clinic, The Hospital for Sick Children
   * Sunnybrook Health Sciences Centre
   * Guelph MS clinic, Guelph ON
   * Thunder Bay MS Clinic, St Joseph's Care Group

   *Note: Requests for patients who is under the care of a community neurologist working outside of one of the MS Society recognized Ontario MS clinics can be considered on a case-by-case basis (please include MRI and relevant history with your request).

6. The patient has a current Expanded Disability Status Scale (EDSS) score less than or equal to 6.0.

Exclusion Criteria: No reimbursement if the patient satisfies any of the following exclusion criteria:

* the patient is receiving combination therapy of Lemtrada with other disease modifying therapies, such as Aubagio, Avonex, Betaseron, Copaxone, Extavia, Rebif, Extavia, Tysabri, Gilenya and Tecfidera;
* the patient has an EDSS greater than 7.0
* the patient is less than 18 years old.

Dosage: 12mg/day for two treatment courses. Initial course: 12mg/day for 5 consecutive days (60mg total dose). Second course: 12mg/day for 3 consecutive days (36mg total dose) administered 12 months after the initial treatment course.

Cladribine
Brand(s): Mavenclad
DOSAGE FORM/ STRENGTH: 10 mg tablet

Initiation Criteria

For the treatment of Relapsing Remitting Multiple Sclerosis (RRMS) in adult patients with active disease meeting ALL the following criteria:

1. 18 years of age or older

2. Diagnosis of RRMS is in accordance with the McDonald 2017 criteria demonstrating dissemination of lesions in the central nervous system in space and time meeting the following;
   i) 2 or more attacks[1] and clinical evidence of 2 or more lesions[2];
   OR
   ii) 2 or more attacks[1] and clinical evidence of 1 lesion with clear historical evidence of prior attack involving lesion in different location;

   [1]If the patient has experienced only one attack, the patient must meet ONE of the additional criteria of dissemination in time in the list below:
   - Additional clinical attack
   - Simultaneous presence of both enhancing and non-enhancing, symptomatic or asymptomatic MS-typical MRI lesions; OR new T2 or enhancing MRI lesion compared to baseline scan (without regard to timing of baseline scan)
   - Presence of cerebrospinal fluid (CSF)-specific oligoclonal bands

   [2] If the patient has evidence of only one lesion the patient must meet ONE of the additional criteria of dissemination in space in the list below:
   - Additional clinical attack implicating different CNS site
   - 1 or more MS-typical T2 lesions in 2 or more areas of the Central Nervous System (CNS): periventricular, cortical, juxtacortical, infratentorial or spinal cord

   AND

3. Failure or documented intolerance to at least one of an interferon **OR** glatiramer acetate **OR** dimethyl fumarate **OR** teriflunomide **OR** ocrelizumab; AND

4. Patient has experienced a clinical relapse and/or new MS lesions in the last 2 years; AND
5. Patient has an EDSS score less than 6.0 before start of therapy; AND

6. Cladribine is used as monotherapy for the treatment of RRMS; AND

Cladribine
Brand(s): Mavenclad
DOSAGE FORM/ STRENGTH: 10 mg tablet

7. The drug request is from a neurologist experienced in the management of RRMS or includes a consult note from a neurologist from an MS clinical recognized by the MS Society of Canada supporting the diagnosis.

   Requests from community neurologists not working with an MS Clinic will be considered case-by-case. (Please include MRI reports or labwork to support the diagnosis pf RRMS aligned with McDonald 2017 criteria.)

   *Note: Requests for patients who is under the care of a community neurologist working outside of one of the MS Society recognized Ontario MS clinics can be considered on a case-by-case basis. Submit MRI and relevant history with your request.

Exclusion criteria:

1. Combination therapy with another disease modifying therapy for RRMS will not be reimbursed.
2. Patients with an EDSS score equal to or greater than 7.0

Dosage: Refer to the Mavenclad product monograph for dosing regimen based on body weight.

Taken as two treatment courses over 2 years. Each treatment course consists of 2 treatment weeks, which are one month apart at the beginning of each treatment year.

1.75 mg/kg per year administered as a treatment course in year 1 and a second treatment course starting 12 months after the first course in the respective year upon monitoring for recovery of lymphocytes before the second course of treatment is administered in accordance with prescribing information.

The recommended cumulative dose of is 3.5 mg/kg body weight over 2 years (1.75 mg/kg per year).

Approval Duration: Two treatment courses over 2 years are funded

Dimethyl fumarate
Brand(s): Tecfidera and generics
DOSAGE FORM/ STRENGTH: 120 mg delayed-release capsule

For the treatment of Relapsing–Remitting Multiple Sclerosis (RRMS) in patients who meet all of the following criteria**:**

- The patient's physician provides documentation setting out the details of the patient's most recent neurological examination (which must have been conducted within ninety [90] days of the request, including a description of any recent attacks, the dates of attacks, and neurological findings).
- Patient has had one (1) or more clinical relapses in the previous year.
- The drug is requested by and followed by a neurologist experienced in the management of RRMS.
- The patient has a recent Expanded Disability Status Scale (EDSS) score ≤ 5.

Dosage: Initial: 120 mg twice daily

Maintenance: 240 mg twice daily

Renewal requests will be considered. Renewals for Tecfidera can be submitted through the Telephone Request Service.

The date and details of the most recent neurological examination and EDSS scores must be provided (exam must have occurred within the last ninety [90] days); **AND**

- The patient must be stable or experienced no more than one clinical relapse* in the past year; **AND**
- The patient has a recent EDSS score ≤ 5.

Dosage: 120 mg twice daily.
Maintenance: 240 mg twice daily

Duration of Approval: 1 year

***Renewal** requests where patients have experienced more than one (1) clinical relapse in the past year are to be externally reviewed.

As applicable, please also include information regarding the requesting physician's specialty (e.g. is the physician a neurologist or a physician with specialized experience with multiple sclerosis (MS), the name of the MS clinic where the patient was examined, or an MS consult note as this information may reduce the turnaround times for assessment.

Duration of Approval: First Renewal: 2 years

Second and subsequent renewals: 5 years

Fingolimod
Brand(s): Gilenya and generics
DOSAGE FORM/ STRENGTH: 0.5 mg capsule

As monotherapy for the treatment of patients with Relapsing Remitting Multiple Sclerosis (RRMS) who meet all of the following criteria:

- The patient's physician provides documentation setting out the details of the patient's most recent neurological examination within ninety (90) days of the submitted request. This must include a description of any recent attack(s), the date(s) of the attack(s), and the neurological findings; AND
- Failure to respond to full and adequate courses[1] of at least one of interferon **OR** glatiramer acetate **OR** dimethyl fumarate; **OR** teriflunomide **OR** ocrelizumab **OR** documented intolerance or contraindication to 2 of the above listed therapies; AND
- Experienced one or more clinically disabling relapses in the previous year; AND
- Has had a significant increase in T2 lesion load compared with that from a previous MRI scan (i.e. 3 or more new lesions) **OR** at least one gadolinium-enhancing lesion.
- Is being followed by a neurologist experienced in the management of RRMS.
- Has a current EDSS of less than or equal to 5.5 (i.e. patients must be able to ambulate at least 100 meters without assistance).

Exclusion Criteria (Patients meeting any of the following exclusion criteria will not be funded)**:**

- Patient's receiving combination therapy of Gilenya with other disease modifying therapies (e.g. Aubagio, Avonex, Betaseron, Copaxone/Glatect, Extavia, Rebif, Extavia, Ocrevus, Tysabri, and Tecfidera).
- Patients with EDSS greater than 5.5
- Patients who have had a heart attack or stroke in the last 6 months of the funding request, history of sick sinus syndrome, atrioventricular block, significant QT prolongation, bradycardia, ischemic heart disease, or congestive heart failure.
- Patients younger than 18 years of age.
- Patients requesting Gilenya due to needle phobia or preference for oral therapy over injection who do not have a clinical contraindication to interferon or glatiramer therapy.
- Skin reactions at the site of injection do NOT qualify as a contraindication to interferon or glatiramer therapy.

Fingolimod
Brand(s): Gilenya and generics
DOSAGE FORM/ STRENGTH: 0.5 mg capsule

Dosage: 0.5 mg once daily

[1]Failure to respond to full and adequate courses: defined as having received a trial of at least 6 months of interferon or glatiramer or dimethyl fumarate therapy or teriflunomide **AND** experienced at least one disabling relapse (attack) while on interferon or glatiramer or dimethyl fumarate or teriflunomide.

MRI reports do NOT need to be submitted with the initial request.

Duration of Approval: 1 year

Renewals are considered. Renewals can be submitted through the Telephone Request Service and will be considered for patients who have benefited from therapy.

Physicians must provide the following information:

- Documentation providing the date and details of the Patient's most recent neurological examination and EDSS scores (exam must have occurred within the last ninety (90) days); AND

- Evidence that the patient is stable and has experienced no more than one (1) disabling attack/relapse in the past year. (Note: If the Patient has had more than one attack/relapse, the request will be sent for external review. Please include details of the attack(s) including the dates on which they occurred); AND

- A recent Expanded Disability Status Scale (EDSS) that is less than or equal to 5.5 (Note: Requests with an EDSS greater than 5.5 will not be funded).

Dosage: 0.5 mg once daily.

Duration of Approval: First Renewal: 2 years

Second and subsequent renewals: 5 years

Glatiramer acetate – See Formulary listing for Glatect
Brand(s): Copaxone, Glatect (available as Limited Use drug on ODB formulary)
DOSAGE FORM/ STRENGTH: 20 mg/mL pre-filled syringe for subcutaneous injection

Refer to the Executive Officer Communications on the Ministry website for the Ministry's Biosimilar Policy including frequently asked questions and updates for the biosimilar policy updates.
http://www.health.gov.on.ca/en/pro/programs/drugs/opdp_eo/eo_communiq.aspx

Effective March 31, 2023, the ODB program will start transitioning coverage for Copaxone®, Enbrel®, Humalog®, Humira®, Lantus®, NovoRapid®, Remicade®, and Rituxan® to their biosimilar versions.

Effective December 29, 2023, coverage for these originator biologic drugs through the ODB program will not be available for patients and the ODB program will only provide coverage for the biosimilar version of these drugs for all ODB program recipients, with limited exemptions. In general, for ODB program recipients who are already on these biologic drugs, there is up to a 9-month transition period (see the biosimilar switch policy described on page 6 to 8 of this document).

It should be noted that after the date when a biosimilar becomes publicly funded for an approved indication, patients initiated on an originator biologic for this same provincially funded indication through support from a manufacturer's patient support program, will be expected to be provided ongoing access of the originator biologic through the patient's original payer mechanism (e.g. manufacturer's patient support program) or to switch to an ODB funded biosimilar version upon meeting specified criteria. The Ministry will no longer consider funding of originator biologics that are part of the biosimilar policy with limited exemptions on or after December 29, 2023.

Interferon beta-1a
Brand(s): Avonex PS, Avonex Pen
DOSAGE FORM/ STRENGTH: 30 mcg/ 0.5mL prefilled syringe for intramuscular injection, 30 mcg single-use prefilled auto-injector

For the treatment of Clinically Definite Multiple Sclerosis (CDMS) or Clinically Isolated Syndrome (CIS) (see CIS criteria in next section).

For CDMS: Avonex requests for patients with CDMS will be reviewed by external medical experts when the following information is provided:

- Details of the most recent neurological examination within the last ninety (90) days, including a description of any recent attacks (date and neurological findings)

- The patient has experienced at least two clinical attacks including one clinical attack within the past year

- MRI findings as applicable

- The patient's EDSS is less than or equal to 6.0

Renewal requests for Avonex can be submitted through the Telephone Request Service. Avonex renewals will be considered for patients who have benefited from therapy. Patients must be stable (i.e. no relapses or attacks during the last year) and the patient's EDSS must be less than or equal to 6.0

The physician must provide the following information:

- Description of the patient's clinical course in the last year, including details of all attacks;

- Date and details of the most recent neurological examination (within the last 90 days); and

- The patient's most recent EDSS score.

As applicable, include information regarding the requesting physician's specialty (e.g. is the physician a neurologist or a physician with specialized experience with multiple sclerosis (MS), the name of the MS clinic where the neurologist is based, or an MS consult note supporting the diagnosis as this information may reduce the turnaround times for assessment.

Duration of Approval: First Renewal: 2 years

Second and subsequent renewals: 5 years

Interferon beta-1a
Brand(s): Rebif
DOSAGE FORM/ STRENGTH: 22 mcg and 44 mcg prefilled syringe for subcutaneous injection, 66 mcg/ml and 132 mcg/ml pre-filled cartridge

For the treatment of Clinically Definite Multiple Sclerosis (CDMS) or Clinically Isolated Syndrome (CIS) (see CIS criteria in next section).

For CDMS: Rebif requests for patients with CDMS will be reviewed by external medical experts when the following information is provided:

- Date and details of the most recent neurological examination (within the last 90 days); and
- Dates and details (e.g., neurological findings) of at least two clinical attacks, including one clinical attack within the past year; and
- EDSS score ≤ 6.

Duration of Approval: 1 year

Renewal requests for Rebif can be submitted through the Telephone Request Service and will be considered for patients who have benefited from therapy and have an EDSS score ≤ 6. The physician must provide the following information:

- Description of the patient's clinical course in the last year, including details of all attacks;
- Date and details of the most recent neurological examination (within the last 90 days); and
- The patient's most recent EDSS score.

As applicable, include information regarding the requesting physician's specialty (e.g. is the physician a neurologist or a physician with specialized experience with multiple sclerosis (MS), the name of the MS clinic where the neurologist is based, or an MS consult note supporting the diagnosis as this information may reduce the turnaround times for assessment.

Duration of Approval: First Renewal: 2 years

Second and subsequent renewals: 5 years

Interferon beta-1b
Brand(s): Betaseron
DOSAGE FORM/ STRENGTH: 0.3 mg/vial subcutaneous injection

For the treatment of Clinically Definite Multiple Sclerosis (CDMS) or Clinically Isolated Syndrome (CIS) (see criteria in next section)

For CDMS: Betaseron requests for patients will be reviewed by external medical experts when the following information is provided:

- Date and details of the most recent neurological examination (within the last 90 days); AND
- Dates and details (e.g., neurological findings) of at least two clinical attacks, including one clinical attack within the past year; AND
- EDSS score ≤ 6.

Duration of Approval: 1 year

Renewal requests for Betaseron can be submitted through the Telephone Request Service and will be considered for patients who have benefited from therapy and have an EDSS score ≤ 6.

The physician must provide the following information:

- Description of the patient's clinical course in the last year, including details of all attacks; AND
- Date and details of the most recent neurological examination (within the last 90 days); AND
- The patient's most recent EDSS score.

As applicable, include information regarding the requesting physician's specialty (e.g. is the physician a neurologist or a physician with specialized experience with multiple sclerosis (MS), the name of the MS clinic where the neurologist is based, or an MS consult note supporting the diagnosis as this information may reduce the turnaround times for assessment.

Duration of Approval: First Renewal: 2 years

Second and subsequent renewals**:** 5 years

Interferon beta-1b
Brand(s): Extavia
DOSAGE FORM/ STRENGTH: 0.3 mg/vial subcutaneous injection

For the treatment of Clinically Definite Multiple Sclerosis (CDMS) or Clinically Isolated Syndrome (CIS) (see criteria in next section).

For CDMS: Extavia requests for patients will be reviewed by external medical experts when the following information is provided:

- Date and details of the most recent neurological examination (within the last 90 days) AND
- Dates and details (e.g., neurological findings) of at least two clinical attacks, including one clinical attack within the past year AND
- EDSS score ≤ 6.

Duration of Approval: 1 year

Renewal requests for Extavia can be submitted through the Telephone Request Service and will be considered for patients who have benefited from therapy and have an EDSS score ≤ 6.

The physician must provide the following information:

- Description of the patient's clinical course in the last year, including details of all attacks;
- Date and details of the most recent neurological examination (within the last 90 days); and
- The patient's most recent EDSS score.

As applicable, include information regarding the requesting physician's specialty (e.g. is the physician a neurologist or a physician with specialized experience with multiple sclerosis (MS), the name of the MS clinic where the neurologist is based, or an MS consult note supporting the diagnosis as this information may reduce the turnaround times for assessment.

Duration of Approval: 2 years

Second and subsequent renewals: 5 years

Modafinil
Brand(s): Alertec
DOSAGE FORM/ STRENGTH: 100 mg tablet

For the treatment of fatigue in patients with multiple sclerosis who have demonstrated a lack of response to or an inability to tolerate amantadine.

Note: See additional indications and criteria under “CNS” drugs

Duration of Approval: Lifetime

Natalizumab
Brand(s): Tysabri
DOSAGE FORM/ STRENGTH: 300 mg/15 mL concentrate for solution for intravenous infusion

Initiation Criteria:

As monotherapy for the treatment of Rapidly Evolving Severe Relapsing-Remitting Multiple Sclerosis (RES-RRMS) for the patient who meets all the following:

a) The patient’s physician provides documentation setting out the details of the patient’s most recent neurological examination within ninety (90) days of the submitted request. This must include a description of any recent attacks, including the corresponding dates, and the neurological findings; AND

b) Has been diagnosed with MS; AND

c) Is 18 to 65 years of age; AND

d) Has a current EDSS of less than or equal to 5.0; AND

e) Has had ONE of the following types of relapses in the past year:

- The occurrence of one relapse with partial recovery during the past year AND has at least ONE gadolinium-enhancing lesion on brain MRI, OR significant increase in T2 lesion load compared to a previous MRI (i.e. 3 or more new lesions); OR
- The occurrence of two or more relapses with partial recovery during the past year; OR
- The occurrence of two or more relapses with complete recovery during the past year AND has at least ONE gadolinium-enhancing lesion on brain MRI, OR significant increase in T2 lesion load compared to a previous MRI;

f) has failed to respond to full and adequate courses[1] of at least one of interferon **OR** glatiramer acetate **OR** dimethyl fumarate; **OR** teriflunomide **OR** documented intolerance or contraindication to 2 of the 3 therapies. (Note that needle phobia is not acceptable.)

Natalizumab
Brand(s): Tysabri
DOSAGE FORM/ STRENGTH: 300 mg/15 mL concentrate for solution for intravenous infusion

g) is being followed by a neurologist experienced in the management of RRMS

h) details of past treatment, including dates and Patient response;

[1]Failure to respond to a full and adequate course: defined as a trial of at least 6 months of interferon or glatiramer therapy or dimethyl fumarate AND experienced at least one disabling relapse (attack) while on interferon or glatiramer or dimethyl fumarate.

MRI reports do NOT need to be submitted with the initial request.

Duration of Approval: 1 year

Renewals will be considered for requests meeting the following;

(a) Documentation providing the date and details of the patient's most recent neurological examination and EDSS scores (exam must have occurred within the last ninety (90) days); AND

(b) Evidence that the Patient is stable and has experienced no more than one (1) disabling attack/relapse in the past year (Note: if the Patient has had more than one attack/relapse, the request will be sent for external review); AND

(c) A recent Expanded Disability Status Scale (EDSS) that is less than or equal to 5.0 (Note that the request will be rejected if the EDSS is greater than 5.0).

Duration of Approval: First Renewal: 2 years

Second and subsequent renewals: 5 years

Ocrelizumab
Brand(s): Ocrevus
DOSAGE FORM/ STRENGTH: 300 mg Injection

Initiation Criteria

For treatment of Early Primary Progressive Multiple Sclerosis (PPMS) in adult patients who meet ALL of the following criteria:

1. 18 years of age or older;
2. Diagnosis of early PPMS is confirmed based on McDonald 2017 diagnostic criteria meeting the following;
   i) Patient has had one year of disability progression (retrospectively or prospectively determined) independent of clinical relapse; AND
   ii) Two or more of the following;
   - One or more T2-hyperintense lesions (symptomatic or asymptomatic) characteristic of multiple sclerosis in one of more of the following brain regions periventricular, cortical, juxtacortical or infratentorial
   - Two or more T2-hyperintense lesions (symptomatic or asymptomatic) in the spinal cord
   - Presence of CSF-specific oligoclonal bands
3. Level of disability from disease meeting the below:

   i) A recent Expanded Disability Status Scale (EDSS)[1] score between 3.0 and 6.5 prior to initiation of ocrelizumab; AND
   ii) A Functional Systems Scale (FSS) score of at least 2.0 for the pyramidal system due to lower extremity findings (Note that FSS scores associated with disability in other systems such as brainstem or cerebellar can be considered);

4. Disease duration from onset of multiple sclerosis meeting one of the below:
   i) Less than 15 years for those with an EDSS score greater than 5.0
   ii) Less than 10 years for those with an EDSS score equal to or less than 5.0
   iii) PPMS has been progressive in the last 3 years in the absence of activity

5. The drug request is from a neurologist experienced in the management of PPMS from one of the MS Society recognized Ontario MS clinics[2] or includes a consult note from a neurologist from one of these clinics supporting the diagnosis and the treatment with ocrelizumab.

[1]A “recent” score is an EDSS evaluated within the prior 6 months. Consideration will be provided for results from a neurological exam within the prior 12 months upon confirmation that the patient’s clinical status has not deteriorated.

Ocrelizumab
Brand(s): Ocrevus
DOSAGE FORM/ STRENGTH: 300 mg Injection

[2]MS Society recognized Ontario MS clinics*:

Hamilton MS Clinic HHS, McMaster University
Kingston MS Clinic, Kingston General Hospital
London MS Clinic, London Health Sciences Centre
Ottawa MS Research clinic, Ottawa Hospital General Campus
Ottawa Pediatric MS Clinic, CHEO
Toronto MS Clinic, St Michael's Hospital
Toronto Pediatric MS Clinic, The Hospital for Sick Children
Sunnybrook Health Sciences Centre

*Note: Requests for patients who is under the care of a community neurologist working outside of one of the MS Society recognized Ontario MS clinics can be considered on a case-by-case basis.

Exclusion Criteria:

Patients with an EDSS score equal to or greater than 7.0

Dosage: Initial dose of 300 mg intravenous infusion, followed 2 weeks later by a second 300 mg intravenous infusion. Subsequent doses of single 600 mg intravenous infusion every 6 months after the first initial dose.

Renewal Criteria:

Ongoing funding will be provided for those who continue to benefit from treatment and who have an Expanded Disability Status Scale (EDSS) score less than 7.0 .

Duration of Approval of Initials and Renewals: 18 months

Ocrelizumab
Brand(s): Ocrevus
DOSAGE FORM/ STRENGTH: 300 mg Injection

Initiation Criteria:

For the treatment of Relapsing Remitting Multiple Sclerosis (RRMS) in adult patients with active disease meeting ALL the following criteria:

1. 18 years of age or older
2. Diagnosis of RRMS is in accordance with the McDonald 2017 criteria demonstrating dissemination of lesions in the central nervous system in space and time meeting the following;
   - 2 or more attacks[1] and clinical evidence of 2 or more lesions[2];
     OR
   - 2 or more attacks and clinical evidence of 1 lesion with clear historical evidence of prior attack involving lesion in different location;

   [1]If the patient has experienced only one attack, the patient must meet ONE of the additional criteria of dissemination in time in the list below:
   - Additional clinical attack
   - Simultaneous presence of both enhancing and non-enhancing, symptomatic or asymptomatic MS-typical MRI lesions; OR new T2 or enhancing MRI lesion compared to baseline scan (without regard to timing of baseline scan)
   - Presence of cerebrospinal fluid (CSF)-specific oligoclonal bands

   [2]If the patient has evidence of only one lesion the patient must meet ONE of the additional criteria of dissemination in space in the list below:
   - additional clinical attack implicating different CNS site
   - 1 or more MS-typical T2 lesions in 2 or more areas of the Central Nervous System (CNS): periventricular, cortical, juxtacortical, infratentorial or spinal cord

   AND
3. Patient has experienced a clinical relapse and/or new MS lesions in the last 2 years; AND
4. Patient has an EDSS score less than 6.0 before start of therapy; AND
5. Ocrelizumab is used as monotherapy; AND
6. The drug request is from a neurologist experienced in the management of RRMS from one of the MS Society recognized Ontario MS clinics[3] or includes a consult note from a neurologist from one of these clinics supporting the diagnosis.

Ocrelizumab
Brand(s): Ocrevus
DOSAGE FORM/ STRENGTH: 300 mg Injection

[3]MS Society recognized Ontario MS clinics*:

Hamilton MS Clinic HHS, McMaster University
Kingston MS Clinic, Kingston General Hospital
London MS Clinic, London Health Sciences Centre
Ottawa MS Research clinic, Ottawa Hospital General Campus
Ottawa Pediatric MS Clinic, CHEO
Toronto MS Clinic, St Michael's Hospital
Toronto Pediatric MS Clinic, The Hospital for Sick Children
Sunnybrook Health Sciences Centre

*Note: Requests for patients who is under the care of a community neurologist working outside of one of the MS Society recognized Ontario MS clinics can be considered on a case-by-case basis.

Exclusion criteria:
1. Combination therapy with another disease modifying therapy for RRMS will not be reimbursed.
2. Patients with an EDSS score equal to or greater than 7.0

Dosage: Initial dose of 300 mg intravenous infusion, followed 2 weeks later by a second 300 mg intravenous infusion. Subsequent doses of single 600 mg intravenous infusion every 6 months after the first dose.

Renewal Criteria:

Ongoing funding will be provided for those who continue to benefit from treatment and who have an Expanded Disability Status Scale (EDSS) score less than 7.0

When requesting renewal of funding, information that should be provided should include:

- Date and details of the most recent neurological examination and EDSS scores to support ongoing benefit from therapy.
- Clinical details of the date and onset of clinical attacks/relapses
- Information to support that the patient is stable/not demonstrating a sub-optimal response

Renewal requests where patients have experienced more than 1 attack in the past year will be externally reviewed.

Approval Duration of Initial and Renewals: 18 months

Ofatumumab
Brand(s): Kesimpta
DOSAGE FORM/ STRENGTH: 20 mg/0.4 mL pre-filled pen for injection
Effective date: March 25, 2022

Initiation Criteria

For the **treatment of Relapsing Remitting Multiple Sclerosis (RRMS)** in patients who meet all the following criteria**:**

1. 18 years of age or older; AND

2. Diagnosis of RRMS is in accordance with the McDonald 2017 criteria demonstrating dissemination of lesions in the central nervous system in space and time meeting the following;
   - 2 or more attacks[1] and clinical evidence of 2 or more lesions[2]
     OR
   - 2 or more attacks and clinical evidence of 1 lesion with clear historical evidence of prior attack involving lesion in different location

   [1]If the patient has experienced only one attack, the patient must meet ONE of the additional criteria of dissemination in time in the list below:
   - Additional clinical attack
   - Simultaneous presence of both enhancing and non-enhancing, symptomatic or asymptomatic MS-typical MRI lesions; OR new T2 or enhancing MRI lesion compared to baseline scan (without regard to timing of baseline scan)
   - Presence of cerebrospinal fluid (CSF)-specific oligoclonal bands.

   [2]If the patient has evidence of only one lesion the patient must meet ONE of the additional criteria of dissemination in space in the list below:
   - Additional clinical attack implicating different CNS site
   - 1 or more MS-typical T2 lesions in 2 or more areas of the Central Nervous System (CNS): periventricular, cortical, juxtacortical, infratentorial or spinal cord

   AND
3. An Expanded Disability Status Scale (EDSS) score of less than 6.0; AND

4. Evidence of active disease defined as at least ONE of the following:
   - One relapse during the previous year
   - Two relapses during the previous 2 years
   - A positive gadolinium (Gd)-enhancing magnetic resonance imaging (MRI) scan during the year before starting treatment with ofatumumab

   AND
5. Ofatumumab is used as monotherapy; AND

Ofatumumab
Brand(s): Kesimpta
DOSAGE FORM/ STRENGTH: 20 mg/0.4mL Prefilled pen for Injection

6. The drug request is from a neurologist experienced in the management of RRMS from one of the MS Society recognized Ontario MS clinics[3] or includes a consult note from a neurologist from one of these clinics supporting the diagnosis.

[3]MS Society recognized Ontario MS clinics*:

Hamilton MS Clinic HHS, McMaster University
Kingston MS Clinic, Kingston General Hospital
London MS Clinic, London Health Sciences Centre
Ottawa MS Research clinic, Ottawa Hospital General Campus
Ottawa Pediatric MS Clinic, CHEO
Toronto MS Clinic, St Michael's Hospital
Toronto Pediatric MS Clinic, The Hospital for Sick Children
Sunnybrook Health Sciences Centre
Thunder Bay MS Clinic (35 Algoma Street North, Thunder Bay, ON)

*Note: Requests for patients who is under the care of a community neurologist working outside of one of the MS Society recognized Ontario MS clinics can be considered on a case-by-case basis.

Exclusion criteria:
1. Combination therapy with another disease modifying therapy for RRMS will not be reimbursed.
2. Patients with an EDSS score equal to or greater than 7.0.

Renewal Criteria
Ongoing funding will be provided for those who continue to benefit from treatment and who have an Expanded Disability Status Scale (EDSS) score less than 7.0.
When requesting renewal of funding, information that should be provided should include:
- Date and details of the most recent neurological examination and EDSS scores to support ongoing benefit from therapy.
- Clinical details of the date and onset of clinical attacks/relapses
- Information to support that the patient is stable/not demonstrating a sub-optimal response

Renewal requests where patients have experienced more than 1 attack in the past year will be externally reviewed.

Duration of Approvals for initial and renewals: 12 months

Siponimod
Brand(s): Mayzent
DOSAGE FORM/ STRENGTH: 0.25 mg, 2 mg tablet
Effective Date: March 25, 2022

For the **treatment of secondary progressive multiple sclerosis (SPMS)** in patients who meet the following criteria**:**

1. Documented history of relapsing-remitting multiple sclerosis (RRMS); AND
2. Diagnosis of active SPMS disease as evidenced by the ALL the following:
   i) The patient has had one year of disability progression (retrospectively or prospectively determined) independent of clinical relapse; AND

   ii) Patient has experienced one (1) or more clinical attacks/relapses in the last 2 years AND/OR Patient has imaging features characteristic of multiple sclerosis inflammatory activity (e.g. New T2 lesions, gadolinium enhanced lesions) in the last year;

   AND
3. A recent[1] Expanded Disability Status Scale (EDSS) score between 3.0 and 6.5 prior to initiation of siponimod; AND
4. The drug request is from a neurologist experienced in the management of SPMS from one of the MS Society recognized Ontario MS clinics[2] or includes a consult note from a neurologist from one of these clinics supporting the diagnosis and the treatment with siponimod; AND
5. Siponimod is not being used as combination therapy with other disease-modifying treatments (DMTs) used to treat multiple sclerosis.

[1]A "recent" score is an EDSS evaluated within the prior 6 months. Consideration will be provided for results from a neurological exam within the prior 12 months upon confirmation that the patient's clinical status has not deteriorated.

[2]MS Society recognized Ontario MS clinics at the following website: https://mssociety.ca/about-ms/diagnosing-ms/ms-clinics

- Hamilton MS Clinic HHS, McMaster University
- Kingston MS Clinic, Kingston General Hospital
- London MS Clinic, London Health Sciences Centre
- Ottawa MS Research clinic, Ottawa Hospital General Campus
- Ottawa Pediatric MS Clinic, CHEO
- Toronto MS Clinic, St Michael's Hospital
- Toronto Pediatric MS Clinic, The Hospital for Sick Children
- Sunnybrook Health Sciences Centre
- Guelph MS Clinic
- Thunder Bay MS Clinic, St Joseph's Care Group

Siponimod
Brand(s): Mayzent
DOSAGE FORM/ STRENGTH: 0.25 mg, 2 mg tablet

*Note: Requests for patients who is under the care of a community neurologist working outside of one of the MS Society recognized Ontario MS clinics can be considered on a case-by-case basis.

Renewal Criteria:

Ongoing funding will be provided for those who continue to benefit from treatment and who have an Expanded Disability Status Scale (EDSS) score less than 7.0.

Duration of Approval of Initials and Renewals: 12 months

Approved Dose: Dose titration to the daily maintenance dose of 2 mg daily

Peginterferon beta-1a
Brand(s): Plegridy
DOSAGE FORM/ STRENGTH: 125mcg/0.5mL, 94mcg/0.5mL Injection, Starter Pack:
63mcg/0.5mL, 94mcg/0.5mL

For the treatment of Clinically Definite Multiple Sclerosis (CDMS)/ Relapsing remitting multiple sclerosis (RRMS) in patients meeting the following criteria:

Plegridy requests will be reviewed by external medical experts when the following information is provided:

- Details of the most recent neurological examination within the last ninety (90) days, including a description of any recent attacks (date and neurological findings)
- The patient has experienced at least two clinical attacks in his or her lifetime, including one clinical attack within the past 12 months preceding the EAP request;
- MRI findings as applicable
- The patient's EDSS is less than or equal to 6.0

Duration of Approval: 1 year

Renewal requests for Plegridy can be submitted through the Telephone Request Service. Plegridy renewals will be considered for patients who have benefited from therapy. Patients must be stable (i.e. no relapses or attacks during the last year) and the patient's EDSS must be less than or equal to 6.0

Peginterferon beta-1a
Brand(s): Plegridy
DOSAGE FORM/ STRENGTH: 125 mcg/0.5 mL, 94 mcg/0.5 mL Injection;
Starter pack: 63 mcg/0.5mL and 94 mcg/0.5 mL injection.

The physician must provide the following information:

- Description of the patient's clinical course in the last year, including details of all attacks;
- Date and details of the most recent neurological examination (within the last 90 days); and
- The patient's most recent EDSS score.

*__Renewal__ requests where patients have experienced more than one (1) clinical relapse in the past year will be considered on a case-by-case basis through an external review.

As applicable, include information regarding the requesting physician's specialty (e.g. is the physician a neurologist or a physician with specialized experience with multiple sclerosis (MS), the name of the MS clinic where the neurologist is based, or an MS consult note supporting the diagnosis as this information may reduce the turnaround times for assessment.

Duration of Approval: First Renewal: 2 years

Second and subsequent renewals: 5 years

Teriflunomide
Brand(s): Aubagio
DOSAGE FORM/ STRENGTH: 14 mg tablet
Moved to ODB formulary effective May 31, 2023

This drug is available on the ODB formulary as a Limited Use Benefit.

Please refer to the formulary for the updated ODB funding criteria.

CLINICALLY ISOLATED SYNDROME DRUGS

Glatiramer acetate (Coverage is provided for Glatect)

Brand(s): Glatect; Copaxone will only be funded for patients who meet a medical exemption as of December 29, 2023 (Refer to the Biosimilar policy)
DOSAGE FORM/ STRENGTH: 20 mg/mL pre-filled syringe for subcutaneous injection

Interferon beta-1a

Brand(s): Avonex PS, Avonex Pen
DOSAGE FORM/ STRENGTH: 30 mcg/0.5mL prefilled syringe for intramuscular injection, 30 mcg single-use prefilled autoinjector

Brand(s): Rebif
DOSAGE FORM/ STRENGTH: 22 mcg and 44 mcg prefilled syringe for subcutaneous injection, 66 mcg/ml and 132 mcg/ml pre-filled cartridge

Interferon beta-1b

Brand(s): Betaseron
DOSAGE FORM/ STRENGTH: 0.3 mg/vial subcutaneous injection

Brand(s): Extavia
DOSAGE FORM/ STRENGTH: 0.3 mg/vial subcutaneous injection

For the treatment of Clinically Isolated Syndrome (CIS): requests for patients who have experienced a single demyelinating event will be reviewed by external medical experts when the following information is provided:

- Date and details of the most recent neurological examination which must have been conducted within the last ninety days of the request;
- The patient's EDSS is less than or equal to 6.0 (please provide EDSS score); AND
- The patient's clinically isolated syndrome occurred within the last twelve months.

Duration of Approval: 1 year

Renewal requests will be assessed according to the following criteria:

- the requesting physician provides the date and details of the patient's most recent neurological examination and EDSS scores;
- the patient's neurological examination occurred within that last ninety days;
- the patient is stable (i.e. no relapses or attacks during the last year) and
- the patient's EDSS is less than or equal to 6.0

NEPHROLOGY TREATMENTS

Anifrolumab

Brand(s): Saphnelo
DOSAGE FORM/ STRENGTH: 150 mg/mL (300 mg vial) Injection
Effective Date: December 19, 2023

Initiation criteria:

For the treatment of adult patients with active, moderate to severe systemic lupus erythematosus (SLE) meeting all the following criteria;

1. Patient is at least 18 years of age; AND
2. Documented autoantibody positive SLE; AND
3. Moderate-to-severe SLE as defined by SLE Disease Activity Index 2000 (SLEDAI-2K) score of 6 or higher (Note 1); AND
4. Inadequate disease control in spite of treatment with an oral corticosteroid (OCS) dose of at least 10 mg daily of prednisone (or another equivalent corticosteroid) in addition to standard of care therapy for SLE (i.e. one or any combination of OCS, antimalarials, and/or immunosuppressants) (Note 2); AND
5. Request is provided by a prescriber with expertise in the diagnosis and management of SLE.

Exclusion Criteria:

1. Anifrolumab will not be reimbursed when used in combination with other biologic treatments for SLE.
2. Anifrolumab will not be reimbursed in patients with severe or unstable neuropsychiatric SLE.
3. Anifrolumab will not be reimbursed in patients with severe active SLE nephritis.

Initial renewal criteria:

Renewal of funding for anifrolumab will be provided upon meeting the following criteria:

1. The dose of OCS is decreased to atleast 7.5 mg daily day of prednisone (or equivalent)

   OR

   The OCS dose remains higher than 7.5 mg daily of prednisone (or equivalent) but has decreased by at least 50% from the baseline OCS dose; AND
2. There is a reduction in disease activity as demonstrated by a reduction of the SLEDAI-2K score to 5 or less OR by BILAG-2004 improvement in organ systems and no new worsening.

Anifrolumab
Brand(s):Saphnelo
DOSAGE FORM/ STRENGTH: 150 mg/mL (300 mg vial) Injection

Subsequent renewal criteria:

Subsequent renewal of funding will be provided for those who are able to maintain their initial response that was demonstrated after 12 months of therapy with anifrolumab.

Notes:

1. For this funding criteria, the SLEDAI-2K should be used as the validated measure to assess disease activity at baseline, however, the British Isles Lupus Assessment Group (BILAG)-2004 index can be considered on a case-by-case basis where the SLEDAI-2K was not available. The same index/scale should be used at baseline and all subsequent renewals.
2. Note that if BILAG-2004 is the index used to evaluate response at baseline compared to after 12 months of treatment, the interpretation of improvement may be as described below: Improvement in involved BILAG organs (A [severe] and B [moderate]) at baseline (e.g., reduction of all baseline BILAG-2004 A to B, C, or D and baseline BILAG-2004 B to C or D, and no BILAG) with no worsening (where worsening is defined as 1 or more new BILAG-2004 A items or 2 or more new BILAG-2004 B items)
3. Standard of care for SLE is defined as using an antimalarial drug (e.g., hydroxychloroquine) (discontinuation upon developing toxicity), at least one immunosuppressive drug (e.g., cyclophosphamide, azathioprine, methotrexate, cyclosporine, and mycophenolate), and OCS (e.g. prednisone), with or without (non-steroidal anti-inflammatory drugs) NSAIDs.
4. Pediatric patients with SLE meeting the anifrolumab criteria may be considered on a case-by-case basis.

Approved dose: Up to 300 mg IV every 4 weeks

Approval duration for initials and renewals: 1 year

Belimumab
Brand(s): Benlysta
DOSAGE FORM/ STRENGTH: 120 mg/5 mL, 400 mg/20 mL Vial for Injection
Effective Date: April 17, 2024

Initiation criteria:

For the treatment of active lupus nephritis (LN) in patients on standard therapy who meet the following criteria:

1. Age 18 years and older; AND
2. Diagnosed with biopsy-proven (note 1) active LN of International Society of Nephrology and Renal Pathology Society class III (focal LN) or IV (diffuse LN) with or without class V (membranous LN), or pure class V disease; AND
3. Belimumab is being administered in addition to standard therapy for LN (Note 2); AND
4. Patient has started standard induction therapy within the prior 60 days before the request for belimumab; AND
5. Patient has not demonstrated treatment failure to both cyclophosphamide and mycophenolate mofetil (or other forms of mycophenolate) used previously as induction therapies; AND
6. Patient has an eGFR greater than or equal to 30 mL/min/1.73 m^2; AND
7. Prescribed by a rheumatologist or nephrologist with experience in managing Lupus nephritis.

Discontinuation criteria: Treatment with belimumab must be discontinued if the patient does not meet all of the renewal criteria or if the patient has any of the following:

1. An eGFR decrease to less than 30 mL/min/1.73 m^2
2. Patient requires addition of other immunosuppressant agents (other than as part of the induction and maintenance regimens), corticosteroid use outside of the limits, anti– tumour necrosis factor therapy, or other biologics to manage their LN.

Renewal Criteria:

<u>First renewal</u>

Renewal of funding will be considered for patients who do not meet the discontinuation criteria and who meet the following criteria after the first 12 months of treatment with belimumab:

1. Patient has reduced their baseline oral corticosteroid doses to at least 7.5 mg per day or lower OR for those who remain at doses higher than 7.5 mg per day, patients will be considered for renewal if they are able to reduce their corticosteroid dose to at least 50% from their baseline levels; AND

2. Patient must demonstrate stabilization or improvement in eGFR with a documented estimated eGFR that is no more than 20% below the value before the renal flare (preflare value) or that is greater than or the same as 60 mL/min/1.73 m^2 after 12 months of therapy; AND

3. Patient has documented improvement in proteinuria defined as one of the following:
   a. proteinuria no greater than 0.7 g/24 hours after 12 months of therapy if baseline proteinuria was less than 3.5 g/24 hours;
   b. proteinuria no greater than 0.7 g/24 hours after 18 to 24 months of therapy if baseline proteinuria was greater than 3.5 g/24 hours;

(Note: Patients who meet the corticosteroid and renal improvement in the renewal criteria above but who had baseline “nephrotic” levels of proteinuria, will be approved for an additional 6 to 12 months on a case-by-case basis if they have been unable to reduce their proteinuria level to at least 0.7g/24 hours after the first 12 months of belimumab treatment.)

Second and Subsequent renewals

The prescriber must provide documentation that the initial response achieved after the first 12 months of therapy with belimumab has been maintained.

Notes:

Patients unable to provide a kidney biopsy may be considered on a case-by-case basis. Applications must include documented rationale and relevant clinical details as to why a kidney biopsy cannot be provided.

1. Standard induction therapy is defined as corticosteroids with either cyclophosphamide or mycophenolate mofetil or other forms of mycophenolate, or azathioprine. Outside of induction therapy, patients are expected to be receiving other standard-of-care therapies for LN (e.g., antimalarials and angiotensin-converting enzyme inhibitors or angiotensin receptor blockers) as appropriate and indicated.
2. Prescribers must submit laboratory reports with documentation of relevant lab work required within the belimumab funding criteria. (e.g. eGFR, serum creatinine, albumin, urine protein, etc.)

Exclusion criteria: Patients with a diagnosis of active Systemic Lupus Erythematosus (SLE) but without active LN are excluded from funding of belimumab.

Recommended Dose for LN:10 mg/kg IV at 2-week intervals for the first 3 doses and at 4-week intervals thereafter.

Approval duration for initials and renewals: Up to 12 months

Calcitriol
Brand(s): Sterimax Calcitriol Injection
DOSAGE FORM/ STRENGTH: 1 mcg/mL

Case-by-case funding is provided for dialysis patients. Please submit all relevant clinical data to enable an assessment by the EAP.

Calcitriol Injection, USP (calcitriol) 1mcg/mL Inj Sol – 1mL Pk (imported by STE) – Effective Date: July 17, 2024

This imported US product (PIN 09858344) is funded under the EAP on a temporary basis case by case and for those stabilized with an existing EAP approval. This is to manage a product shortage of calcitriol injection 1 mcg/mL (STE) DIN 02399334 that is funded under the EAP.

Cinacalcet
Brand(s): Sensipar and generics
DOSAGE FORM/ STRENGTH: 30 mg, 60 mg, 90 mg tablets

For the treatment of severe hyperparathyroidism* in patients with chronic kidney disease who are on dialysis who meet the following criteria;

i) the patient is refractory to other treatments; AND

ii) the patient has symptoms clearly related to hyperparathyroidism that are causing significant impairment in quality of life (e.g. calciphylaxis or bone pain); AND

iii) additionally, **ONE** of the following criteria is present:

a) the patient has been reviewed by a surgeon, anesthetist or nephrologist and has been deemed to not be a candidate for parathyroidectomy due to high surgical risk or anesthetic risk. [Please note: This must be accompanied by a clinical note explaining the high surgical risk or anesthetic risk and the patient's parathyroid hormone (PTH) level]; OR

b) the patient has been wait-listed for a parathyroidectomy and requires Sensipar for bridge therapy; OR

c) the patient is awaiting an imminent renal transplant and a nephrologist indicates a preference for pre-transplant treatment with Sensipar instead of a parathyroidectomy.

*Severe hyperparathyroidism is considered to be patients with PTH levels greater than 88 pmol/L confirmed on two laboratory tests for PTH taken at least 1 month apart.

Exclusion Criteria:

Patients with primary hyperparathyroidism or parathyroid carcinoma.

Initial Approval durations:

i) Patients meeting the above criteria and iii a) above – 1 year

ii) Patients who meet the above criteria and iii b) above – period of time until the estimated date of the parathyroidectomy

iii) Patients wait-listed for a parathyroidectomy requiring bridge therapy with Sensipar or awaiting an imminent renal transplant will be approved to the estimated date of the surgery.

Cinacalcet

Brand(s): Sensipar and generics
DOSAGE FORM/ STRENGTH: 30 mg, 60 mg, 90 mg tablets

Duration of Approval: 1 year or to the estimated date of the procedure for those using for bridge therapy and awaiting surgery

Renewals will be considered for patients who are not candidates for parathyroidectomy and who continue to benefit from therapy. Requests for renewals should include the patient's PTH level.

Renewals will NOT be considered for patients who have had a parathyroidectomy.

Duration of Approval: 1 year

Rituximab

Brand(s): Riximyo, Ruxience, and Truxima (biosimilar); Rituxan (only for those approved for biosimilar exemption)
DOSAGE FORM/ STRENGTH: 10 mg/mL intravenous injection
Effective date: July 29, 2022

Refer to the Executive Officer Communications on the Ministry website for the Ministry's Biosimilar Policy including frequently asked questions and updates for the biosimilar policy updates.
http://www.health.gov.on.ca/en/pro/programs/drugs/opdp_eo/eo_communiq.aspx

Effective March 31, 2023, the ODB program will start transitioning coverage for Copaxone®, Enbrel®, Humalog®, Humira®, Lantus®, NovoRapid®, Remicade®, and Rituxan® to their biosimilar versions.

Effective December 29, 2023, coverage for these originator biologic drugs through the ODB program will not be available for patients and the ODB program will only provide coverage for the biosimilar version of these drugs for all ODB program recipients, with limited exemptions. In general, for ODB program recipients who are already on these biologic drugs, there is up to a 9-month transition period (see the biosimilar switch policy described on page 6 to 8 of this document).

It should be noted that after the date when a biosimilar becomes publicly funded for an approved indication, patients initiated on an originator biologic for this same provincially funded indication through support from a manufacturer's patient support program, will be expected to be provided ongoing access of the originator biologic through the patient's original payer mechanism (e.g. manufacturer's patient support program) or to switch to an ODB funded biosimilar version upon meeting specified criteria. The Ministry will no longer consider funding of originator biologics that are part of the biosimilar policy with limited exemptions on or after December 29, 2023.

Rituximab (See formulary for funded biosimilars)

Brand(s): Riximyo, Ruxience, Truxima, Rituxan (Approved EAP exemptions only)
DOSAGE FORM/ STRENGTH: 10 mg/mL Intravenous injection

Initiation Criteria:

For the treatment of adult patients with primary membranous nephropathy (PMN) who are at moderate to high risk of developing progressive kidney injury or complications of nephrotic syndrome meeting the following criteria:

1. Patient is 18 years of age or older (see Note 3): AND
2. Prescribed by a nephrologist with expertise in the diagnosis and treatment of (PMN); AND
3. Patient meets one of the following clinical circumstances:
    a. Has documented proteinuria greater than 5 g per day despite 6 months of therapy with an angiotensin-converting enzyme (ACE) inhibitor or angiotensin II receptor blocker (ARB) (Note that a shorter period of observation may be provided for patients with documented proteinuria greater than 8 g per day or high anti-PLA2R titres greater than 50 or eGFR less than 60 mL/min/1.73m^2); OR
    b. Has documented proteinuria greater than 3.5 g per day with life- or organ-threatening complication(s) of nephrotic syndrome (i.e., venous thrombosis, arterial thrombosis, infection, or rapid decline in kidney function not otherwise explained); OR
    c. Has biopsy-proven or serology(anti-PLA2R)-proven recurrence in a patient who has received a kidney transplant and has proteinuria greater than 3.5 g per day.

Approved dosage:

1,000 mg IV on day 0 and day 15 (i.e. 1,000 mg IV administered two weeks apart)

No additional doses are required in patients who demonstrate complete remission.

An additional course of rituximab may be administered at the above dosage after a minimum of 6 months has elapsed from the prior treatment course, if treatment with rituximab has resulted in a reduction in proteinuria from baseline by at least 25% without complete remission OR if the patient relapses following complete remission.

Approval duration of initial criteria: 12 months

Rituximab (See formulary for funded biosimilars)

Brand(s): Riximyo, Ruxience, Truxima, Rituxan (Approved EAP exemptions only)
DOSAGE FORM/ STRENGTH: 10 mg/mL Intravenous injection

Notes:

1. Rituximab can be discontinued in patients who have achieved complete remission.

2. Rituximab can be discontinued in non-responders. Retreatment of non-responders is not recommended.

3. Pediatric patients 17 years of age and younger may be considered on a case-by-case basis through external review. Please include relevant laboratory results, consult notes, and medications that have been used to manage the patient's condition.

4. Definitions:

   Complete remission: Proteinuria less than 0.3 g per day or protein-creatinine ratio less than 30 mg/mmoL

   Partial remission: Reduction in proteinuria of at least 50% from baseline and final proteinuria between 0.3 g and 3.5 g per day

   Relapse: Recurrence of proteinuria (as per the initiation criteria) accompanied by a decrease in serum albumin to less than 30 g/L in patients who have achieved a complete or partial remission following prior rituximab treatment.

   Nonresponse: Lower than 25% reduction in proteinuria by 6 months after initial treatment course

Sodium Thiosulfate

Brand(s): Seacalphyx DIN 02386666 and Hope pharmaceuticals DIN 02428393
DOSAGE FORM/ STRENGTH: 250mg/mL Injection; 12.5 g/50 mL Injection
Effective date: March 28, 2017

Approval of sodium thiosulfate for the treatment of calciphylaxis will be provided where all of the following criteria have been met:

Patients with G4 or G5 chronic kidney disease**; AND**

i) Have been diagnosed with calciphylaxis either by**:**
   a. 99m Technicium scintigraphy (bone scan) showing deposits that correspond to clinical lesions; OR
   b. Biopsy; OR
   c. Where scintigraphy negative and biopsy is not feasible, then diagnosis must be confirmed by nephrologist with submission of anonymized photographs of lesions AND a differential diagnosis checklist (e.g. warfarin-induced necrosis if on warfarin; lipohypertrophy if on insulin; cellulitis, nephrogenic sclerosing dermopathy, emboli, thrombi, fibrointimal hyperplasia and so on which depends on the site of lesion); **AND**

ii) Patient has either:
   a. Ulcerated lesions; OR
   b. Non-ulcerated lesions which have not improved after 2 weeks of multimodal treatment with replacement of calcium-containing phosphate binders with non-calcium containing binders (i.e. sevelamer), discontinuation of vitamin D analogs and initiation of calcimimetic (i.e. cinacalcet), changes in dialysis prescription (reduction in dialysate calcium; consideration of increased dialysis intensity), replacement of warfarin with alternative anticoagulants where possible, wound management strategies, and analgesia for lesion pain.

   Requests for patients with calciphylaxis who do not meet the above criteria will be considered on a case-by-case basis.

Duration of Approval: 2 months

Renewals will be considered for patients responding to treatment with improved pain control AND reduction in lesion number or size, reduction in ulcer size, or complete ulcer healing.

Recommended dose: 25g three times weekly.

Duration of Approval: Two months at a time until lesions are completely resolved, and for additional 2 months after complete healing.

OCULAR TREATMENTS

Tocilizumab
Brand(s): Actemra
DOSAGE FORM/ STRENGTH: 162 mg/0.9 mL inj (PFS), 162mg/0.9mL Auto Inj.

For the treatment of new onset or relapsed Giant Cell Arteritis (GCA) in adult patients meeting all the following criteria,

- Symptomatic for GCA; AND
- Diagnosis of GCA confirmed by temporal artery biopsy and/or imaging tests (i.e. magnetic resonance angiography, computed tomography angiography or positron emission scanning)[1]; AND
- Tocilizumab subcutaneous is used as combination therapy with 20 mg to 60 mg of prednisone (or an equivalent corticosteroid) with subsequent corticosteroid tapering as symptoms stabilize; AND
- Prescribed by a rheumatologist or a prescriber with expertise in the diagnosis and management of GCA.

[1]Where these tests are not available or where a result may be deemed unreliable (e.g. a negative biopsy in a patient on corticosteroids), the prescriber may C-reactive protein and/or Erythrocyte Sedimentation Rate results with the request.

Recommended dose:

162 mg sc once a week (or once every other week, based on clinical considerations) in combination with a tapering course of corticosteroid.

Approval Duration: 1 year

Renewals will be considered on a case-by-case basis.

Approval Duration of renewals: 1 year

Adalimumab – See Formulary for funded biosimilars

Brand(s): Humira (Only for those approved for biosimilar exemption)
DOSAGE FORM/ STRENGTH: 40 mg/0.8 mL prefilled syringe, 40mg/0.8mL and 20 mg/0.2 mL prefilled pens for subcutaneous injection

Infliximab - See formulary for funded biosimilars

Brand(s): Remicade (Only for those approved for biosimilar exemption)
DOSAGE FORM/ STRENGTH: 100 mg/Vial Injection for infusion

Refer to the Executive Officer Communications on the Ministry website for the Ministry's Biosimilar Policy including frequently asked questions and updates for the biosimilar policy updates. http://www.health.gov.on.ca/en/pro/programs/drugs/opdp_eo/eo_communiq.aspx

Effective March 31, 2023, the ODB program will start transitioning coverage for Copaxone®, Enbrel®, Humalog®, Humira®, Lantus®, NovoRapid®, Remicade®, and Rituxan® to their biosimilar versions.

Effective December 29, 2023, coverage for these originator biologic drugs through the ODB program will not be available for patients and the ODB program will only provide coverage for the biosimilar version of these drugs for all ODB program recipients, with limited exemptions. In general, for ODB program recipients who are already on these biologic drugs, there is up to a 9-month transition period (see the biosimilar switch policy described on page 6 to 8 of this document).

It should be noted that after the date when a biosimilar becomes publicly funded for an approved indication, patients initiated on an originator biologic for this same provincially funded indication through support from a manufacturer's patient support program, will be expected to be provided ongoing access of the originator biologic through the patient's original payer mechanism (e.g. manufacturer's patient support program) or to switch to an ODB funded biosimilar version upon meeting specified criteria. The Ministry will no longer consider funding of originator biologics that are part of the biosimilar policy with limited exemptions on or after December 29, 2023.

For the treatment of severe non-infectious ocular inflammatory disease (OID) in patients meeting one of the following criteria;

- Experienced failure, intolerance, or contraindication to oral corticosteroid (or topical corticosteroid for anterior uveitis) and failure or intolerance to at least one immunosuppressive therapy; OR
- For the treatment of chronic Juvenile Idiopathic Arthritis (JIA)-associated uveitis after failure or intolerance to a first-line immunosuppressive agent; OR

- For patients who have immediately vision-threatening OID and do not meet the above criteria, where consultation notes/ letter from an ophthalmologist expert specializing in OIDs (who may be the requesting physician) confirm the severity of the patient's condition and indicate detailed rationale for an immediate biologic therapy (e.g. ocular inflammation associated with Behcet's disease; severe non-necrotizing scleritis; necrotizing scleritis; etc.); AND

- Patient must be followed by a uveitis specialist, a retina specialist familiar with ocular inflammatory diseases, or a pediatric ophthalmologist.

Approved Dose:

Adalimumab 40 mg subcutaneous every 1 to 2 weeks.

Infliximab 5-10 mg/kg IV at weeks 0, 2, 6 and maintenance every 4-8 weeks

Duration of Approval: 1 year

Renewals will be considered for requests where consultation notes or a letter is provided by the requesting physician to confirm that treatment has resulted in improvement/stability of vision and other treatment goals (e.g., remission from/control of ocular inflammation) have been met.

Duration of Approval: 2 years

Cyclosporine 0.1% eye drops
Brand(s): Verkazia
DOSAGE FORM/ STRENGTH: 0.1% eye drops
Effective date: March 3, 2021

Initiation criteria:

For the treatment of severe vernal keratoconjunctivitis (VKC) in patients who meet ALL the following criteria:

- Patient is between 4 and 18 years of age inclusive; AND
- Diagnosis of severe VKC as defined by one of the following evaluations of severity:
  - Grade 3 (severe) or 4 (very severe) on the Bonini Scale; OR
  - Grade 4 (marked) or 5 (severe) on the modified Oxford Scale;

  AND
- Documentation detailing the patient's baseline severity of signs and symptoms of VKC is provided prior to treatment initiation with Verkazia; AND
- Patient is under the care of a physician with expertise in the diagnosis and management of VKC.

Note: Patients previously treated with cyclosporine 0.1% but who discontinued treatment upon resolution of VKC signs and symptoms are eligible to reinitiate treatment if signs and symptoms of severe VKC recur and they meet the first and second initiation criteria.

Initial approval period: 6 months

Exclusion criteria:

Verkazia will not be funded in patients meeting ANY of the following criteria:

- Patient is older than 18 years of age;
- Patient has asymptomatic, pre-symptomatic, or moderate VKC;
- Patients with active or suspected ocular or peri-ocular infection;
- Patients with ocular malignancies or premalignant conditions.

Discontinuation Criteria:

Verkazia will not be funded upon meeting ONE or more of the following;

- There is no demonstrated observable improvement in the patient's VKC signs and symptoms after 4 months of Verkazia therapy (compared to baseline); OR
- The patient's VKC signs and symptoms have been resolved.

Case-by-case consideration may be provided for patients who have responded to therapy but who continue to experience recurrent VKC symptoms

Rituximab

Brand(s): Riximyo, Ruxience, and Truxima (biosimilar); Rituxan (Only for those approved for biosimilar exemption)
DOSAGE FORM/ STRENGTH: 10 mg/mL intravenous injection
Effective date: August 11, 2015

Refer to the Executive Officer Communications on the Ministry website for the Ministry's Biosimilar Policy including frequently asked questions and updates for the biosimilar policy updates. http://www.health.gov.on.ca/en/pro/programs/drugs/opdp_eo/eo_communiq.aspx

Effective March 31, 2023, the ODB program will start transitioning coverage for Copaxone®, Enbrel®, Humalog®, Humira®, Lantus®, NovoRapid®, Remicade®, and Rituxan® to their biosimilar versions.

Effective December 29, 2023, coverage for these originator biologic drugs through the ODB program will not be available for patients and the ODB program will only provide coverage for the biosimilar version of these drugs for all ODB program recipients, with limited exemptions. In general, for ODB program recipients who are already on these biologic drugs, there is up to a 9-month transition period (see the biosimilar switch policy described on page 6 to 8 of this document).

It should be noted that after the date when a biosimilar becomes publicly funded for an approved indication, patients initiated on an originator biologic for this same provincially funded indication through support from a manufacturer's patient support program, will be expected to be provided ongoing access of the originator biologic through the patient's original payer mechanism (e.g. manufacturer's patient support program) or to switch to an ODB funded biosimilar version upon meeting specified criteria. The Ministry will no longer consider funding of originator biologics that are part of the biosimilar policy with limited exemptions on or after December 29, 2023.

For the treatment of severe non-infectious ocular inflammatory disease (OID) in patients failed or did not tolerate treatment with infliximab or adalimumab; OR has contraindication to anti-TNF therapy AND who meet one of the following criteria;

- Experienced failure, intolerance, or contraindication to oral corticosteroid (or topical corticosteroid for anterior uveitis) and failure or intolerance to at least one immunosuppressive therapy; OR
- For the treatment of chronic Juvenile Idiopathic Arthritis (JIA)-associated uveitis after failure or intolerance to a first-line immunosuppressive agent; OR
- For patients who have immediately vision-threatening OID and do not meet the above criteria, where consultation notes/ letter from an ophthalmologist expert
- specializing in OIDs (who may be the requesting physician) confirm the severity of the patient's condition and indicate detailed rationale for an immediate biologic

therapy (e.g. ocular inflammation associated with Behcet's disease; severe non-necrotizing scleritis; necrotizing scleritis; etc.); AND

- Patient must be followed by a uveitis specialist, a retina specialist familiar with ocular inflammatory diseases, or a pediatric ophthalmologist.

Approved Dose: Rituximab up to 1000 mg IV per infusion at days 1 & 15 and 3rd infusion at 6-12 months.

Note that maintenance rituximab infusions are not funded.

Duration of Approval: 1 year

Renewals will be considered for requests where;

- Consultation notes or a letter is provided by the requesting physician to confirm that treatment has resulted in improvement/stability of vision and other treatment goals (e.g., remission from/control of ocular inflammation) have been met; AND

Patients must also have demonstrated subsequent deterioration of symptoms, at least 6 months from the last dose of rituximab.

Duration of Approval: 2 years

Rituximab

Brand(s): Riximyo, Ruxience, and Truxima (biosimilar); Rituxan ((biologic originator for those meeting biosimilar exemption)
DOSAGE FORM/ STRENGTH: 10 mg/mL intravenous injection
Effective date: July 29, 2022

Neuromyelitis Optica Spectrum Disorder (NMOSD)

Initiation Criteria:

For the treatment of Neuromyelitis Optica Spectrum Disorder (NMOSD) in patients meeting the following criteria

1. NMOSD diagnosis meets international diagnostic criteria; AND
2. Patient is seropositive for the aquaporin-4 (AQP-4) antibody **OR** patient is AQP-4 antibody negative, but has had more than one attack within a 6-month timeframe while on azathioprine/mycophenolate with or without corticosteroids (i.e. aggressive disease); AND
3. The prescriber is a neurologist with expertise in the diagnosis and treatment of NMOSD.

Rituximab (See formulary for funded biosimilars)

Brand(s): Riximyo, Ruxience, Truxima, Rituxan (Approved EAP exemptions only)
DOSAGE FORM/ STRENGTH: 10 mg/mL Intravenous injection

Notes:
1. Rituximab should not be initiated during an acute episode of NMOSD.
2. Patients to be re-evaluated every 12 months.

Exclusion:

Rituximab will not be funded in combination with other biologics for NMOSD

Dosage:

Induction with 1,000mg IV x 2 doses 2 weeks apart for adults (4 weekly treatments of 375 mg/m^2 for children)

Repeat every 6 months

Approval duration of initial criteria: 12 months

Renewal criteria:

Renewal of funding will be considered in patients who have not experienced a relapse of NMOSD or unacceptable toxicities from rituximab. Consideration of funding in patients who have experienced a relapse will require a description of the relapse, including any associated bloodwork to support the ongoing efficacy and safety of rituximab. Please submit relevant consult notes to support the request.

Renewals: 2 years

Satralizumab
Brand(s): Enspryng
DOSAGE FORM/ STRENGTH: 120 mg/mL Prefilled Syringe
Effective date: February 3, 2023

Initiation Criteria

For the treatment of Neuromyelitis Optica Spectrum Disorder (NMOSD) in patients meeting the following criteria

1. Patient is 12 years of age or older; AND
2. NMOSD diagnosis meets international diagnostic criteria; AND
3. Patient is seropositive for the aquaporin-4 (AQP-4) antibody; AND
4. The patient must have had at least ONE relapse of NMOSD in the previous 12 months despite an adequate trial of rituximab for NMOSD (Note that if the patient is not appropriate for rituximab, an adequate trial of another preventative treatment such as azathioprine or mycophenolate must have been used); AND
5. Patients must have an Expanded Disability Status Scale (EDSS) score of 6.5 points or less; AND
6. The prescriber is a neurologist with expertise in the diagnosis and treatment of NMOSD.

Notes:
1. Satralizumab should not be initiated during a NMOSD relapse episode.
2. Patients should be evaluated every 6 months.
3. Satralizumab may be used alone or in combination with an immunosuppressant therapy.
4. Case-by-case consideration will be provided for patients with EDSS score higher than 6.5 and higher than 8.0 (i.e.per the discontinuation criteria).

Exclusion Criteria:

1. Satralizumab will not be funded in combination with other biologics for NMOSD.
2. Satriluzumab will not be funded as acute treatment of an NMOSD relapse.

Renewal Criteria:

Renewal of satralizumab should be provided for those who continue to benefit from preventative treatment and who do not meet the discontinuation criteria.

At the time of renewal, the number of relapses in the prior 12 months on treatment and a recent EDSS score must be provided.

Discontinuation criteria:

Reimbursement should be discontinued for patients with an EDSS of 8 or higher.

Satralizumab
Brand(s): Enspryng
DOSAGE FORM/ STRENGTH: 120 mg/mL Prefilled Syringe

Approved dose:

120 mg by subcutaneous injection at weeks 0, 2, and 4 for the first 3 administrations, followed by a maintenance dose of 120 mg every 4 weeks.

Approval duration: 1 year

ONCOLOGY DRUGS

Abemaciclib

Brand(s): Verzenio
DOSAGE FORM/ STRENGTH: 50 mg, 100 mg, 150 mg tablet
Effective date: October 16, 2023

Initiation Criteria:

For the adjuvant treatment of adult patients with hormone receptor (HR)–positive, human epidermal growth factor receptor 2 (HER2)–negative, node-positive early breast cancer at high risk of disease recurrence meeting ALL of the following criteria:

1. Patient is 18 years of age or older; AND
2. Has documented HR-positive and HER2-negative breast cancer (Note 1); AND
3. Has resected invasive early breast cancer without metastases; AND
4. Has a documented Ki-67 immunohistochemistry (IHC) test with an index score of at least 20% or higher; AND
5. Patient's breast cancer meets one of the following pathological features;
   a. Pathological tumour involvement in at least 4 ipsilateral axillary lymph nodes; OR
   b. Pathological tumour involvement in 1 to 3 ipsilateral axillary lymph node(s) AND patient has a primary tumour at least 5 cm in size or larger or has histologic grade 3 disease OR has both (Note 2 and 3);

   AND
6. Abemaciclib is being used in combination with an endocrine therapy (e.g. tamoxifen, anastrozole, letrozole, exemestane); AND
7. Abemaciclib is initiated within 16 months following completion of definitive surgery of primary breast tumour.

Exclusion criteria:

1. Patients are not eligible for funding of adjuvant abemaciclib if they have inflammatory breast cancer.

2. Patients are not eligible for funding of adjuvant abemaciclib if they have metastatic breast cancer.

3. Patients are not eligible for funding of adjuvant abemaciclib if they have received prior treatment with a CDK 4/6 inhibitor (e.g. palbociclib, ribociclib).

4. Monotherapy with adjuvant abemaciclib will not be funded.

Abemaciclib

Brand(s): Verzenio

DOSAGE FORM/ STRENGTH: 50 mg, 100 mg, 150 mg

Notes:

1. Include the following reports with your request application as objective confirmation: HER2 status, hormone receptor status (i.e. estrogen and progesterone receptor status), pathology reports associated with axillary nodal involvement and size of tumours, and the Ki-67 IHC test report.
2. For patients who received neoadjuvant therapy, primary tumour size greater than 5 cm on breast imaging is allowed. If tumour size is needed to meet eligibility criteria, patients with multifocal/multicentric tumours may be eligible based on the addition of diameters of the individual lesions on a case-by-case basis.
3. Histologic grade 3 disease as defined by a combined score of at least 8 points per the modified Bloom-Richardson grading system, also known as the Nottingham score or equivalent.
4. Patients who progress early on adjuvant abemaciclib within the first 6 months of treatment will not be eligible for another CDK 4/6 inhibitor in the curative adjuvant or the metastatic state.
5. Patients who have experienced treatment interruptions within the 2 years from starting treatment and have not experienced disease recurrence or disease progression may be considered to resume treatment with abemaciclib on a case-by-case basis to a maximum total of 2 years (i.e. 24 months) of adjuvant treatment with abemaciclib combined with an endocrine therapy.

Discontinuation criteria:

Abemiciclib in the adjuvant setting will be funded until the occurrence of any of the following, whichever occurs first:

1. Completion of a total of 2 years of treatment; OR
2. Until disease recurrence; OR
3. Until development of unacceptable toxicities from treatment with abemaciclib; OR
4. If patient meets any of the exclusion criteria.

Renewal Criteria:

Renewals will be considered in patients who do not meet any of the discontinuation criteria for a maximum of 2 years of adjuvant treatment duration. (Note 5)

Approved dose: Up to 150 mg twice daily with dose adjustments as necessary based on the product monograph.

Duration of Approvals: 1 year (A maximum total of 2 years of adjuvant treatment will be funded.)

Abiraterone

Brand(s): Zytiga and generics (see formulary for full list of funded generics)
DOSAGE FORM/ STRENGTH: 250 mg, 500 mg tablet (Refer to ODB formulary for funded options.

Abiraterone products moved to the Ontario drug benefit (ODB) formulary as a general benefit effective with the ODB formulary update edition No.43 effective on July 31, 2024.

Acalabrutinib

Brand(s): Calquence
DOSAGE FORM/ STRENGTH: acalabrutinib 100 mg tablets
Effective date: December 3, 2021 (Updated August 10, 2023 – added tablet format)

For the treatment of adult patients with chronic lymphocytic leukemia (CLL) who meet the following criteria:

1. Diagnosed with active disease according to one or more of the International Workshop on Chronic Lymphocytic Leukemia (iwCLL) 2008 criteria; AND

2. Meets one of the following circumstances of use:
   i. First line use in a previously untreated patient who presents with one or more of the following cytogenic markers:
      - chromosome 17p deletion; OR
      - TP53 mutation, OR
      - unmutated immunoglobulin heavy chain variable region (IgHV);

      OR

   ii. Patient with relapsed or refractory CLL who has experienced disease progression on at least one prior systemic therapy/regimen.*

      AND

3. Acalabrutinib will be used as monotherapy; AND

4. Patient has good performance status.

*A prior line of therapy should include a fludarabine-based regimen in fit patients.

Renewal Criteria:

Renewals will be considered in patients until disease progression (as defined based on published iwCLL [2018]) or unacceptable toxicity.

Acalabrutinib
Brand(s): Calquence
DOSAGE FORM/ STRENGTH: 100 mg Capsule

Exclusion Criteria: (Patients meeting the below will not be funded.)

1. Patients who have experienced disease progression on another Bruton's tyrosine kinase (BTK) inhibitor (e.g. ibrutinib) for the treatment of CLL.

2. Patients with prolymphocytic leukemia.

3. Patients with current or history of Richter's syndrome.

4. Patients with central nervous system (CNS) lymphoma or leukemia.

Notes:

1. The Ministry will fund only one line of treatment with a BTK inhibitor for CLL.

2. The Ministry will not fund idelalisib following progression on a BTK inhibitor.

3. Patients may switch to acalabrutinib from another BTK inhibitor (e.g. Ibrutinib) as long as they have not experienced disease progression on another BTK inhibitor. Please include the reasons for requesting the switch with the application (e.g. intolerances, contraindications, etc.).

4. Acalabrutinib may be considered in patients diagnosed with small lymphocytic lymphoma (SLL) on a case-by-case basis upon meeting the above treatment eligibility criteria for CLL.

Approved Dosage for Initials and Renewals: 100 mg orally twice daily

Duration for Approval of Initials and Renewals: 1 year

Afatinib
Brand(s): Giotrif
DOSAGE FORM/ STRENGTH: 20 mg, 30 mg, 40 mg tablet

Initial requests:

For the treatment of patients with advanced or metastatic non-small cell lung cancer (NSCLC) who meet the following criteria;

- Afatanib is being used as first line therapy; AND
- Afatanib is being used as monotherapy; AND
- Patient's cancer is EGFR positive

Dose: 40 mg orally once daily

Exclusion Criteria:
- Patients with EGFR wild-type, negative, or unknown mutation.
- Afatinib will not be considered for funding in patients who have progressed on a prior EGFR TKI targeted therapy.
- Not funded for 2nd or 3rd line or maintenance NSCLC.

Notes:
- Patients should be assessed for disease status at least every two months. Afatinib may be continued until evidence of disease progression or development of unacceptable toxicity requiring discontinuation of afatinib.
- Patients who receive afatinib 1st line are NOT eligible for erlotinib in the 2nd or 3rd line or maintenance NSCLC setting.
- Requests for afatinib for patients who have initiated another EGFR TKI therapy (i.e. Iressa [gefitinib]) in the first line setting and who have not had disease progression will be considered on a case-by- case basis.

Renewal requests will be considered based on the following;

Afatinib 40 mg once daily may be continued until evidence of disease progression or development of unacceptable toxicity at which point the drug should be discontinued. Patients should have their disease status assessed at least every two months.

Exclusion Criteria:
- Patients with EGFR wild-type, negative, or unknown mutation.
- Afatinib will not be considered for funding in patients who have progressed on a prior EGFR TKI targeted therapy. Not funded for 2nd or 3rd line or maintenance NSCLC.

Alectinib
Brand(s): Alecensaro
DOSAGE FORM/ STRENGTH: 150 mg capsule

Initial Criteria:

For the treatment of anaplastic lymphoma kinase ("ALK") – positive locally advanced (not amenable to curative therapy) or metastatic non-small cell lung cancer (NSCLC) in patients meeting ALL the following criteria;

- Alectinib is used as first line treatment OR after experiencing disease progression or intolerance on crizotinib[1, 2, 3]; AND
- Alectinib is used as monotherapy; AND
- Patient has good performance status (ECOG ≤ 2).

[1]Patients who have progressed during or following first-line therapy with alectinib are not eligible to receive alectinib as a subsequent-line therapy.

[2]Time-limited funding will be considered case-by-case in patients with ALK-positive NSCLC who have progressed on chemotherapy and crizotinib OR crizotinib and an immune checkpoint inhibitor commenced prior to the public funding of alectinib.

[3]Include details of the intolerance including the grade of toxicity and reasons why crizotinib was not able to be used.

Exclusion criteria:

- Alectinib will not be funded if the patient has experienced disease progression while on an ALK inhibitor other than crizotinib.
- Alectinib will not be funded beyond third line.

Public funding will be considered for only one of Alectinib (Alecensaro) OR Ceritinib (Zykadia) and vice versa.

Recommended dose: 600 mg twice daily

Renewal Criteria:

Ongoing funding will be considered in patients who have not experienced disease progression or unacceptable toxicities to treatment with Alectinib.

Approval duration of initial and renewal requests: 1 year

Apalutamide
Brand(s): Erleada
DOSAGE FORM/ STRENGTH: 60 mg capsule, 240 mg tablet (added April 16, 2024)
Effective date: January 14, 2020 (nmCRPC) Updated: November 18, 2021 (mCSPC)

Non-metastatic Castrate Resistant Prostate Cancer (nmCRPC)

Initiation criteria:

For the treatment of high risk non-metastatic castration resistant prostate cancer (nmCRPC) in patients who meet all the following criteria:

1. Patient using apalutamide in combination with androgen deprivation therapy (ADT); AND
2. Has no detectable distant metastases as determined by CT, MRI, or technetium-99m bone scan; AND
3. Patient has castration resistant disease based on meeting all the following indicia observed while on continuous ADT treatment or post orchiectomy:
   a. Castrate serum testosterone levels: AND
   b. Biochemical progression defined as Three (3) prostate-specific antigen (PSA) rises at least 1 week apart, with the last PSA greater than 2ng/mL; and
4. Patient is at high risk for developing metastatic disease based on a Prostate-specific antigen doubling time (PSADT) of less than or equal to 10 months during continuous ADT; AND
5. Has Eastern Cooperative Oncology Group (ECOG) Performance Status less than or equal to 2.

Exclusion criteria: The following will not be reimbursed.

1. The patient received prior chemotherapy for the treatment of prostate cancer unless it was in the adjuvant or neoadjuvant setting.
2. The patient has previously experienced disease progression on prior treatment with enzalutamide or darolutamide used for prostate cancer.

Definitions for the purpose of the EAP funding criteria:

***ADT** – A first generation androgen deprivation therapy (e.g. goserelin, leuprolide, triptorelin, buserelin, degarelix).*

***ARI**- A second generation androgen receptor inhibitor (e.g. apalutamide, darolutamide, enzalutamide).*

Notes:

1. The Ministry will fund only one second generation androgen receptor inhibitor (ARI) in patients with non-metastatic castrate resistant prostate cancer.

2. Requests for apalutamide in patients who have initiated another ARI therapy in the nmCRPC setting and who have not experienced disease progression will be considered on a case-by-case basis.
3. Patients treated with an ARI as part of a clinical trial may be eligible for apalutamide and will be considered on a case-by-case basis.

Approved Dosage: 240 mg administered orally once daily.

Renewal Criteria:

Renewals will be considered in patients without evidence of radiographic disease progression or unacceptable toxicity while on apalutamide therapy.

Duration of initial and renewal approvals: 1 year

Metastatic castration sensitive prostate cancer (mCSPC)

Initiation Criteria:

For the treatment metastatic castration sensitive prostate cancer (mCSPC) in patients who meet all of the following criteria:

1. Apalutamide is used in combination with androgen deprivation therapy (ADT)[1]; AND
2. Metastatic lesions detected on technetium-99m bone scan, computed tomography (CT), and/or magnetic resonance imaging (MRI); AND
3. Castration sensitive as defined by the patient being treatment naïve to an ADT OR ADT initiated within the prior 6 months before start of therapy with apalutamide OR ADT used in the neoadjuvant or adjuvant setting where the patient has been off treatment for 12 months or more prior to start of apalutamide; AND
4. Has not experienced disease progression with another androgen receptor axis targeted therapy (ARAT) for castration sensitive prostate cancer; AND
5. Patient has good performance status.

[1]ADT is not required for patients with bilateral orchiectomy

Definitions for the purpose of the EAP funding criteria:

***ADT** – A first generation androgen deprivation therapy (e.g. goserelin, leuprolide, triptorelin, buserelin, degarelix)*

***ARI** - A second generation androgen receptor inhibitor (e.g. apalutamide, darolutamide, enzalutamide)*

***ARAT**- An androgen receptor axis targeted therapy (e.g. abiraterone, apalutamide, darolutamide, enzalutamide)*

Apalutamide
Brand(s): Erleada
DOSAGE FORM/ STRENGTH: 60 mg Capsule, 240 mg Tablet

The following baseline levels are to be provided with the initial application:
i) Number of metastatic lesions on bone scan and in soft tissues
ii) Testosterone level
iii) Baseline (pre-treatment) PSA level
iv) Pre-treatment Gleason score (optional)

Notes:

1. Patients who have previously progressed on an ARI for prostate cancer will not be eligible for apalutamide in mCSPC. The Ministry will fund only one of apalutamide or enzalutamide in patients with mCSPC.
2. Patients treated with enzalutamide or darolutamide as part of a clinical trial may be eligible for apalutamide and will be considered on a case-by-case basis.
3. Patients who are currently on a treatment regimen with an ARAT for prostate cancer, must meet the initiation criteria if they wish to switch to publicly funded apalutamide for mCSPC.
4. Time limited funding consideration will be provided on a case-by case basis for those patients who are using docetaxel in combination with ADT as long as there has been no progression and the treatment regimen has not been used for more than 6 months.

Approved Dosage for Initials and Renewals: 240 mg administered orally once daily.

Renewal Criteria:

Renewals will be considered in patients until disease progression (i.e. PSA elevation in addition to radiographic disease progression, or PSA progression in addition to clinical symptoms associated with cancer progression), development of castration resistant disease, or experiencing unacceptable toxicity while on apalutamide.

Exclusion Criteria: (Patients meeting any of the following will not be funded.)

1. Patients who have previously experienced disease progression on apalutamide or another ARI used in the setting of prostate cancer.
2. Apalutamide will not be funded as combination therapy with another ARAT.

Duration of initial and renewal approvals: 1 year

Asciminib

Brand(s): Scemblix
DOSAGE FORM/ STRENGTH: 20 mg, 40 mg tablets
Effective date: May 19, 2023

Initiation Criteria:

For the treatment of adult patients with chronic phase Philadelphia chromosome positive (Ph+) Chronic Myelogenous Leukemia (CML) in patients meeting the following criteria:

1. 18 years of age or older; AND
2. Diagnosis of (Ph+) chronic phase CML; AND
3. Asciminib is used in one of the following clinical situations:
   i) As third line therapy after experiencing disease progression or intolerance to two or more prior tyrosine kinase Inhibitor (TKI) therapies (imatinib, dasatinib, nilotinib, bosutinib or ponatinib); OR
   ii) As first or second line in patients who have a documented mutational drug resistance to imatinib, dasatinib, and nilotinib, which makes them clinically inappropriate treatment choices for first or second line therapy; OR
   iii) As second or subsequent line therapy in patients who progressed on bosutinib in first line and who have a documented mutational drug resistance to imatinib, dasatinib, and nilotinib, which makes them clinically inappropriate treatment choices.

Exclusion Criteria:

1. Asciminib is not funded for blast or accelerated phase CML.
2. Asciminib will not be funded for patients with V299L or T315I mutation.
3. Asciminib will not be funded in combination with another oral TKI for treatment of CML.
4. Asciminib will not be funded as 5th line treatment for CML or beyond. (Note 1)

Notes:

1. For a time-limited period, patients who have used 4 lines of treatment that included bosutinib and ponatinib for (Ph+) chronic phase CML, prior to provincial reimbursement of asciminib, will be considered for asciminib on a case-by-case basis.

Renewal criteria:

Renewal of funding will be considered upon confirmation from the patient's clinician that the patient has experienced hematologic and/or cytogenic response and is expected to continue to do so

Recommended Dosing:

40 mg twice daily or 80 mg once daily.

Approval period for initials & renewals: 1 year

Axitinib
Brand(s): Inlyta
DOSAGE FORM/ STRENGTH: 1 mg, 5 mg tablet
Updated: March 15, 2021

For the treatment of advanced renal cell carcinoma (MRCC) in patients who meet the following criteria:

1. Axitinib is being requested as treatment for a patient with advanced renal cell carcinoma in one of the following settings:

    i) Axitinib is being used in treatment naïve patients as first line therapy in combination with pembrolizumab in patients with disease in any risk category (Note that in this first line setting, cabozantinib may be funded as second line following progression to axitinib);
    OR
    ii) As second line therapy after failure to sunitinib or pazopanib in patients with disease in any risk category (Note that in this second line setting, only one of axitinib OR nivolumab OR cabozantinib will be funded);
    OR
    iii) As third line therapy in patients in the intermediate or poor risk disease category who have progressed on combination therapy with ipilimumab and nivolumab in first line and sunitinib or pazopanib used in second line. (Note that in this third line setting, only one of axitinib or cabozantinib will be funded.)

2. Patients must have good performance status.

NOTES:
- When used in combination with pembrolizumab in the first line setting, patients who are intolerant to pembrolizumab may stop pembrolizumab and continue treatment with axitinib as monotherapy until disease progression or development of unacceptable toxicities.
- When used in combination with pembrolizumab in the first line setting, patients experiencing disease progression or unacceptable toxicities may be considered for cabozantinib in second line, however, only two lines of treatment will be funded in this setting.
- Case-by-case consideration may be provided for patient with MRCC who have used and progressed on publicly funded older treatment regimens for MRCC such as everolimus, sorafenib, temsirolimus and/or interferons.

Funded Dosing Regimen: 5 mg twice a day. Dose may be adjusted based on individual response and tolerability.

Renewal Criteria: Renewals will be considered in patients who have not experienced disease progression or unacceptable toxicity while being treated with axitinib.

Approval duration of initials and renewals: 1 year

Azacitidine
Brand(s): Onureg
DOSAGE FORM/ STRENGTH: 200 mg, 300 mg tablet
Updated: November 14, 2022

Initiation Criteria:
For maintenance treatment of adult patients with newly diagnosed acute myeloid leukemia (AML) following induction therapy with or without consolidation therapy in patients who meet ALL the following criteria;

1. 18 years of age or older; AND
2. Has newly diagnosed AML (de novo or secondary to prior myelodysplastic syndrome (MDS) or chronic myelomonocytic leukemia (CMML)) with intermediate- or poor-risk cytogenetics; AND
3. Ineligible for hematopoietic stem cell transplant (HSCT); AND
4. Patient is in first remission with complete remission (CR) or complete remission with incomplete blood count recovery (CRi) following induction therapy with or without consolidation chemotherapy; AND
5. Has Eastern Cooperative Oncology Group (ECOG) performance status less than or equal to 3; AND
6. Has adequate organ function; AND
7. Prescribed by a clinician with expertise in the diagnosis and treatment of AML.

Notes:

1. Oral azacitidine should be started within 4 months of achieving CR or CRi.
2. Patients with FMS-Like Tyrosine Kinase 3 (FLT3) mutation positive AML meeting the initiation criteria can be funded.
3. If the ANC is less than 500/mcL on Day 1 of a cycle, oral azacitidine should not be administered and the start of the cycle should be delayed until the ANC is 500/mcLor more.

Discontinuation criteria:

Oral azacitidine should be discontinued upon the occurrence of any of the following:

a. Disease relapse (i.e., appearance of >5% blasts in the bone marrow or peripheral blood)
b. Unacceptable toxicity
c. Patient becomes eligible (at the discretion of the treating clinician) for allogeneic bone marrow or stem cell transplantation during the treatment period

Azacitidine
Brand(s): Onureg
DOSAGE FORM/ STRENGTH: 200 mg, 300 mg tablet

Exclusion Criteria

1. Patients who are eligible for HSCT are not funded.
2. Patients with favourable risk genetics.
3. Maintenance following re-induction/re-consolidation in relapsed AML will not be funded.

Renewal Criteria

Renewal of funding will be considered for patient who do not meet any of the discontinuation criteria or exclusion criteria.

Lab reports to confirm that the patient has not relapsed must be submitted.

Approved Dose: Up to 300 mg orally once daily on Days 1 through 14 with each 28-days cycle.

Note that dose escalations to reinitiate remission in those experiencing a disease relapse will not be funded.
Approval duration (Initials and Renewals): 1 year

Belzutifan
Brand(s): Welireg
DOSAGE FORM/ STRENGTH: 40 mg Tablet
Effective date: November 25, 2024

Initiation criteria:

For the treatment of patients with von Hippel-Lindau (VHL) disease meeting ALL the following criteria:

1. 18 years of age or older: AND

2. Documented confirmation of a germline mutation and/or deletion of the VHL gene; AND

3. Patient with VHL disease-associated tumours not requiring immediate surgery that is associated with one or more of the following conditions:
a. non-metastatic renal cell carcinoma
b. central nervous system (CNS) hemangioblastomas
c. non-metastatic pancreatic neuroendocrine tumours (pNET);

AND
4. Provides the baseline radiographic report prior to initiation of treatment with belzutifan; AND

5. Belzutifan will be used as monotherapy; AND

6. Patient must have a good performance status; AND

7. Initiated by a specialist with expertise in the management of VHL disease-associated tumours.

Discontinuation criteria:
Funding of Belzutifan will be discontinued upon meeting any of the following scenarios:

1. Clinical disease progression (i.e. worsening of symptoms)
2. Radiographic disease progression with clinical disease progression
3. Patient develops metastatic RCC or metastatic pNET or another metastatic cancer
4. Patient experiences intolerable side effects to belzutifan therapy (e.g becoming transfusion dependent due to anemia)

Belzutifan

Brand(s): Welireg
DOSAGE FORM/ STRENGTH: 40 mg tablet

Renewal Criteria:

Renewal of funding will be approved in those who continue to use belzutifan as monotherapy for vHL disease-associated tumours and who do not meet the discontinuation criteria.

Patients with tumours in multiple sites, who demonstrate radiographic progression without clinical disease progression may continue on treatment with belzutifan if the clinician deems that the patient is continuing benefit from treatment.

Approved dose:

Up to 120 mg orally daily

Approval duration of initials and renewals: 1 year

Binimetinib
Brand(s): Mektovi
DOSAGE FORM/STRENGTH: 15 mg Tablet
Effective date: December 6, 2022

Initiation Criteria

For the mutation-targeted treatment of BRAF V600 mutation-positive locally advanced, unresectable melanoma or metastatic melanoma in patients who meet ALL the following criteria:

1. Binimetinib will be used in combination with encorafenib; AND
2. Has histologically confirmed BRAF V600 mutation positive locally advanced unresectable or metastatic cutaneous melanoma or unknown primary melanoma (stage IIIB, IIIC, or IV per AJCC); AND
3. Has not received a previous treatment (i.e. treatment naïve) for locally advanced or metastatic disease OR has progressed on a prior first line immunotherapy for locally advanced or metastatic disease; AND
4. Good performance status; AND
5. Has adequate organ, bone marrow and cardiac function; AND
6. Prescribed by a clinician with expertise in the diagnosis and management of melanoma.

Notes:

1. Binimetinib and encorafenib may be considered in patients who have previously received a BRAF inhibitor (BRAFi)/MEK inhibitor (MEKi) in the adjuvant setting if disease relapse occurs more than 6 months after completion of adjuvant BRAFi/MEKi treatment.
2. The Ministry will fund only one BRAF mutation targeted treatment/treatment regimen for locally advanced or metastatic melanoma.
3. If brain metastases are present, they should be treated or asymptomatic and stable.
4. For a time-limited period, requests in patients who have initiated another BRAFi or MEKi treatment regimen will be considered for a switch to encorafenib/bimetinib on a case-by-case basis upon having met the above initiation criteria at the time of BRAFi/MEKi initiation and ONLY IF there has been no disease progression.
5. Patients should be assessed for a response (as per RECIST 1.1) to treatment with encorafenib and binimetinib every 2 to 3 months.
6. Treatment should be discontinued in those who develop adverse reactions that do not resolve despite dose delays or dose reductions

Binimetinib
Brand(s): Mektovi
DOSAGE FORM/ STRENGTH: 15 mg capsule

Exclusion Criteria

1. Uveal or mucosal melanoma are not funded.
2. BRAF V600 negative, or wild type tumors, or unknown status will not be funded
3. Patients who have experienced disease progression on a BRAF targeted regimen for locally advanced or metastatic melanoma
4. Binimetinib monotherapy will not be funded.

Renewal requests:

Renewal of binimetinib in combination with encorafenib may be continued until evidence of disease progression or development of unacceptable toxicity requiring discontinuation.

A letter from the prescriber confirming no clinical or radiological disease progression by RECIST 1.1 should be included.

Recommended dose:

Binimetinib 45 mg twice daily in combination with Encorafenib 450 mg once daily

Approval duration (both initial and renewal requests):

6 months (patients should have their disease status assessed at least every 6 months)

Bosutinib
Brand(s): Bosulif
DOSAGE FORM/ STRENGTH: 100 mg, 500 mg tablet
(Last Update: September 3, 2020)

For the treatment of patients with Philadelphia chromosome-positive (Ph+) chronic myelogenous leukemia (CML) in patients meeting the following criteria;

1. 18 years of age or older; AND

2. Diagnosis of (Ph+) chronic phase, accelerated phase, or blast phase CML; AND

3. Bosutinib is used in one of the following clinical situations:

    i) As second line therapy after experiencing disease progression on imatinib, dasatinib, or nilotinib[1] in first line: OR

    ii) as third line therapy after experiencing disease progression to imatinib, dasatinib, nilotinib[1], or ponatinib in second line; OR

    iii) In patients who have not progressed on one or more prior TKIs but who have documented mutational drug resistance to imatinib, dasatinib, and/or nilotinib[1] which make them clinically inappropriate treatment choices; OR

    iv) In patients who have not progressed on one or more TKIs but have experienced unacceptable intolerance or toxicity to one prior TKI (i.e. imatinib, dasatinib, or nilotinib[1])

Exclusion Criteria:

1. Bosutinib will not be funded in combination with another oral TKI (e.g. imatinib, nilotinib, dasatinib, or ponatinib)
2. Bosutinib will not be funded as 4th line treatment for CML or beyond.

[1]Note that nilotinib is not funded in blast phase CML, therefore, considerations will only be applied for imatinib and dasatinib in patients with blast phase CML

Renewal criteria:

Renewal of funding will be considered upon confirmation from the patient's clinician that the patient has experienced hematologic and/or cytogenic response and is expected to continue to do so

Recommended Dosing: 500mg per day

Approval period for initials & renewals: 1 year

Brigatinib
Brand(s): Alunbrig
DOSAGE FORM/ STRENGTH: 30 mg, 90 mg, 180 mg tablet; 7x90 mg and 21x180 mg oral starter kit
Effective date: February 10, 2022

Initial Criteria

For the treatment of anaplastic lymphoma kinase ("ALK") – positive locally advanced (not amenable to curative therapy) or metastatic non-small cell lung cancer (NSCLC) in patients meeting ALL the following criteria;

1. 18 years of age or older; AND
2. Patient has not been treated with another ALK inhibitor for NSCLC; AND
3. Brigatinib is used as monotherapy; AND
4. Patient has good performance status.

Exclusion criteria:

1. Brigatinib will not be funded in patients who have experienced disease progression on an ALK inhibitor.
2. Brigatinib will not be funded as combination therapy with another ALK-inhibitor.

Notes:
1. Patients who have received chemotherapy or radiation therapy should wait 2 weeks before starting brigatinib.
2. On a time-limited basis, patients who have developed intolerances to crizotinib or alectinib used within a first line setting, and who meet the above criteria, may be considered for a switch to brigatinib on a case-by-case basis. Provide details of the intolerances including the grade of toxicity (as applicable) and reasons for the switch.

Renewal Criteria:

Ongoing funding will be considered in patients who have not experienced disease progression or unacceptable toxicities to treatment with brigatinib.

Recommended dose: Starting dose of 90 mg daily for the first 7 days and, if tolerated, dose increased to 180 mg daily.

Approval duration of initial and renewal requests: 1 year

Cabozantinib
Brand(s): Cabometyx
DOSAGE FORM/ STRENGTH: 20 mg, 40 mg, 60 mg tablet
Effective date: May 6, 2020 (mRCC); Updated: December 29, 2021 (HCC); February 8, 2024 (DTC); October 18, 2024 (mRCC)

Advanced Renal Cell Carcinoma

Initiation Criteria:

For the treatment of patients with advanced or metastatic renal cell carcinoma (RCC) meeting all of the following criteria prior to starting treatment with cabozantinib:

1. Patient is 18 years of age and older; AND
2. Diagnosed with advanced (i.e. not amenable to curative surgery or radiation therapy) or metastatic renal cell carcinoma (RCC); AND
3. Patient will be using cabozantinib in one of the following clinical settings:

i) As first line treatment in combination with nivolumab in patients with any risk category (i.e. good, intermediate or poor risk) (Note 1) who have not received prior systemic therapy for advanced or metastatic RCC (Note 2 and 3); OR

ii) As second line monotherapy treatment in patients with any risk category (i.e. good, intermediate or poor risk) (Note 1) after progression on sunitinib or pazopanib used as first line.
If used in this second line setting after monotherapy, only one of cabozantinib or axitinib or nivolumab will be funded.
OR

iii) As second line monotherapy treatment in patients with any risk category (i.e. good, intermediate or poor risk) (Note 1) after progression on a combination regimen of lenvatinib and pembrolizumab used as first line. In this setting, only one of cabozantinib or axitinib will be funded.
OR

iv) As second line monotherapy treatment in in patients with any risk category (i.e. good, intermediate or poor risk) (Note 1) after progression on a combination regimen of axitinib and pembrolizumab used as first line; OR

v) As third line monotherapy treatment in patients with any risk category (i.e. good, intermediate or poor risk) (Note 1) after progression on sunitinib or pazopanib in first line AND nivolumab monotherapy in second line. OR

vi) As third line monotherapy treatment in patients with intermediate or poor risk (Note 1) after progression on ipilimumab-nivolumab combination in first line and sunitinib or pazopanib in second line. If used in this third line setting, only one of cabozantinib or axitinib will be funded.

Cabozantinib
Brand(s): Cabometyx
DOSAGE FORM/ STRENGTH: 20 mg, 40 mg, 60 mg tablet

Exclusion Criteria:

1. Patients who have experienced progression on cabozantinib for advanced or metastatic RCC will not be considered for EAP reimbursement for retreatment with cabozantinib in a subsequent line.
2. Cabozantinib will not be funded for patients with advanced or metastatic RCC when used as fourth or later line therapy.*

*Case-by-case consideration may be provided for patients who have experienced disease progression or intolerance to everolimus or temsirolimus or sorafenib used for advanced or metastatic RCC.

Notes:

1. Patient's risk stratification as per the International Metastatic RCC Database Consortium (IMDC), however, other equivalent risk stratifications will be considered on a case-by-case basis.
2. Patients who have used pembrolizumab in the adjuvant setting will only be eligible for funding of first line combination of cabozantinib and nivolumab for advanced or metastatic RCC if they have experienced a disease-free interval of 6 months or longer after completion of adjuvant therapy. It should be noted that patients will only be eligible for one line of an immune checkpoint inhibitor-based therapy for advanced or metastatic RCC.
3. Patients who experience unacceptable toxicity to either cabozantinib or nivolumab may continue treatment with the other agent until disease progression (up to a maximum of 2 years for nivolumab).

Renewal criteria:

Renewals for cabozantinib will be considered until clinically meaningful disease progression or the patient has experienced unacceptable toxicity.

Recommended dose:

Requests for 20 mg should include reasons why the lower dosed tablets are required.

Monotherapy: Cabozantinib 60 mg daily as monotherapy.

Combination therapy: Cabozantinib 40 mg daily until disease progression with 240 mg of nivolumab intravenously every 2 weeks for a maximum period of 24 months

Approval duration (initials and renewals): 1 year

Cabozantinib
Brand(s): Cabometyx
DOSAGE FORM/ STRENGTH: 20 mg, 40 mg, 60 mg tablet

Advanced Hepatocellular Carcinoma

Initiation Criteria:

For the treatment of unresectable, advanced hepatocellular carcinoma (HCC) in adult patients meeting all of the following criteria prior to starting treatment with cabozantinib:

1. Patient is 18 years of age and older;**AND**
2. Cabozantinib will be used as monotherapy for HCC; **AND**
3. Cabozantinib will be used as second line therapy in a patient who has experienced disease progression during treatment with sorafenib OR lenvatinib for HCC; **AND**
4. Patient has good performance status with Eastern Cooperative Oncology Group (ECOG) Performance status less than or equal to 1; **AND**
5. Has a Child-Pugh class A liver function.

Exclusion criteria: Patients meeting any of the following criteria will not be funded:

1. Cabozantinib will not be funded in combination therapy with another therapy for HCC.
2. Cabozantinib will not be funded in patients with Child-Pugh class status of B or C.
3. Cabozantinib will not be funded as first-line therapy.

Notes

1. Only one of regorafenib or cabozantinib for the treatment of unresectable HCC will be funded in the second line setting.
2. Cabozantinib can be funded in patients who develop intolerances or toxicities to regorafenib and wish to switch to cabozantinib as long as they have not experienced disease progression on regorafenib and meet the initial funding criteria for cabozantinib.

Recommended dose: 60 mg orally once daily

Requests for 20mg and 40mg tablets should include reasons why the lower dosed tablets are required.

Cabozantinib
Brand(s): Cabometyx
DOSAGE FORM/ STRENGTH: 20 mg, 40 mg, 60 mg tablet

Renewal criteria:

Renewals will be considered until clinically meaningful disease progression[1] or the patient has experienced unacceptable toxicity.

Please provide radiographic and/or scan results indicating no progression.

[1] Evaluation according to Response Evaluation Criteria in Solid Tumors RECIST 1.1 criteria.

Duration of Approval for Initials and Renewals: 3 months

Cabozantinib for differentiated thyroid cancer

Initiation Criteria:

For the treatment of adult patients with locally advanced or metastatic differentiated thyroid carcinoma (DTC) who meet the following criteria:

1. Patient is 18 years of age or older; AND
2. Has locally advanced or metastatic differentiated thyroid carcinoma that is histologically or cytologically confirmed; AND
3. Patient's DTC is refractory or resistant to radioactive iodine (RAI) (Note 1); AND
4. Patient has been previously treated with at least one other vascular endothelial growth factor receptor (VEGFR)-targeted tyrosine kinase inhibitor (TKI) (Note 2); AND
5. Patient will be using cabozantinib meeting one of the following circumstances:

i) Patient is using cabozantinib as third line treatment after experiencing failure of, or resistance to first-line treatment with RAI (Note 1) and second line-treatment with lenvatinib or sorafenib (Note 2);
OR
ii) Patient is using cabozantinib as fourth line after experiencing failure or resistance to first line treatment with RAI (Note 1), then second line-treatment with lenvatinib or sorafenib (Note 2), and third-line treatment with selpercatinib;
AND

Cabozantinib
Brand(s): Cabometyx
DOSAGE FORM/ STRENGTH: 20 mg, 40 mg, 60 mg tablet

6. Patient has good performance status; AND

7. Cabozantinib is not being used in combination with other anticancer therapies for DTC: AND

8. Prescribed by an authorized prescriber with expertise in the management of thyroid cancer.

Renewal criteria:

Renewal of funding will be considered in patients who are not experiencing disease progression (Note 3) or unacceptable toxicity to cabozantinib.

Notes:

1. Patients with an intolerance, contraindication or deemed ineligible for the use of radioactive iodine therapy can be considered for funding on a case-by-case basis. Please provide details of the intolerance or contraindication with your request.

2. Although sorafenib is not funded for the treatment of DTC under the Ontario drug benefit program, patients who have used sorafenib for DTC rather than lenvatinib can be considered.

3. Response should be measured using clinical assessment, biochemical markers, and radiological imaging.

Recommended dose: Up to 60 mg once daily.

Requests for 20 mg and 40 mg tablets should include reasons why the lower dosed tablets are required.

Approval duration of initials and renewals: 1 year

Ceritinib
Brand(s): Zykadia
DOSAGE FORM/ STRENGTH: 150mg capsule

Initial Criteria:

For the treatment of anaplastic lymphoma kinase ("ALK") – positive locally advanced (not amenable to curative therapy) or metastatic non-small cell lung cancer (NSCLC) in patients meeting ALL the following criteria;

- Patient is using ceritinib as monotherapy; AND
- Ceritinib is being used as second line[1] therapy in patients who have experienced disease progression to crizotinib OR in patients who have experienced intolerance[2] to crizotinib.

Exclusion criteria:

- Ceritinib will not be funded if the patient has experienced disease progression while on an ALK inhibitor other than crizotinib.
- Ceritinib will not be funded beyond third line therapy .[2]

[1]Time-limited funding will be considered case-by-case in patients with ALK-positive NSCLC who have progressed on chemotherapy and crizotinib OR crizotinib and an immune checkpoint inhibitor commenced prior to the public funding of ceritinib.

[2]Include details of the intolerance including the grade of toxicity and reasons why crizotinib was not able to be used, particularly in situations where a toxicity was deemed to be grade 1 or 2.

Recommended dose: 450 mg daily (Product Monograph dose update December 2018)

Renewal Criteria:

Ongoing funding will be considered in patients who have not experienced disease progression or unacceptable toxicities to treatment with ceritinib.

Approval duration of initial and renewal requests: 1 year

Cobimetinib
Brand(s): Cotellic
DOSAGE FORM/ STRENGTH: 20 mg tablet

Initial criteria:

For the treatment of patients with previously untreated BRAF V600 mutation-positive unresectable stage III or stage IV melanoma who have a good performance status (ECOG ≤ 2).

- As first-line combination therapy with vemurafenib; AND
- If brain metastases are present, they should be asymptomatic or stable

Recommended Dose as combination dual therapy with Vemurafenib:
Cobimetinib 60 mg once daily for 21 days, followed by seven days off treatment; AND
Vemurafenib 960 mg twice daily for 28 days.
Both drugs are given until disease progression or unacceptable toxicity.

Renewal criteria:

Combination dual therapy may be continued until evidence of disease progression[1] or development of unacceptable toxicity requiring discontinuation.

[1] Letter from physician outlining radiological and clinical benefit requiring continuation of the drug and verification of no disease progression or development of unacceptable toxicity must be submitted.

Approval duration (both initial and renewal requests): 6 months (patients should have their disease status assessed at least every 6 months)

Exclusion Criteria:

- BRAF V600 negative, or wild type tumors, or unknown status will not be funded

Cobimetinib therapy will not be considered for funding in patients who have progressed on a prior BRAF inhibitor therapy used as monotherapy or in combination.

Crizotinib
Brand(s): Xalkori
DOSAGE FORM/ STRENGTH: 200 mg, 250 mg capsule
Updated December 4, 2020

Initial Criteria:

For the treatment of locally advanced (not amenable to curative therapy) or metastatic non-small cell lung cancer (NSCLC) in patients who meet the following criteria:

1. Crizotinib is being used as the first-line oral treatment for a patient with ROS1-positive NSCLC

   OR

   Crizotinib is being used as the first-line oral treatment for a patient with anaplastic lymphoma kinase (ALK)-positive NSCLC

   OR

   Crizotinib is being used as second line oral treatment for a patient with anaplastic lymphoma kinase (ALK)-positive NSCLC

   Note: Patients with ALK-positive NSCL who have progressed on Crizotinib in first line will not be eligible for funding in second line.

2. Patient has good performance status.

3. Patient is using crizotinib as monotherapy.

Renewal Criteria:

Renewals will be considered until clinically meaningful disease progression or the patient has experienced unacceptable toxicity.

Exclusion Criteria:

Crizotinib will not be funded as combination therapy with another treatment for the treatment of ROS1-positive NSCLC or for ALK-positive NSCLC.

Dosing: 250 mg orally twice daily

Approval duration of Initials and Renewals: 1 year

Dabrafenib
Brand(s): Tafinlar
DOSAGE FORM/ STRENGTH: 50 mg, 75 mg capsule
Effective date: August 19, 2014; Updated August 10, 2016; Updated January 7, 2020 (adjuvant)

Initial Criteria:

For the mutation-targeted treatment of patients with BRAF V600 mutation-positive unresectable melanoma or metastatic melanoma meeting the following criteria:

1. As monotherapy or as combination therapy with trametinib;
2. If brain metastases are present, they should be asymptomatic or stable

Requests in patients who have initiated another single-agent BRAF or MEK inhibitor therapy will be considered on a **case-by-case** basis ONLY IF there has been no disease progression.

Exclusion Criteria:

1. BRAF V600 negative, or wild type tumors, or unknown status will not be funded
2. Funding will not be considered in patients who have experienced progression on a BRAF mutation targeted therapy. The Ministry will fund only one BRAF mutation targeted treatment/treatment regimen.
3. May be sequenced after immunotherapies or other funded treatments, however, treatment beyond third line will not be considered for funding.

Renewal Criteria:

Therapy as monotherapy OR as combination dual therapy (as above) may be continued until evidence of disease progression[1] or development of unacceptable toxicity requiring discontinuation.

[1] Letter from physician outlining radiological and clinical benefit requiring continuation of the drug and verification of no disease progression must be submitted.

Approval duration (both initial and renewal requests): 6 months (patients should have their disease status assessed at least every 6 months)

Recommended Dose as Monotherapy:

150 mg twice daily until disease progression or development of unacceptable toxicity requiring discontinuation of dabrafenib

Recommended Dose as combination dual therapy with Trametinib:

Dabrabenib 150 mg twice daily and Trametinib 2mg once daily until disease progression or development of unacceptable toxicity requiring discontinuation

Dabrafenib
Brand(s): Tafinlar
DOSAGE FORM/ STRENGTH: 50 mg and 75 mg capsule

Adjuvant treatment of resected Stage III cutaneous melanoma

Initiation Criteria:

For the adjuvant treatment of resected Stage III cutaneous melanoma in patients meeting ALL the following criteria;

1. Dabrafenib is being used as combination therapy with Trametinib
2. Patient's cutaneous melanoma met the following requirements prior to resection:
    a. Histologically confirmed stage IIIA (limited to lymph node metastases of > 1 mm), IIIB, IIIC, or IIID cutaneous melanoma [8th edition of the American Joint Committee on Cancer staging system]
    b. BRAF V600 mutated (all BRAF V600 mutations)
3. Post-resection, clinical or radiographic confirmation of complete disease resection including absence of in-transit metastases must be provided.[1]
4. Eastern Cooperative Oncology Group (ECOG) Performance Status 0 to 2

[1]Micrometastatic lymph node involvement detected by sentinel lymph node biopsy will be allowed.

Exclusion Criteria:

1. Patients with stage IIIA cutaneous melanoma with lymph node metastases less than 1 mm.
2. Monotherapy with Dabrafenib
3. Combinations with other anticancer therapies

Recommended Dose in adjuvant therapy:

Dabrabenib 150 mg twice daily and Trametinib 2 mg once daily

Notes: Treatment administered post-resection until disease recurrence or unacceptable toxicity to a maximum of 12 months of treatment in total. (Note: 12 months refers to duration of adjuvant treatment accessed through all sources of funding (i.e. private and public).

Approval duration: Maximum of 12 months. Renewals are not considered.

Dabrafenib
Brand(s): Tafinlar
DOSAGE FORM/ STRENGTH: 50 mg and 75 mg capsule

Notes:

1. The Ministry will reimburse for provincially funded treatments for use in the adjuvant setting in patients with cutaneous melanoma for a total duration of up to 12 months. Overall access to adjuvant therapy will be limited to 12 months in total and combines the duration of use of all treatments administered in the adjuvant setting.

2. Funding will not be granted for dabrafenif-trametinib in patients who have used another treatment in the adjuvant setting for cutaneous melanoma for a duration of 3 months or longer.

3. A one-time switch to dabrafenif-trametinib in the adjuvant cutaneous melanoma setting will be permitted for BRAF-mutated patients who switch from another adjuvant treatment that has been used for less than 3 months and upon meeting the above funding criteria.

4. Patients who experience disease progression within 6 months of completion of adjuvant BRAF therapy will not be funded for another BRAF targeted therapy.

5. Switching to cobimetinib-vemurafenib from dabrafenib-trametinib will not be permitted in BRAF-positive patients.

Darolutamide
Brand(s): Nubeqa
DOSAGE FORM/ STRENGTH: 300 mg tablet
Effective date: June 8, 2021 (nmCRPC) Updated: March 8, 2024 (mCSPC)

High risk non-metastatic castration resistant prostate cancer

Initiation Criteria:

For the treatment of high risk non-metastatic castration resistant prostate cancer (nmCRPC) in patients who meet all the following criteria:

1. Patient using darolutamide (Nubeqa) in combination with androgen deprivation therapy (ADT); AND
2. Has no detectable distant metastases as determined by CT, MRI, or technetium-99m bone scan; AND
3. Patient has castrate resistant disease based on meeting all the following indicia observed while on continuous ADT treatment or post orchiectomy:
   - Castrate serum testosterone levels: AND
   - Biochemical progression defined as three (3) prostate-specific antigen (PSA) rises at least 1 week apart, with the last PSA greater than 2ng/mL (if the patient has a history of antiandrogen use, the most recent PSA value must be obtained at least 4 weeks after anti-androgen withdrawal); AND
4. Patient is at high risk for developing metastatic disease based on a prostate-specific antigen doubling time (PSADT) of less than or equal to 10 months during continuous ADT; AND
5. Has an Eastern Cooperative Oncology Group (ECOG) Performance Status less than or equal to 2.

Exclusion Criteria:

Patients meeting one or more of the below exclusion criteria will not be funded.

1. The patient received prior chemotherapy or immunotherapy for the treatment of prostate cancer, unless it was in the adjuvant or neoadjuvant setting completed more than 2 years previously.
2. The patient has experienced disease progression on prior treatment with Erleada (apalutamide) or Xtandi (enzalutamide)/
3. The patient has a high risk for disease progression by other definitions (such as a high Gleason score 8-10, high PSA level at diagnosis, etc.) AND has not had a PSA progression in the non-metastatic setting.

Darolutamide
Brand(s): Nubeqa
DOSAGE FORM/ STRENGTH: 300 mg tablet

Approved Dosage: 600 mg administered orally twice daily.

Notes:

1. The Ministry will fund only one of Nubeqa (darolutamide) or Erleada (apalutamide) or Xtandi (enzalutamide) in patients with non-metastatic castrate resistant prostate cancer.

2. While doses may be withheld or reduced to 300 mg twice daily to manage grade 3 toxicities until symptoms improve, treatment doses should be resumed at a dose of 600 mg twice daily.

3. Requests for Nubeqa in patients who initiated Erleada or Xtandi therapy in the nmCRPC setting and who have not had disease progression will be considered on a case-by-case basis.

4. Following progression on darolutamide in non-metastatic castrate resistant prostate cancer, the patient would not be eligible for darolutamide, apalatumide or enzalutamide in metastatic castrate resistant state.

Renewal Criteria:

Renewals will be considered in patients without evidence of radiographic disease progression or unacceptable toxicity while on Nubeqa therapy.

Approved Dosage: 600 mg administered orally twice daily.

Approval Duration of initials and renewals: 1 year

Darolutamide
Brand(s): Nubeqa
DOSAGE FORM/ STRENGTH: 300 mg tablet

Metastatic castration sensitive prostate cancer

Initiation Criteria:

For the treatment of metastatic castration sensitive prostate cancer (mCSPC) in patients who meet all of the following criteria:

1. Darolutamide is used in combination with docetaxel and an androgen deprivation therapy (ADT)[1]; AND
2. Metastatic lesions detected on technetium-99m bone scan, computed tomography (CT), and/or magnetic resonance imaging (MRI)[2]; AND
3. Castration sensitive as defined by the patient being treatment naïve to an ADT OR ADT initiated within the prior 6 months before start of therapy with darolutamide OR ADT was used in the neoadjuvant or adjuvant setting and the patient has not been treated with ADT for 12 months or more prior to start of darolutamide; AND
4. Has not experienced disease progression with another androgen receptor axis targeted therapy (ARAT) for castration sensitive prostate cancer; AND
5. Patient has good performance status and is deemed to be chemotherapy eligible.

[1]ADT is not required for patients with bilateral orchiectomy.

[2]Positron emission tomography (PET) imaging results may be considered.

Definitions for the purpose of the EAP funding criteria:

***ADT** – A first generation androgen deprivation therapy (e.g. goserelin, leuprolide, triptorelin, buserelin, degarelix)*

***ARI** - A second generation androgen receptor inhibitor (e.g. apalutamide, darolutamide, enzalutamide)*

***ARAT**- An androgen receptor axis targeted therapy (e.g. abiraterone, apalutamide, darolutamide, enzalutamide)*

The following baseline levels are to be provided with the initial application:
i) Number of metastatic lesions on bone scan and in soft tissues
ii)Testosterone level
iii) Baseline (pre-treatment) PSA level
iv) Pre-treatment Gleason score (optional)

Darolutamide
Brand(s): Nubeqa
DOSAGE FORM/ STRENGTH: 300 mg tablet

Notes:

1. Patients must not have received prior treatment with an androgen receptor axis–targeted therapy, chemotherapy, or immunotherapy for prostate cancer.

2. Patients who have previously progressed on an ARI for prostate cancer will not be eligible for darolutamide in mCSPC. The Ministry will fund only one of apalutamide or enzalutamide or darolutamide in patients with mCSPC.

3. Patients treated with apalutamide or enzalutamide as part of a clinical trial may be eligible for darolutamide in mCSPC and will be considered on a case-by-case basis.

4. Patients who progress on treatment with darolutamide, for mCSPC will not be eligible for another ARI in the metastatic castration resistant setting.

5. Patients who are currently on a treatment regimen with an ARAT for prostate cancer, must meet the initiation criteria if they wish to switch to publicly funded darolutamide for mCSPC.

6. Time limited funding consideration will be provided on a case-by case basis to add darolutamide in those patients who are using docetaxel in combination with ADT as long as there has been no progression and the treatment regimen has not been used for more than 6 months.

Approved Dosage for Initials and Renewals: 600 mg twice a day

(The dose of docetaxel used in combination with darolutamide should be based on the recommendations from the docetaxel product monograph or information from Ontario Health Cancer Care Ontario.)

Renewal Criteria:

Renewals will be considered in patients until disease progression (i.e. disease progression based on clinical, PSA and radiographic factors) or experiencing unacceptable toxicity due to darolutamide.

Exclusion Criteria: (Patients meeting any of the following will not be funded.)

1. Patients who have previously experienced disease progression on darolutamide or another ARI used in the setting of prostate cancer.
2. Darolutamide will not be funded as combination therapy with another ARAT.

Duration of initial and renewal approvals: 1 year

Dasatinib

Brand(s): Sprycel and generics (see formulary for list of funded generics)
DOSAGE FORM/ STRENGTH: 20 mg, 50 mg, 70 mg, 100 mg tablet

For the treatment of Philadelphia chromosome positive (Ph+) chronic myelogenous leukemia (CML) in the chronic phase.[1]

Dosing recommendation: 100 mg per day.

Renewals will be considered for patients who have experienced hematologic and/or cytogenic response and is expected to continue to do so.

Duration of Approval: 1 Year

Exclusion criteria:

Combination treatment with any two or more of the oral tyrosine-kinase inhibitors (TKI) (i.e. imatinib, nilotinib or dasatinib) will not be funded.

[1]Note: Funding is only considered for any two oral TKIs* per patient in a lifetime for chronic phase CML (*TKIs: imatinib, nilotinib, or dasatinib). If a patient develops grade 3 or grade 4 toxicity on one of the listed TKI's within 3 months of initiating therapy, funding for a third oral TKI will be allowed.

For the treatment of patients with accelerated phase or blast phase Philadelphia chromosome positive (Ph+) chronic myelogenous leukemia (CML) with documented resistance[1] or intolerance[2] (as defined below) to imatinib therapy

Dosing recommendation: 140 mg per day.

Definitions of resistance and intolerance:

[1]Imatinib resistance is defined as primary or acquired resistance to imatinib at doses of at least 600 mg/day or through a mutational analysis report.

[2]Intolerance to imatinib (at any dose) is defined as persistent grade 3 or grade 4 toxicity requiring discontinuation of therapy.

Renewals will be considered for patients who have experienced hematologic and/or cytogenic response and are expected to continue to do so.

Duration of Approval: 1 Year

Dasatinib

Brand(s): Sprycel and generics (see formulary for list of funded generics)
DOSAGE FORM/ STRENGTH: 20 mg, 50 mg, 70 mg, 100 mg tablet

Exclusion criteria:

- Combination treatment with any 2 or more of the oral TKIs (i.e. imatinib, nilotinib or dasatinib) will not be funded.

- Dasatinib is not funded as a sequential third line therapy in patients who experience primary or acquired resistance (not including mutational resistance) to nilotinib.

For the treatment of Philadelphia chromosome positive acute lymphoblastic leukemia (Ph+ ALL) in patients meeting the following criteria:

i) An adult patient with Philadelphia chromosome positive acute lymphoblastic leukemia (Ph +ALL); AND

ii) Patient's disease is resistant[1] to imatinib-containing chemotherapy (patient must have tried 600 mg/day); O

iii) Patient has experienced intolerance[2] to imatinib therapy.

[1]Imatinib resistance is defined as primary or acquired resistance to imatinib at doses of at least 600 mg/day or through a mutational analysis report.

[2]Intolerance to imatinib (at any dose) is defined as the patient has experienced persistent grade 3 or grade 4 toxicity requiring discontinuation of therapy.

Renewals will be considered after confirmation from the patient's physician that the patient has benefited or continues to benefit from therapy with Sprycel and is expected to continue to do so.

Duration of Approval: 1 Year

Reimbursement of dasatinib for children with acute lymphoblastic leukemia will be considered on a case-by-case basis.

Decitabine and Cedazuridine
Brand(s): Inqovi
DOSAGE FORM/STRENGTH: 35 mg/100mg tablet
Effective date: December 19, 2022

Initiation Criteria:

For the treatment of adult patients with myelodysplastic syndromes (MDS) who meet ALL the following criteria;

1. 18 years of age or older; AND
2. Has International Prognostic Scoring System (IPSS) intermediate-1, intermediate-2, and/or high-risk MDS (see Note 1); AND
3. Has adequate organ function; AND
4. Inqovi is used as monotherapy; AND
5. Prescribed by a clinician with experience in the diagnosis and treatment of MDS.

Notes:

1. Patient may have previously treated or untreated, de novo or secondary MDS, including all French-American-British (FAB) subtypes (Refractory anemia (RA),refractory anemia with ringed sideroblasts (RARS), refractory anemia with excess blasts (RAEB), and chronic myelomonocytic leukemia (CMML).
2. Inqovi may be used as a bridge to hematopoietic stem cell transplant (HSCT) in patients with MDS who are transplant eligible.
3. Inqovi can be used as a bridge to intensive chemotherapy (with curative intent) for MDS.
4. In patients with MDS with deletion 5q chromosome, Inqovi should be used only if lenalidomide is not appropriate or after progression on lenalidomide.
5. Time-limited access to Inqovi will be provided for patients currently receiving treatment with azacitidine for MDS who wish to switch to Inqovi as long as criteria are met and there is no evidence of disease progression on azacitidine.

Renewal Criteria: Renewals will be considered until disease progression or development of unacceptable toxicities requiring discontinuation.

Exclusion Criteria

1. Patients with MDS who have experienced disease progression while on a hypomethylating agent (e.g. azacitidine, decitabine) for MDS will not be eligible for treatment with Inqovi.
2. Inqovi is not funded for the treatment of acute myeloid leukemia (AML).
3. Inqovi is not funded for patients with low-risk MDS.

Decitabine and Cedazuridine
Brand(s): Inqovi
DOSAGE FORM/ STRENGTH: 35 mg/100 mg tablet

Recommended dose: 1 tablet containing (35 mg of decitabine and 100 mg of cedazuridine) orally once daily on Days 1 through 5 of each 28-day cycle until disease progression or unacceptable toxicity

Approval duration (initials and renewals): 1 year

Encorafenib
Brand(s): Braftovi
DOSAGE FORM/STRENGTH: 75 mg capsule
Effective date: December 6, 2022 Updated January 10, 2024

Encorafenib for Colorectal, Small Bowel or Appendiceal cancers

Initiation Criteria:

For the treatment of patients with **previously treated metastatic colorectal cancer (mCRC)** with a BRAF V600E mutation as combination therapy with cetuximab in patients meeting ALL the following criteria;

1. Documented BRAF V600E-mutated mCRC detected by a validated test; AND
2. Has received at least 1 previous systemic treatment for mCRC but the previous treatment received was not with an epidermal growth factor receptor (EGFR) inhibitor or a BRAF inhibitor; AND
3. Patients must have good performance status (Eastern Cooperative Oncology Group (ECOG) equal to or less than 2); AND
4. Patients must have adequate organ function; AND
5. Encorafenib must be used in combination with cetuximab; AND
6. Prescribed by a clinician with expertise in the diagnosis and treatment of colorectal cancer.

Notes:

1. Patients with metastatic small bowel adenocarcinoma or appendiceal adenocarcinoma may be considered case-by-case for funding of encorafenib provided all other eligibility criteria are met.
2. Combination therapy of encorafenib and panitumumab may be considered as an option to combination with cetuximab.
3. Patients should be assessed clinically every 2 to 4 weeks, with radiological assessments performed every 8 to 12 weeks.

Encorafenib
Brand(s): Braftovi
DOSAGE FORM/ STRENGTH: 75 mg capsule

4. In the event that encorafenib or cetuximab is discontinued due to unacceptable toxicity, the other drug must also be discontinued.
5. For a time-limited period, patients who are using cetuximab or panitumumab for mCRC who have not experienced disease progression on their current regimen and otherwise meet the above initiation criteria, may change their treatment regimen to add encorafenib to be used as dual combination therapy with cetuximab or panitumumab.

Exclusion Criteria;

1. Patients with other types of BRAF mutations or whose BRAF status cannot be determined will not be funded.
2. Encorafenib will not be funded as first line treatment for mCRC.
3. Encorafenib will not be funded as monotherapy.

Renewal Criteria:

Combination dual therapy may be continued until evidence of disease progression based on RECIST criteria as determined by radiographic scans or development of unacceptable toxicity due to encorafenib or cetuximab (or panitumumab as applicable).

Approved dose: 300 mg orally once daily.

Approval duration: 1 year

Encorafenib
Brand(s): Braftovi
DOSAGE FORM/ STRENGTH: 75 mg capsule

Encorafenib for Melanoma

Initiation Criteria:

For the mutation-targeted treatment of BRAF V600 mutation-positive locally advanced, unresectable melanoma or metastatic melanoma in patients who meet ALL the following criteria:

1. Encorafenib will be used in combination with binimetinib; AND
2. Has histologically confirmed BRAF V600 mutation positive locally advanced unresectable or metastatic cutaneous melanoma or unknown primary melanoma (stage IIIB, IIIC, or IV per AJCC); AND
3. Has not received a previous treatment (i.e. treatment naïve) for locally advanced or metastatic disease OR has progressed on a prior first line immunotherapy for locally advanced or metastatic disease; AND
4. Good performance status; AND
5. Has adequate organ, bone marrow and cardiac function; AND
6. Prescribed by a clinician with expertise in the diagnosis and management of melanoma.

Notes:
1. Encorafenib and binimetinib may be considered in patients who have previously received a BRAF inhibitor (BRAFi)/MEK inhibitor (MEKi) in the adjuvant setting if disease relapse occurs more than 6 months after completion of adjuvant BRAFi/MEKi treatment.
2. The Ministry will fund only one BRAF mutation targeted treatment/treatment regimen for locally advanced or metastatic melanoma.
3. If brain metastases are present, they should be treated or asymptomatic and stable.
4. For a time-limited period, requests in patients who have initiated another BRAFi or MEKi treatment regimen will be considered for a switch to encorafenib/bimetinib
5. on a case-by-case basis upon having met the above initiation criteria at the time of BRAFi/MEKi initiation and ONLY IF there has been no disease progression.
6. Patients should be assessed for a response (as per RECIST 1.1) to treatment with encorafenib and binimetinib every 2 to 3 months.
7. Treatment should be discontinued in those who develop adverse reactions that do not resolve despite dose delays or dose reductions.

Encorafenib
Brand(s): Braftovi
DOSAGE FORM/ STRENGTH: 75 mg capsule

Exclusion Criteria

1. Uveal or mucosal melanoma are not funded.
2. BRAF V600 negative, or wild type tumors, or unknown status will not be funded
3. Patients who have experienced disease progression on a BRAF targeted regimen for locally advanced or metastatic melanoma.

Renewal requests:

Renewal of encorafenib in combination with binimetinib may be continued until evidence of disease progression or development of unacceptable toxicity requiring discontinuation.

A letter from the prescriber confirming no clinical or radiological disease progression by RECIST 1.1 should be included.

Recommended dose:

Encorafenib 450 mg once daily in combination with Binimetinib 45 mg twice daily

Approval duration (both initial and renewal requests): 6 months (patients should have their disease status assessed at least every 6 months)

Entrectinib
Brand(s): Rozlytrek
DOSAGE FORM/STRENGTH: 100 mg, 200 mg capsule
Effective date: December 23, 2021

Initial Criteria:

For the treatment of locally advanced (not amenable to curative therapy) or metastatic non-small cell lung cancer (NSCLC) in patients who meet the following criteria:

1. Entrectinib is being used as the first-line oral treatment for a patient with ROS1-positive NSCLC[1]; AND

2. Patient has good performance status; AND

3. Patient is using entrectinib as monotherapy.

[1]Include the ROS1 laboratory report with the application.

Renewal Criteria:

Renewals will be considered until clinically meaningful disease progression or the patient has experienced unacceptable toxicity.

Exclusion Criteria:

1. Entrectinib will not be funded as combination therapy with another treatment for the treatment of ROS1-positive NSCLC.

2. Entrectinib will not be funded in patients who have previously experienced disease progression while on crizotinib for ROS1-positive NSCLC.

Notes:

1. Patients who have initiated on a first-line platinum-based doublet chemotherapy, chemotherapy-immunotherapy combination, or single agent immunotherapy and have not progressed, may be considered for entrectinib if they have not received an ROS-1 targeted treatment previously.

Approved Dose: Maximum of 600 mg orally once daily

Approval duration of Initials and Renewals: 1 year

Entrectinib
Brand(s): Rozlytrek
DOSAGE FORM/STRENGTH: 100 mg, 200 mg capsule
Effective date: May 16, 2023

Rozlytrek for NTRK gene fusion tumours:

For the treatment of adult patients with unresectable locally advanced, or metastatic solid extracranial tumours in patients meeting ALL the following criteria:

1. Tumour is documented to have a neurotrophic tyrosine receptor kinase (NTRK) gene fusion without a known acquired resistance mutation; AND
2. Has failed all standard treatment for their tumour site; AND
3. Where surgery is not an option as it may lead to substantial morbidity; AND
4. Patient has a good performance status (i.e. an Eastern Cooperative Oncology Group (ECOG) Performance Status of 0 to 2); AND
5. Entrectinib should be administered as monotherapy

Exclusion: Entrectinib will not be funded in patients who have experienced disease progression on an NTRK inhibitor

Notes:

1. The patient's NTRK gene fusion report must be submitted with the application.
2. The patient's baseline radiographic evaluation (i.e. CT and/or MRI) should be provided on the initial funding application to EAP.
3. Reimbursement with entrectinib can include patients meeting the above initiation criteria who have brain metastases that are controlled or asymptomatic but entrectinib should not be initiated in patients who have primary CNS tumours.

Renewal Criteria:

Renewals will be considered in patients who have not experienced disease progression or unacceptable toxicities requiring discontinuation while on entrectinib.

Please provide radiographic and/or scan results indicating no progression with requests for renewal of funding.

Evaluation according to modified Response Evaluation Criteria in Solid Tumors (mRECIST) or RECIST 1.1 criteria and Response Assessment in Neuro-Oncology for CNS tumours.

Approved dose: Up to 600 mg orally once daily
Approval duration of initials: 3 months
Approval duration of first renewal: 3 months
Approval duration of 2nd renewal: 6 months
Approval duration of 3rd and subsequent renewals: 1 year

Enzalutamide
Brand(s): Xtandi
DOSAGE FORM/STRENGTH: 40 mg capsule
Updated: December 1, 2021

Initiation criteria for metastatic castration sensitive prostate cancer (mCSPC):

For the treatment metastatic castration sensitive prostate cancer (mCSPC) in patients who meet all of the following criteria:

1. Enzalutamide is used in combination with androgen deprivation therapy (ADT)[1]; AND
2. Metastatic lesions detected on technetium-99m bone scan, computed tomography (CT), and/or magnetic resonance imaging (MRI); AND
3. Castration sensitive as defined by the patient being treatment naïve to an ADT OR ADT initiated within the prior 6 months before start of therapy with enzalutamide OR ADT used in the neoadjuvant or adjuvant setting where the patient has been off treatment for 12 months or more prior to start of enzalutamide; AND
4. Has not experienced disease progression with another an androgen receptor axis targeted therapy (ARAT) for castration sensitive prostate cancer; AND
5. Patient has good performance status.

[1]ADT is not required for patients with bilateral orchiectomy

Definitions for the purpose of the EAP funding criteria:

***ADT** – A first generation androgen deprivation therapy (e.g. goserelin, leuprolide, triptorelin, buserelin, degarelix)*

***ARI**- A second generation androgen receptor inhibitor (e.g. apalutamide, darolutamide, enzalutamide)*

***ARAT**- An androgen receptor axis targeted therapy (e.g. abiraterone, apalutamide, darolutamide, enzalutamide)*

The following baseline levels are to be provided with the initial application;

i) Number of metastatic lesions on bone scan and in soft tissues

ii) Testosterone level

iii) Baseline (pre-treatment) PSA level

iv) *Pre-treatment Gleason score (optional)*

Enzalutamide
Brand(s): Xtandi
DOSAGE FORM/STRENGTH: 40 mg capsule

Notes:

1. Patients who have previously progressed on a second-generation androgen receptor inhibitor (e.g. apalutamide, enzalutamide, darolutamide) for prostate cancer will not be eligible for enzalutamide in mCSPC. The Ministry will fund only one of enzalutamide or apalutamide in patients with mCSPC.

2. Patients treated with apalutamide or darolutamide as part of a clinical trial may be eligible for enzalutamide and will be considered on a case-by-case basis.

3. Patients who progress on treatment with enzalutamide or apalutamide mCSPC will not be eligible for enzalutamide in the metastatic castration resistant setting.

4. Patients who are currently on a treatment regimen with an androgen receptor axis targeted therapy (e.g. abiraterone or a second-generation androgen receptor inhibitor) for prostate cancer, must meet the initiation criteria if they wish to switch to publicly funded enzalutamide for mCSPC.

5. Time limited funding consideration will be provided on a case-by case basis for those patients who are using docetaxel in combination with ADT as long as there has been no progression and the treatment regimen has not been used for more than 6 months.

Approved Dosage: 160 mg administered orally once daily.

Renewal Criteria:

Renewals will be considered in patients until disease progression (i.e. PSA elevation in addition to radiographic disease progression, or PSA progression in addition to clinical symptoms associated with cancer progression), development of castration resistant disease, or experiencing unacceptable toxicity while on enzalutamide.

Exclusion Criteria: (Patients meeting any of the following will not be funded.)

1. Patients who have previously experienced disease progression on enzalutamide or another ARI used in the setting of prostate cancer.

2. Patients who have risk factors for seizures

3. Enzalutamide will not be funded as combination therapy with another androgen receptor axis targeted therapy.

Approved Dosage for Initials and Renewals:160 mg administered orally once daily.
Duration of initial and renewal approvals: 1 year

Enzalutamide
Brand(s): Xtandi
DOSAGE FORM/STRENGTH: 40 mg capsule

Initiation Criteria for high risk non-metastatic castration resistant prostate cancer (nmCRPC):

For the treatment of high risk non-metastatic castration resistant prostate cancer (nmCRPC) in patients who meet all the following criteria:

1. Patient using Xtandi in combination with androgen deprivation therapy (ADT); AND

2. Has no detectable distant metastases as determined by CT, MRI, or technetium-99m bone scan; AND

3. Patient has castration resistant disease based on meeting all the following indicia observed while on continuous ADT treatment or post orchiectomy:

    - Castrate serum testosterone levels: AND

    - Biochemical progression defined as Three (3) prostate-specific antigen (PSA) rises at least 1 week apart, with the last PSA greater than 2ng/mL; and

4. Patient is at high risk for developing metastatic disease based on a Prostate-specific antigen doubling time (PSADT) of less than or equal to 10 months during continuous ADT.

5. Has an Eastern Cooperative Oncology Group (ECOG) Performance Status less than or equal to 2.

Approval Duration: 1 year

Exclusion Criteria:

1. The patient received prior chemotherapy for the treatment of prostate cancer, unless it was in the adjuvant or neoadjuvant setting.

2. The patient has previously experienced disease progression on apalutamide or **darolutamide** used for prostate cancer.

3. The patient has risk factors for seizures.

Enzalutamide
Brand(s): Xtandi
DOSAGE FORM/STRENGTH: 40 mg capsule

Definitions for the purpose of the EAP funding criteria:

***ADT** – A first generation androgen deprivation therapy (e.g. goserelin, leuprolide, triptorelin, buserelin, degarelix)*

***ARI**- A second generation androgen receptor inhibitor (e.g. apalutamide, darolutamide, enzalutamide)*

Approved Dosage: 160mg administered orally once daily

Notes:

1. The Ministry will fund only one second generation androgen receptor inhibitor (e.g. apalutamide, darolutamide, or enzalutamide) in patients with nmCRPC.

2. Patients who have progressed on enzalutamide in nmCRPC will not be eligible for enzalutamide in metastatic castration resistant prostate cancer (mCRPC).

3. Requests for enzalutamide in patients who have initiated another ARI therapy in the nmCRPC setting and who have not experienced disease progression will be considered on a case-by-case basis.

Renewal Criteria:

Renewals will be considered in patients without evidence of radiographic disease progression or unacceptable toxicity while on enzalutamide therapy.

Approval Duration: 1 year

Enzalutamide
Brand(s): Xtandi
DOSAGE FORM/STRENGTH: 40 mg capsule

Initiation criteria for metastatic castration resistant prostate cancer (mCRPC):

For the treatment of metastatic castration resistant prostate cancer (mCRPC) in patients meeting the following criteria:

1. Enzalutamide is used in combination with androgen deprivation therapy (ADT)[1]; AND
2. Metastatic lesions detected on a bone scan, computed tomography (CT), and/or magnetic resonance imaging (MRI); AND
3. Patient has castration resistant disease based on meeting the following indicia observed while on continuous ADT treatment or post orchiectomy:
4. Castrate serum testosterone levels; AND
5. Biochemical progression defined as three (3) prostate-specific antigen (PSA) rises at least 1 week apart, with the last PSA greater than 2ng/mL AND/OR radiographic progression of new or pre-existing disease as determined by the detection of 2 or more lesions on bone scan or presence of new soft tissue lesions by RECIST criteria; AND
6. Patient has progressed on a docetaxel-based chemotherapy
   OR
   Patient is using enzalutamide pre-docetaxel for metastatic castration resistant prostate cancer and has not previously experienced disease progression on enzalutamide or another second generation androgen receptor inhibitor (e.g. apalutamide, darolutamide,) used for prostate cancer
   OR
   Patient is using enzalutamide pre-docetaxel for mCRPC and has not previously experienced disease progression on abiraterone used in mCRPC sequenced immediately prior to enzalutamide;
   AND
7. Patient has good performance status defined as an Eastern Cooperative Oncology Group (ECOG) Performance status less than or equal to 2.

[1]ADT is not required for patients with bilateral orchiectomy

Definitions for the purpose of the EAP funding criteria:

***ADT** – A first generation androgen deprivation therapy (e.g. goserelin, leuprolide, triptorelin, buserelin, degarelix)*

***ARI**- A second generation androgen receptor inhibitor (e.g. apalutamide, darolutamide, enzalutamide)*

***ARAT**- An androgen receptor axis targeted therapy (e.g. abiraterone, apalutamide, darolutamide, enzalutamide)*

Enzalutamide
Brand(s): Xtandi
DOSAGE FORM/STRENGTH: 40 mg capsule

Notes:

1. Patients who have progressed on treatment with second generation androgen receptor inhibitors (e.g. apalutamide, enzalutamide, darolutamide) used in prior stages of prostate cancer will not be eligible for enzalutamide in the metastatic castration resistant setting.

2. Patients treated with apalutamide or darolutamide as part of a clinical trial may be eligible for enzalutamide and will be considered on a case-by-case basis.

3. Requests for enzalutamide in patients who initiated abiraterone therapy and who have not had disease progression while on abiraterone will be considered on a case-by-case basis.

Exclusion criteria: (Patients meeting any of the following will not be funded)

1. The patient has risk factors for seizures;

2. Enzalutamide will not be funded as combination therapy with another androgen receptor axis targeted therapy or cabazitaxel.

Renewals:

Renewals will be considered in patients who have not experienced disease progression while on enzalutamide therapy.

Approved Dosage for Initials and Renewals:160 mg administered orally once daily.

Duration of initial and renewal approvals: 1 year

Erlotinib

Brand(s): Tarceva and generics see formulary for a funded list of generics
DOSAGE FORM/ STRENGTH: 25 mg,100 mg, 150 mg tablet

For the treatment of clinically documented incurable progressive non-small cell lung cancer (NSCLC) where:

- Erlotinib is used as monotherapy for the 2nd- or 3rd-line treatment after failure of prior chemotherapy (any regimen) in patients 70 years of age or older.
- Erlotinib is used as monotherapy for the 2nd- or 3rd-line treatment of patients with clinically documented incurable progressive non-small cell lung cancer (NSCLC) despite prior chemotherapy including both docetaxel and a platinum-based treatment (i.e. cisplatin or carboplatin).
- Erlotinib is used as monotherapy for the 3rd-line treatment of patients with clinically documented incurable progressive non-small cell lung cancer (NSCLC) despite prior chemotherapy including both a platinum-based therapy (i.e. cisplatin or carboplatin) AND either pemetrexed or topotecan.
- Erlotinib is used as monotherapy for 2nd line treatment of NSCLC after 1st line platinum-based therapy, where no other chemotherapy will be given and erlotinib is used as the last treatment for the patient

Patients should be assessed for disease status at least every two months. Erlotinib should be discontinued if there is evidence of disease progression.

Note that erlotinib is not indicated and therefore, is not considered for reimbursement as 1st line therapy in treatment of NSCLC.

Requests for 2nd-line and 3rd-line use of erlotinib in patients 70 years of age or older and have not received treatment with either platinum-based combinations will be considered on a case-by-case basis.

Approved dosage: 150 mg/day

Duration of Approval: 6 Months

Renewal will be considered for patients who respond to therapy with no evidence of disease progression. Patients should be assessed for disease status at least every two months. Erlotinib should be discontinued if there is evidence of disease progression.

Duration of Approval: 6 Months

Everolimus

Brand(s): Afinitor and generics see formulary for a funded list of generics
DOSAGE FORM/ STRENGTH: 2.5 mg, 5 mg, 10 mg tablet

Noting that provincial funding algorithms for treatment of mRCC no longer list the use of everolimus within the funding sequence. EAP will apply the criteria as was originally intended case-by-case for received requests. You may wish to review the provincial mRCC algorithm when requesting an anticancer treatment for mRCC.

For the treatment of metastatic renal cell carcinoma (mRCC) as second or third line[1] therapy in patients previously treated for mRCC with a funded tyrosine kinase inhibitor (TKI).

Exclusion criteria: Use in the 4th line setting or later in the treatment course of their disease

Dosage: 10 mg daily

Renewal will be considered for those who have demonstrated benefit from Afinitor therapy (i.e. no disease progression) and is expected to continue to do so.

[1]Funded TKIs include sunitinib (Sutent), sorafenib (Nexavar), and pazopanib (Votrient). The criteria are derived from the review of everolimus for provincial funding for the treatment of MRCC at the time of the original review. Drugs that may have been used as standard treatment in first line may have included interferon and temserolimus. Everolimus is currently not funded after progression on axitinib (Inlyta) or nivolumab.

For the treatment of patients who have progressive, unresectable, well or moderately differentiated, locally advanced or metastatic pancreatic neuroendocrine tumors (pNET).

Patient must have an ECOG* ≤ 2 (prior to the start of Afinitor therapy).

*ECOG = Eastern Cooperative Oncology Group Status

Exclusion criteria: the patient's disease progressed while taking sunitinib (Sutent) to treat pNET.

Dosage: 10 mg daily

Duration of Approval: 1 year

Renewal will be considered for those who have benefited from Afinitor therapy (i.e. no disease progression) and is expected to continue to do so.

Reimbursement of Afinitor will be considered until disease progression occurs on Afinitor.

Duration of Approval: 1 year

Everolimus

Brand(s): Afinitor and generics (see formulary for a funded list of generics)
DOSAGE FORM/ STRENGTH: 2.5 mg, 5 mg, 10 mg tablet

For the treatment of unresectable, locally advanced or metastatic, well-differentiated non-functional neuroendocrine tumours (NETs) of gastrointestinal or lung origin (GIL) in adult patients meeting the following criteria:

- Documented radiological disease progression within six months; AND
- Good performance status (ECOG 0-2).

Treatment should continue until confirmed disease progression or unacceptable toxicity.

Renewals will be considered where the patient's physician has confirmed that the Patient has benefited or continues to benefit from therapy with Afinitor as evidenced by no disease progression, and that they are expected to continue to do so.

For the treatment of postmenopausal women with hormone-receptor positive, HER2 negative advanced breast cancer meeting the following criteria:

- Afinitor is to be used in combination with exemestane; AND
- Patient must have an ECOG* ≤ 2 after recurrence or progression following a non-steroidal aromatase inhibitor (NSAI).

  *ECOG = Eastern Cooperative Oncology Group Status

Dosage: 10 mg daily (dose titration is allowed).

Duration of Approval: 1 year

Renewals will be considered for patients who have benefited or continues to benefit from therapy with Afinitor and is expected to continue to do so.

Duration of Approval: 1 year

Everolimus

Brand(s): Afinitor and generics (see formulary for a funded list of generics)
DOSAGE FORM/ STRENGTH: 2.5 mg, 5 mg, 10 mg tablet

For the treatment of renal angiomyolipoma (AML) associated with tuberous sclerosis complex (TSC) in patients who meet all the following conditions:

(i) Presence of coalescent or multifocal AMLs in either one or both kidneys; AND

(ii) AML progression despite previous embolization and/or surgery; AND

(iii) Further embolization and/or surgery is not recommended due to a documented clinical reason (Note: The physician must submit a clinical note with the request outlining/detailing why invasive therapy cannot be considered);

The approved dosage: 10 mg orally once daily.

Duration of Approval: 1 year

Case-by-Case consideration will be considered in patients who have never been treated with invasive procedures such as embolization and/or surgery. The physician must provide detailed clinical rationale (e.g., from clinical consultation notes) as to why embolization and/or nephrectomy would be medically contraindicated for the patient.

Renewals will be considered in patients with the following documented benefits from therapy;

No AML progression (i.e. no significant new lesions and increase in kidney volume, as well as no significant AML related bleeding);

AND

There is a reduction in volume of AMLs identified prior to treatment with the everolimus.

Duration of Approval: 2 years

Everolimus

Brand(s): Afinitor and generics (see formulary for a funded list of generics)
DOSAGE FORM/ STRENGTH: 2.5 mg, 5 mg, 10 mg tablet

For the treatment of Subependymal giant cell astrocytoma (SEGA) associated with tuberous sclerosis complex (TSC) for whom surgical resection cannot be considered* for reasons such as:

- Location, size, and/or distribution of tumour(s); OR
- SEGA progression despite previous surgical interventions; OR
- Neurocognitive problems/ other complications secondary to previous surgical interventions.
- *Requests must provide details/ consultation notes outlining why the patient cannot be considered for surgical treatment.

Duration of Approval: 1 year

Renewals will be considered in patients with the following documented benefits from therapy:

- Stabilization of SEGA progression (based on assessment of SEGA volume and/or appearance of new lesions); AND
- Improvement of symptoms (e.g., reduced seizure frequency and decreased need for neurosurgical intervention).

Duration of Approval: 2 years

Fedratinib
Brand(s): Inrebic
DOSAGE FORM/ STRENGTH: 100 mg capsule
Effective date: September 8, 2022

Initiation criteria:

For the treatment of splenomegaly and/or disease related symptoms of myelofibrosis in patients meeting the following criteria:

1. Patient is 18 years of age or older; AND
2. Has been diagnosed with one of the following conditions which have resulted in the splenomegaly and/or other constitutional symptoms
    a. intermediate-2 or high risk primary myelofibrosis
    b. post-polycythemia vera myelofibrosis
    c. post-essential thrombocythemia myelofibrosis. AND
3. Has a contraindication to ruxolitnib or has developed intolerances to ruxolitinib but has not experienced disease progression while on ruxolitinib; AND
4. Has a good performance status; AND
5. Patient is using fedratinib under the care of a clinician who is experienced in the treatment of myelofibrosis.

Notes:

- The details of contraindications and intolerances are to be included with the application
- Patients should have documented improvement of spleen size or constitutional symptoms within 6 months of start of fedratinib.
- Patients should be monitored every 3 to 6 months.
- Treatment with fedratinib should be discontinued in patients who demonstrate progressive increase in spleen size, return of constitutional symptoms, development of serious adverse events

Exclusion criteria:

- Fedratinib will not be funded in patients who have experienced disease progression while on ruxolitinib.
- Fedratinib will not be funded in combination with another Janus kinase (JAK) inhibitor or other therapies used to treat MF

Approved dose: Up to 400 mg daily

Renewal Criteria:

Renewal of funding will continue in patients who have demonstrated response to treatment until any one of the following are demonstrated; progressive increase in spleen size, return of constitutional symptoms, or development of serious adverse events.

Approval duration of initials: 7 months; approval duration of renewals: 1 year

Gefitinib

Brand(s): Iressa and generics (see formulary for funded OFIs)
DOSAGE FORM/ STRENGTH: 250 mg tablet

For the first line, monotherapy treatment of locally advanced (not amenable to curative therapy) or metastatic non-small cell lung cancer (NSCLC) in patients who have activating mutations of epidermal growth factor receptor-tyrosine kinase (EGFR-TK). (i.e. Patients who are EGFR Positive)

The patient is to be assessed for disease status at least every two months and treatment will be discontinued if there is evidence of disease progression.

Dose Reimbursed: 250 mg orally once daily.

Duration of Approval: 6 months

Iressa will not be granted funding in the following circumstances;

Patients with EGFR wild-type mutation (i.e. negative for mutation);

Patients with EGFR unknown mutation;

2nd or 3rd line or maintenance NSCLC; or

Patients with unknown EGFR status who start their first chemotherapy while waiting for EGFR testing, then are found/confirmed to be EGFR positive, should continue with the current therapy and will not be eligible for gefitinib (Iressa) in this setting.

Patients who receive gefitinib (Iressa) first line are not eligible for erlotinib in the second- or third-line in the setting of maintenance therapy of NSCLC.

Requests for gefitinib for patients who have initiated another EGFR TKI therapy (i.e. Afatanib [Giotrif]) in the first line setting and who have not had disease progression will be considered on a case-by-case basis.

Renewal will be considered for patients until there is any evidence of disease progression, at which point, treatment with gefitinib (Iressa) must be discontinued. Patients must have their disease status assessed at least every two months.

Dose Reimbursed: 250 mg orally once daily.

Duration of Approval: 6 months

Gilteritinib
Brand(s): Xospata
DOSAGE FORM/ STRENGTH: 40 mg tablet
Effective date: December 1, 2021

Initiation Criteria:

For the treatment of adult patients diagnosed with relapsed or refractory FMS-like tyrosine kinase 3 (FLT3)-mutated acute myeloid leukemia (AML) who meet the following criteria;

1. Patient has relapsed or is considered to be refractory to a prior chemotherapy regimen used for AML.
2. FLT3 mutation with either a FLT3-ITD, FLT3-TKD/D835 or FLT3-TKD/I836 is confirmed by an approved test taken after relapse on a chemotherapy regimen; AND
3. Patient has good performance status (e.g. ECOG less than or equal to 2).

Exclusion criteria:(Requests meeting ANY of the following criteria will not be funded.)

1. Patients with therapy-related AML.
2. Patients who have had a prior relapse while being treated with gilteritinib or another tyrosine kinase inhibitor (TKI) specific to FLT3-mutated AML in the relapsed or refractory AML setting.
3. Gilteritinib is not funded for induction or consolidation therapy for AML (i.e. not funded for earlier lines of treatment prior to refractory or relapsed disease).

Renewal Criteria:

Treatment to continue until disease progression or until unacceptable toxicity occurs. At the time of renewal please include a brief summary of the clinical benefit that has been observed (e.g. partial or complete remission, reduction in transfusions etc.)

Notes:

A delay in clinical response can occur and it is recommended that treatment with gilteritinib be continued for a minimum of six months (i.e. in the absence of disease progression or unacceptable toxicity).

1. Patients may be considered to have refractory AML after progression on a minimum of one cycle of induction chemotherapy in accordance with the prescriber's clinical assessment.
2. Dose escalations to achieve complete remission will be permitted but dose should not be escalated after achieving complete remission.
3. Patients who receive gilteritinib in relapsed or refractory AML who progress to a hematopoietic stem cell transplant will be able to continue on gilteritinib as maintenance until disease progression.

Gilteritinib
Brand(s): Xospata
DOSAGE FORM/ STRENGTH: 40 mg tablet

For a time-limited period, patients currently receiving salvage chemotherapy for relapsed or refractory AML and patients in second hematologic relapse or later may be considered for funding on a case-by-case basis if they did not relapse on a prior TKI in the relapse/refractory setting if they have FLT3 mutated AML.

Recommended dose: 120mg once daily

Duration of approval of initial requests: 7 months

Duration of approval or renewals: 1 year

Ibrutinib
Brand(s): Imbruvica
DOSAGE FORM/ STRENGTH: 140 mg capsule

For the treatment of patients with chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL) who meet the following criteria;

i) Patient has received at least one prior therapy to treat CLL/SLL; AND

ii) Patient's prescriber has deemed that it would be inappropriate for the patient to receive treatment or retreatment with a fludarabine-based regimen.

Duration of Approval: 1 Year

Exclusion criteria:

Patients whose disease has progressed on idelalisib therapy in the relapsed setting are not eligible to receive iburitinib.

Renewals will be considered for patients who have not experienced disease progression while on ibrutinib (Imbruvica) therapy.

Duration of Approval: 1 Year

Initial criteria for Treatment naïve patients with high risk CLL/SLL (First-line therapy):

For patients with previously untreated chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL) who present with one of the following cytogenic markers:

- chromosome 17p deletion; OR
- TP 53 mutation; OR
- unmutated immunoglobulin heavy chain variable region (IgHV)

Renewal criteria :Patient has experienced no disease progression while on Imbruvica therapy.

Initial and renewal approval period: 1 year.

For treatment of patients with relapsed or refractory mantle cell lymphoma who have received at least one prior therapy.

Renewals will be considered if patient has experienced no disease progression while on Imbruvica therapy.

Initial and renewal approval period: 1 year.

Idelalisib
Brand(s): Zydelig
DOSAGE FORM/ STRENGTH: 100 mg, 150 mg Tablets

For the treatment of patients with relapsed chronic lymphocytic leukemia (CLL)/ small lymphocytic lymphoma (SLL) in combination with Rituximab.

Exclusion criteria:

Patients whose disease has progressed on ibrutinib therapy in the relapsed setting are not eligible to receive idelalisib.

Note: Patients who have experienced intolerance but not disease progression to ibrutinib in the relapsed setting may switch to idelalisib. Documentation on the nature of the intolerance is required.

Renewals will be considered for patient who has not experienced disease progression while on idelalisb (Zydelig) therapy.

Funded Dose:

Idelalisib will be funded in combination with up to 8 cycles of rituximab at the recommended dose of 150 mg orally twice daily and will continue following the completion of the rituximab portion of the regimen.

Imatinib (ODB formulary as general benefit)
Brand(s): Gleevec + generics (must meet generic substitution policies under ODB)
DOSAGE FORM/ STRENGTH: all available strengths

Imatinib is a general benefit drug under the ODB program. Refer to listed Health Canada indications for generic imatinib formulations. Patients must meet generic substitution policies for access to Gleevec.

Lapatinib
Brand(s): Tykerb
DOSAGE FORM/ STRENGTH: 250 mg tablet
Effective date: November 14, 2011

For the second-line treatment of HER2-positive metastatic breast cancer when used in combination with chemotherapy after previous exposure to trastuzumab-based treatments.

For the treatment of HER-2 positive metastatic breast cancer when used in combination with chemotherapy after use of trastuzumab in patients who have an adverse drug reaction or contraindication to trastuzumab therapy.

Lapatinib will not be considered in patients who meet the following exclusions:

- Lapatinib (Tykerb) will not be funded in combination with trastuzumab (Herceptin) for second-line HER-2 positive metastatic breast cancer.
- Patients who have progressed while on trastuzumab (Herceptin) for second-line treatment of HER-2 positive metastatic breast cancer, will not be eligible for funding of lapatinib (Tykerb)
- Lapatinib (Tykerb) will not be funded in the adjuvant settting.

Dosing schedule:

- 1250 mg (5 tablets) once daily in combination with capecitabine for days 1 to 14 (in a 21 day cycle) until disease progression, unacceptable toxicity, or withdrawal of consent

Note: Funding of second-line lapatinib for HER-2 positive metastatic breast cancer will be discontinued upon evidence of disease progression

Duration of Approval: 6 Months

Renewal will be considered for lapatinib until there is evidence of disease progression at which point the drug should be discontinued.

Duration of Approval: 6 Months

Larotrectinib
Brand(s): Vitrakvi
DOSAGE FORM/ STRENGTH: 25 mg, 100 mg capsules, 20 mg/mL oral liquid
Effective date: February 24, 2023

For the treatment of unresectable locally advanced, or metastatic solid tumours in patients meeting ALL the following criteria;

1. Tumour is documented to have a neurotrophic tyrosine receptor kinase (NTRK) gene fusion without a known acquired resistance mutation; AND
2. Has failed all standard treatment for their tumour site; AND
3. Is not a candidate for surgery and/or radiation as it may lead to substantial morbidity; AND
4. Has an Eastern Cooperative Oncology Group (ECOG) Performance Status of 0 to 2 for adults or 0 to 3 for children (<18 years old); AND
5. Larotrectinib is used as monotherapy.

Notes:
1. The patient's NTRK gene fusion report must be submitted with the application.
2. The patient's baseline radiographic evaluation (i.e. CT and/or MRI) should be provided on the initial funding application to EAP.
3. Patients with symptomatic brain metastases, unstable cardiovascular disease, or on treatments that are strong CYP3A4 inhibitors or inducers should be carefully considered and monitored.

Renewal Criteria:

Renewals will be considered in patients who have not experienced disease progression or unacceptable toxicities requiring discontinuation while on Larotrectinib.

Please provide radiographic and/or scan results indicating no progression with requests for renewal of funding.

Evaluation according to modified Response Evaluation Criteria in Solid Tumors (mRECIST) or RECIST 1.1 criteria and Response Assessment in Neuro-Oncology for CNS tumours.

Recommended dose:
- 100 mg orally twice daily in patients with Body Surface area (BSA) greater than or equal to 1 m^2
- 100 mg/m^2 orally twice daily for children (less than 18 years old) with BSA less than 1 m^2.

Approval duration of initials: 3 months

Approval duration of first renewal: 3 months

Approval duration of 2nd renewal: 6 months

Approval duration of 3rd and subsequent renewals: 1 year

Lenalidomide

Brand(s): Revlimid and generics (see formulary for funded OFIs)
DOSAGE FORM/ STRENGTH: 2.5mg, 5 mg,10 mg, 15 mg, 20 mg, 25 mg capsule
Updated: August 19, 2022

Effective with the April 29, 2022 formulary update, lenalidomide for the treatment of anemia due to myelodysplastic syndrome (MDS), for multiple myeloma as first line, relapsed refractory or as maintenance therapy may be accessed upon meeting limited use criteria on the Ontario Drug Benefit Formulary.

Requests not meeting LU criteria may be submitted to the Exceptional Access program to be evaluated on a case-by-case basis.

[1]Lenalidomide sensitive" is defined as a patient whose disease has not been refractory to a lenalidomide-based regimen and/or has not experienced disease progression while on a lenalidomide-based regimen.

Refractory disease is defined as;

i) disease progression within 60 days after stopping treatment while on lenalidomide (and/or bortezomib); or

ii) progression while on any dose of lenalidomide (and/or bortezomib) including while on maintenance therapy with these therapies; or

iii) non-responsive disease during therapy (either failure to achieve minimal response or experiencing disease progression)

iv) Patients who are refractory to lenalidomide will not be eligible for daratumumab or carfilzomib-based triplets that are used in combination with lenalidomide.

Progressive disease is defined as having one or more of the following;

i) An increase of 25% from lowest response value in serum M-component (the absolute increase must be greater than or the equal to 0.5g/dL), and/or urine M-component (the absolute increase must be greater than or equal to 200 mg/24 hours).

ii) An absolute increase of greater than 10mg/dL in the difference between involved and uninvolved FLC levels (if no measurable serum and urine M-protein levels).

iii) Definite development of new bone lesions or soft tissue plasmacytomas or definite increase in the size of existing bone lesions or soft tissue plasmacytomas.

iv) Development of hypercalcemia (corrected serum calcium greater than 11.5 mg/dL or 2.5 mmol/L) that can be attributed solely to the plasma cell proliferative disorder.

You may also wish to review the Ontario Health – Cancer Care Ontario website for information for funding of NDFP drugs used for the treatment of multiple myeloma.

Lenvatinib

Brand(s): Lenvima

DOSAGE FORM/ STRENGTH: 4 mg, 10 mg capsules (packaged as 4 mg, 8 mg, 10 mg, 14 mg, 20 mg, and 24 mg daily dose cartons.) (Note: 18 mg is not publicly funded) Updated March 5, 2020; Updated September 1, 2023 for 2 new indications

Initiation criteria for differentiated thyroid cancer (DTC):

For the treatment of patients with locally recurrent or metastatic, progressive, differentiated thyroid cancer (DTC) who meet ALL the following criteria:

- Papillary or Follicular subtypes of DTC that are histologically or cytologically confirmed; AND
- Thyroid cancer is refractory or resistant to radioactive iodine; AND
- DTC shows evidence of disease progression within the past 13 months; AND
- Patient has good performance status with ECOG less than or equal to 2; AND
- Lenvatinib is being used as monotherapy

Exclusion criteria:

- Patients with anaplastic or medullary thyroid cancer
- Patients who have received more than one prior therapy with a tyrosine kinase inhibitor

Duration of Approval: 1 Year

Renewal of funding will be considered until a patient progresses on treatment or develops unacceptable toxicity to lenvatinib.

Duration of Approval: 1 Year

Initiation criteria for advanced hepatocellular carcinoma (HCC)

For the treatment of unresectable advanced[1] hepatocellular carcinoma (HCC) in adult patients who meet ALL the following criteria prior to starting treatment with lenvatinib;

- Patient is 18 years of age or older; AND
- Lenvatinib will be used as monotherapy for HCC; AND
- Patient has good performance status with Eastern Cooperative Oncology Group (ECOG) Performance status less than or equal to 2; AND
- Has a Child-Pugh class A liver function.

[1] Patients with Stage B HCC, based on the Barcelona Clinic Liver Cancer (BCLC) Staging System will be considered for lenvatinib if they have progressed on transarterial chemoembolization (TACE). Case-by-case consideration will be provided for Stage B

Lenvatinib

Brand(s): Lenvima
DOSAGE FORM/ STRENGTH: 4 mg, 10 mg capsules (packaged as 4 mg, 8 mg, 10 mg, 14 mg, 20 mg, and 24 mg daily dose cartons) (Note: 18 mg is not publicly funded)

HCC patients who are not suitable for the TACE procedure. In such situations, please provide additional information to support why the patient is not suitable for TACE.

Exclusion Criteria: Patients meeting any of the following criteria will not be funded.

- Patients with Child-Pugh score greater than 6 (i.e. Child-Pugh class B or C) will not be funded.
- Patients who have progressed on sorafenib for HCC will not be funded for lenvatinib

Only one of sorafenib or lenvatinib for the treatment of HCC will be funded in the first line. Patients will be permitted to switch from sorafenib to lenvatinib if they experience intolerance and have not progressed on sorafenib.

Recommended Dosage:

The recommended daily dose of lenvatinib is 8mg once daily for patients with a body weight of <60kg and 12 mg once daily for patients with a body weight of ≥60 kg

Renewal Criteria:

Renewals will be considered for patients who have not experienced unacceptable toxicities to lenvatinib or until disease progression.

Please provide radiographic results, scan results or both indicating no progression. Progression evaluation will be in accordance with modified Response Evaluation Criteria in Solid Tumors (mRECIST) or RECIST 1.1 criteria.

Approval duration for initials and approvals : 3 months

Lenvatinib

Brand(s): Lenvima
DOSAGE FORM/ STRENGTH: 4 mg, 10 mg capsules (packaged as 4 mg, 8 mg, 10 mg, 14 mg, 20 mg, and 24 mg daily dose cartons) (Note: 18 mg is not publicly funded)

Initiation criteria for metastatic renal cell carcinoma (mRCC)

Lenvatinib will be funded for the treatment of advanced (not amenable to curative surgery or radiation) or metastatic renal cell carcinoma (mRCC) in patients who meet ALL the following criteria;

1. 18 years of age or older; AND
2. Has a confirmed diagnosis of advanced (not amenable to curative surgery or radiation) or metastatic renal cell carcinoma; AND
3. Patient is not a candidate for curative surgery or radiation; AND
4. Patient's disease in any international mRCC database consortium (IMDC) risk group category (Note 1); AND
5. Is using lenvatinib as first line in a patient who has not received a prior systemic therapy for advanced or metastatic renal cell carcinoma; AND
6. Lenvatinib is used in combination with pembrolizumab; AND
7. Patient has good performance status; AND
8. Prescribed by an expert in the diagnosis and management of renal cell carcinoma.

Note:

1. If an IMDC risk classification cannot be provided, the Memorial Sloan Kettering Cancer Center (MSKCC) risk group categories to confirm that the patient's disease is in any MSKCC risk group category may be used.
2. The Ministry will fund only one of pembrolizumab with lenvatinib or pembrolizumab with axitinib for mRCC.
3. Patients with stable or treated central nervous system (CNS) metastases may be considered provided all other eligibility criteria are met.

Exclusions:

Patients meeting any of the following criteria are not eligible for funding of lenvatinib.

1. Using in combination with another anticancer drug other than pembrolizumab.

Renewal Criteria:

Renewal of funding will be considered until disease progression or development of unacceptable toxicities.

Lenvatinib

Brand(s): Lenvima

DOSAGE FORM/ STRENGTH: 4 mg, 10 mg capsules (packaged as 4 mg, 8 mg, 10 mg, 14 mg, 20 mg, and 24 mg daily dose cartons) (Note: 18 mg is not publicly funded)

Recommended dose:

Lenvatinib: 20 mg orally daily modified as needed to manage adverse reactions.

Lenvatinib is continued as monotherapy following 35 cycles of pembrolizumab until disease progression or development of unacceptable toxicities.

Pembrolizumab is funded under the New Drug Funding Program (NDFP) and an application to NDFP will be required.

Pembrolizumab 2 mg/kg intravenously (IV) (up to a maximum of 200 mg) every 3 weeks OR Pembrolizumab 4 mg/kg IV (up to a maximum of 400 mg) every 6 weeks.

Up to a maximum of 2 years (up to 35 doses given every 3 weeks or 18 doses given every 6 weeks), whichever comes first.

Patients who complete 2 years of pembrolizumab without disease progression or recurrence on pembrolizumab may be considered for retreatment upon relapse and may receive up to an additional year of pembrolizumab, with or without lenvatinib, at the point of confirmed disease progression.

Approval Duration of initials and renewals: 1 year

Lenvatinib

Brand(s): Lenvima
DOSAGE FORM/ STRENGTH: 4 mg, 10 mg capsules (packaged as 4 mg, 8 mg, 10 mg, 14 mg, 20 mg, and 24 mg daily dose cartons) (Note: 18 mg is not publicly funded)

Initiation criteria for the treatment of advanced, recurrent, or metastatic, proficient mismatch repair (pMMR) endometrial carcinoma

Lenvatinib will be funded for the treatment of advanced, recurrent, or metastatic, proficient mismatch repair (pMMR) endometrial carcinoma in patients who meet ALL the following criteria;

1. 18 years of age or older; AND
2. Has a confirmed diagnosis of advanced, recurrent, or metastatic endometrial carcinoma that is deemed to be proficient mismatch repair (pMMR); AND
3. Documentation that endometrial carcinoma is not microsatellite instability high (MSI-H) disease; AND
4. Documentation that endometrial carcinoma is not mismatch repair deficient (dMMR) disease;AND
5. Patient is not a candidate for curative surgery or radiation; AND
6. Lenvatinib will be used in combination with pembrolizumab (Note 1 and dosing recommendations); AND
7. Has experienced disease progression (must be radiographically confirmed) after 1 prior systemic regimen using a platinum-based chemotherapy regimen (Note 2); AND
8. Must have a good performance status; AND
9. Prescribed by an expert in the diagnosis and management of endometrial carcinoma.

Notes:

1. Patients who have developed unacceptable toxicities to pembolizumab may continue with lenvatinib monotherapy and vice versa.
2. Patients who have received more than one prior line of platinum-based chemotherapy that is not in the neoadjuvant or adjuvant treatment settings may be considered on a case-by-case basis.
3. Patients with carcinosarcoma (also referred to as malignant mixed Müllerian tumor) will be eligible for funding provided all other eligibility criteria are met.
4. Patients with stable or treated central nervous system (CNS) metastases may be considered.

Exclusions:

Patients meeting any of the following criteria are not eligible for funding of lenvatinib.

1. Patients with sarcoma (e.g., endometrial leiomyosarcoma, endometrial stromal sarcoma).
2. Using in combination with another anticancer drug other than pembrolizumab.

Lenvatinib

Brand(s): Lenvima
DOSAGE FORM/ STRENGTH: 4 mg, 10 mg capsules (packaged as 4 mg, 8 mg, 10 mg, 14 mg, 20 mg, and 24 mg daily dose cartons) (Note: 18 mg is not publicly funded)

Renewal Criteria:

Renewal of funding will be considered until disease progression or development of unacceptable toxicities.

Recommended dose:

Lenvatinib: 20 mg orally daily modified as needed to manage adverse reactions.

Lenvatinib is continued as monotherapy following 35 cycles of pembrolizumab until disease progression or development of unacceptable toxicities.

Pembrolizumab is funded under the New Drug Funding Program (NDFP) and an application to NDFP will be required.

Pembrolizumab 2 mg/kg intravenously (IV) (up to a maximum of 200 mg) every 21 days (max of 35 cycles), or Pembrolizumab 4 mg/kg IV (up to a maximum of 400 mg) every 42 days (maximum of 18 cycles)

Patients who complete 2 years of pembrolizumab without disease progression may be considered for retreatment upon relapse and may receive up to an additional one year of pembrolizumab (i.e., 17 cycles if given every 3 weeks or 9 cycles if given every 6 weeks), with or without lenvatinib, at the point of confirmed disease progression

Approval Duration of initials and renewals: 1 year

Lorlatinib
Brand(s): Lorbrena
DOSAGE FORM/STRENGTH: 25mg, 200 mg tablets
Effective date: July 17, 2023

Initial Criteria:

For the treatment of anaplastic lymphoma kinase ("ALK") – positive locally advanced (not amenable to curative therapy) or metastatic non-small cell lung cancer (NSCLC) in patients meeting ALL the following criteria:

1. 18 years of age or older; AND
2. Patient has not been treated with prior systemic treatment for advanced or metastatic NSCLC; AND
3. Lorlatinib is used as monotherapy; AND
4. Patient has good performance status.

Exclusion criteria:

1. Lorlatinib will not be funded in patients who have experienced disease progression on an ALK inhibitor.
2. Lorlatinib will not be funded as combination therapy with another ALK-inhibitor.

Notes:

1. Patients who have received chemotherapy or radiation therapy before confirmation of ALK status, may switch to lorlatinib once ALK positivity is confirmed.
2. Lorlatinib should not be used in patients with severe acute or chronic medical or psychiatric conditions.
3. On a time-limited basis, patients who have developed intolerances to crizotinib, alectinib, or brigatinib used within a first line setting, and who otherwise meet the above criteria, may be considered for a switch to lorlatinib on a case-by-case basis. Provide details of the intolerances including the grade of toxicity (as applicable) and reasons for the switch.

Renewal Criteria:

Ongoing funding will be considered in patients who have not experienced disease progression or unacceptable toxicities to treatment with lorlatinib.

Recommended dose: 100 mg once daily

Approval duration of initial and renewal requests: 1 year

Midostaurin
Brand(s): Rydapt
DOSAGE FORM/ STRENGTH: 25 mg capsule

For the treatment of adult patients diagnosed with FMS-like tyrosine kinase 3 (FLT3)-mutated acute myeloid leukemia (AML) who meet ALL the following criteria:

- FLT3 mutation is confirmed by an approved test; AND
- Midostaurin is used as first-line[1] for FLT3-mutated AML; AND
- Midostaurin is used in combination with standard induction chemotherapy with cytarabine and daunorubicin followed by standard consolidation chemotherapy with cytarabine OR any 7+3 induction regimen containing idarubicin followed by standard consolidation chemotherapy with cytarabine.

Exclusion criteria:

Midostaurin will not be funded in the following situations:

- As maintenance therapy for AML;
- Patients who have developed therapy-related AML after radiation therapy or chemotherapy for another cancer or disorder;
- Patients receiving other induction chemotherapy regimens aside from those mentioned in the eligibility criteria or upon finishing the consolidation phase of treatment;
- Patients undergoing re-induction and/or re-consolidation.

Recommended Dose(s):

Induction dose: Midostaurin 50 mg twice daily on Days 8 to 21 with each cycle of induction cytarabine and daunorubicin.

A maximum of 2 induction cycles may be funded. (Note: EAP only considers funding of outpatient midostaurin usage.)*

Consolidation phase: Midostaurin 50 mg twice daily on days 8 to 21 of each cycle of consolidation with cytarabine.

A maximum of 4 consolidation cycles may be funded by EAP (for cycles administered as an outpatient)*.

Up to 2 cycles of induction and 4 cycles of consolidation may be funded in accordance with patient response to therapy.*

Midostaurin
Brand(s): Rydapt
DOSAGE FORM/ STRENGTH: 25 mg capsule

Approval duration: Up to 6 months (maximum of 2 cycles of induction and 4 cycles of consolidation)*

[1]For a short-term, time limited period, the Ministry will consider requests from prescribers who wish to add midostaurin to their patients' current regimens that have been initiated prior to the provincial funding of midostaurin. To be considered, patients must currently be on standard induction and consolidation chemotherapy, and have not experienced disease progression or unacceptable intolerance during the first-line treatment with the standard chemotherapies being used.

*EAP will provide coverage for midostaurin administered in the outpatient setting (e.g., consolidation cycles). Those responding to induction therapy may require ongoing access to midostaurin for the consolidation phase of treatment upon discharge from the hospital.

Nilotinib
Brand(s): Tasigna
DOSAGE FORM/ STRENGTH: 150 mg, 200 mg capsule

For the treatment of patients with chronic phase Philadelphia chromosome positive (Ph+) chronic myelogenous leukemia (CML).

*Note: Ministry will only fund any TWO of the oral Tyrosine Kinase inhibitors (TKIs) * used for chronic phase CML per patient in a lifetime. (* TKIs: imatinib, nilotinib, or dasatinib)*

If the patient develops grade 3 or 4 toxicity on one of the above TKI's within 3 months of initiating therapy, access to a 3rd oral TKI will be funded for that patient.

Approved dose: 300 mg twice daily but not exceeding 800 mg/day

Duration of Approval: 1 Year

Nilotinib
Brand(s): Tasigna
DOSAGE FORM/ STRENGTH: 150 mg, 200 mg capsule

For the treatment of patients with accelerated phase Philadelphia chromosome positive (Ph+) chronic myelogenous leukemia (CML) with documented intolerance[1] **or resistance**[2] **to imatinib therapy**.

[1]*Intolerance to imatinib at any dose occurs where the Patient has experienced persistent grade 3 or grade 4 toxicity requiring discontinuation of imatinib therapy; or*

[2]*Imatinib resistance occurs where the Patient has primary or acquired resistance to imatinib at doses of at least 600mg/day or via a mutational analysis report.*

Exclusion Criteria – Patients with the following exclusion criteria will not be funded:

blast phase CML;

a. for Ph+ acute lymphocytic leukemia (ALL);

b. combination treatment with any two or more oral TKIS's (imatinib, nilotinib, or dasatinib) will not be funded

c. For accelerated phase CML, nilotinib is not funded as a sequential third line therapy in patients who experience primary or acquired resistance (not including mutational resistance) to dasatinib.

   Approved dosage: Up to 800 mg/day but doses above 800 mg per day will not be considered

Renewal Criteria:

Renewals are considered for patients who experience hematologic and/or cytogenic response to therapy, is expected to continue to do benefit from therapy with Tasigna.

Duration of Approval: 1 Year

Niraparib
Brand(s): Zejula
DOSAGE FORM/ STRENGTH: 100 mg tablet
Effective date: December 21, 2021 Updated: September 27, 2023

Initiation Criteria:

For the maintenance treatment of newly diagnosed or recurrent high grade epithelial ovarian, fallopian tube, or primary peritoneal cancer in adult patients who meet the following criteria;

1. Patients are diagnosed with high grade serous or endometrioid tumours classified as stage III or IV disease according to the International Federation of Gynecology and Obstetrics (FIGO) criteria at the time of their initial diagnosis; AND

2. Patient is using niraparib as maintenance therapy immediately after one course of first line platinum-based therapy in which radiological response (complete or partial) is demonstrated after completing between 6 and 9 cycles of treatment,[1] OR

   Patient is using niraparib as maintenance therapy in recurrent disease after having received at least two prior courses of chemotherapy in which platinum sensitive disease[2] was demonstrated with at least one completed prior treatment course AND radiological response (complete or partial) must be demonstrated after completing at least 4 cycles of their most recent course of chemotherapy[3];

   AND

3. Patients using niraparib as maintenance as first line or in the recurrent/relapsed setting must initiate niraparib within 12 weeks of the final dose of the chemotherapy;[4]

   AND

4. Niraparib must be used as monotherapy for maintenance therapy; AND

5. Patient has good performance status.

[1]Case-by-case consideration will be provided for newly diagnosed patients who are unable to complete 6 cycles of a platinum-based treatment OR who are unable to use a platinum-based chemotherapy but have achieved complete or partial radiological response after treatment with alternative, non-platinum-based chemotherapy.

[2]Platinum-sensitive disease is defined as disease progression/recurrence/relapse occurring at least 6 months following completion of a platinum-based chemotherapy in which an initial response had been demonstrated.

Niraparib
Brand(s): Zejula
DOSAGE FORM/ STRENGTH: 100mg tablet

[3]Case-by-case consideration will be provided for patients with recurrent disease who are unable to use a platinum-based chemotherapy after having demonstrated platinum-sensitive disease to an earlier line of treatment after achieving complete or partial radiological response with their most recent course of treatment with alternative, non-platinum-based chemotherapy.

[4]If more than 8 weeks have elapsed from the last chemotherapy treatment, consideration should be given to exclude disease progression before start of therapy.

Exclusion Criteria:

1. Patients who have previously progressed while on niraparib maintenance therapy will not be funded.
2. Patients who have experienced disease progression while on treatment with a prior PARP inhibitor regardless of treatment line (i.e. first line or recurrent/relapsed setting) will not be funded for niraparib.
3. Patients who have developed disease progression before start of niraparib maintenance therapy will not be funded.
4. Patients with symptomatic, uncontrolled brain metastases will not be funded.
5. Niraparib is not funded when used as combination therapy with chemotherapy.
6. Niraparib retreatment will not be funded in those who have completed 3 years of maintenance therapy and experienced disease progression.

Renewal Criteria:

Niraparib maintenance therapy after first line platinum-based treatment:

Ongoing funding will be considered until disease progression or development of unacceptable toxicity or up to a maximum of 3 years if there is no evidence of disease recurrence.

Niraparib maintenance therapy in recurrent platinum-sensitive disease:

Ongoing funding will be considered until disease progression or development of unacceptable toxicity

Notes:

1. Niraparib funding will not be considered for patients with histologies other than serous or endometroid unless the patient is BRCA mutated. Patients presenting with non-mucinous histology should be BRCA tested.

Niraparib
Brand(s): Zejula
DOSAGE FORM/ STRENGTH: 100 mg tablet

2. Imaging to rule out disease progression is required for patients delayed in starting maintenance therapy with niraparib. (Note: CA-125 clinical assessments may be considered case-by-case where imaging is not available).
3. Cancer antigen 125 (CA-125) and clinical assessments should be done at least every 3 to 4 months to monitor for disease reoccurrence or progression.
4. Patients with no evidence of disease after chemotherapy who are initiated niraparib in the first line maintenance setting will be funded for a maximum of 3 years.
5. Time-limited access to niraparib will be provided for patients already on maintenance bevacizumab who wish to switch to niraparib monotherapy as long as other criteria are met and there is no evidence of disease progression.
6. Patients on another PARP treatment may switch to niraparib if they have developed intolerances or allergies and if they have not experienced disease progression.
7. Niraparib will not be funded as maintenance therapy in patients who have previously progressed on niraparib or another PARP used as maintenance therapy after one or more lines of chemotherapy.
8. Retreatment with maintenance niraparib will not be funded in patients who previously completed 3 years of niraparib maintenance therapy after first line platinum-based chemotherapy, and then subsequently experienced disease progression.
9. Note that the ministry will only fund one PARP therapy (i.e. niraparib or olaparib) in the maintenance setting upon meeting all initiation criteria.

Recommended dose: 200 mg to 300 mg daily (Refer to the product monograph for dosing information.)

Approval duration of initials and renewals: 1 year

Reimbursement will be provided up to a maximum of 3 years if there is no evidence of disease recurrence.

Olaparib
Brand(s): Lynparza
DOSAGE FORM/ STRENGTH: 100 mg tablets, 150 mg tablets
Effective dates: Updated December 23, 2020 (ovarian), May 2, 2022 (prostate), September 15, 2023 (adjuvant breast); November 4, 2024 (Prostate new regimen)

BRCA-mutated, high grade epithelial ovarian, fallopian tube, or primary peritoneal cancer

Initiation Criteria:

For the maintenance treatment of BRCA-mutated, high grade epithelial ovarian, fallopian tube, or primary peritoneal cancer in adult patients who meet ALL the following criteria;

1. Patient has documented mutation in BRCA1 or BRCA2 genes (germline or somatic detected by an approved testing method); AND

2. Patient is using olaparib as maintenance therapy immediately after one course of first line platinum-based chemotherapy in which radiological response (complete or partial) is demonstrated after at least 4 cycles of treatment;
   OR
   Patient is using olaparib as maintenance therapy in relapsed disease after having received more than one prior course of platinum-based chemotherapy in which platinum sensitive disease[1] was demonstrated with one completed treatment course, and there is radiologic response (complete or partial) to the most recently completed course of platinum-based treatment.[2]
   AND
3. Olaparib is started within 8 weeks of the patient's final dose of platinum-based chemotherapy[2] or within 12 weeks[3] with restaging to confirm no disease progression if delay of more than 8 weeks since last dose of chemotherapy has occurred; AND

4. Olaparib is being used as monotherapy for maintenance treatment; AND

5. Patient has good performance status.

[1] Platinum-sensitive disease is defined as disease progression/recurrence/relapse occurring at least 6 months following completion of a platinum-based chemotherapy in which an initial response had been demonstrated.

[2] Patients who are unable to use a platinum-based chemotherapy after having demonstrated platinum- sensitive disease to an earlier line of treatment may be considered on a case-by-case basis if they have received at least 4 cycles of a non-platinum treatment, submit documentation for clinically relevant allergies or intolerance to platinum treatment, and meet all other aspects of the above criteria.

Olaparib
Brand(s): Lynparza
DOSAGE FORM/ STRENGTH: 100 mg tablets, 150 mg tablets

[3] Patients not able to start olaparib within 12 weeks due to extenuating circumstances may be considered on a case-by-case basis if they have no evidence of disease progression, provide information to explain why treatment could not be started within 12 weeks, and meet all other aspects of the above criteria.

Exclusion Criteria: (Patients meeting any of the below criteria will not be funded.)

- Patients who have relapsed after at least one course of platinum-based chemotherapy and have not demonstrated platinum-sensitive disease[1] will not be funded.
- Patients who have developed disease progression before start of olaparib maintenance therapy will not be funded.
- Retreatment with olaparib as maintenance therapy will not be funded.
- Olaparib is not funded when used as combination with chemotherapy.

Recommended dose: 300 mg twice daily for oral tablets

Approval duration: 1 year

Notes:
1. Imaging to rule out disease progression is required for patients delayed in starting maintenance therapy with olaparib by more than 8 weeks or who have stopped therapy for more than 14 days prior to starting or restarting olaparib (Note: CA-125 clinical assessments may be considered case-by-case where imaging is not available).

2. Cancer antigen 125 (CA-125) and clinical assessments should be done at least every 3 to 4 months to monitor for disease reoccurrence or progression.

3. Olaparib will be funded for a maximum of 2 years in the maintenance setting after first line platinum-based therapy if there is no evidence of disease. Olaparib maintenance therapy will be funded ongoing until disease progression or development of unacceptable toxicity to olaparib for those using in relapsed platinum-sensitive disease.

4. Time limited access to olaparib will be provided for patients already on bevacizumab maintenance who wish to switch to olaparib monotherapy as long as other criteria are met and there is no evidence of disease progression on imaging and within 12 weeks of completing chemotherapy.

Olaparib
Brand(s): Lynparza
DOSAGE FORM/ STRENGTH: 100 mg tablets, 150 mg tablets

Renewal Criteria:

Olaparib maintenance therapy after first line platinum-based treatment.

Ongoing funding will be considered until disease progression or development of unacceptable toxicity or up to a maximum of 2 years if there is no evidence of disease.
Olaparib maintenance therapy in relapsed platinum-sensitive disease:

Ongoing funding will be considered until disease progression or development of unacceptable toxicity

Recommended Dose: 300 mg twice daily for oral tablets

Approval duration of renewals: 1 year

(Note that Olaparib will be funded for a maximum of 2 years in the maintenance setting after first line platinum-based therapy if there is no evidence of disease at 2 years.)

Metastatic castration resistant prostate cancer

Initiation Criteria:

For the treatment of metastatic castration resistant prostate cancer (mCRPC) in patients meeting all of the following criteria;

1. Patient is 18 years of age or older; AND
2. Provides documentation that patient is positive for deleterious or suspected deleterious germline and/or somatic mutations in the BRCA 1 or BRCA 2 genes[1] using an approved testing method; AND
3. Has metastatic lesions detected on a bone scan, computed tomography (CT), and/or magnetic resonance imaging (MRI)[2]; AND
4. Has castration resistant disease based on meeting the following indicia observed while on continuous androgen deprivation therapy (ADT) treatment or post orchiectomy[3]:
    - Castrate serum testosterone levels AND
    - Biochemical progression defined as three (3) prostate-specific antigen (PSA) rises at least 1 week apart, with the last PSA greater than 2ng/mL AND/OR radiographic progression of new or pre-existing disease as determined by the detection of 2 or more lesions on bone scan or presence of new soft tissue lesions by RECIST criteria; AND

Olaparib
Brand(s): Lynparza
DOSAGE FORM/ STRENGTH: 100 mg tablets, 150 mg tablets

5. Patient is treatment naïve to olaparib or another poly-(ADP-ribose) polymerase (PARP) inhibitor used in the setting of mCRPC; AND
6. Patient meets one of the following clinical settings;
   i) Olaparib is used in combination with androgen deprivation therapy (ADT) in a PARP-naive patient who has experienced disease progression on an ARAT/ARPI (e.g. abiraterone, apalutamide, darolutamide, enzalutamide) used at any stage of prostate cancer[2];
   OR
   ii) Olaparib is used in combination with abiraterone, and prednisone or prednisolone in a patient who has not used an ARAT/ARPI at any stage of prostate cancer (i.e. treatment naïve to an ARAT/ARPI). If the patient has already initiated a CYP-17 inhibitor (e.g. abiraterone) in mCRPC, they should not have received more than 4 months of treatment with abiraterone prior to initiation of the olaparib; AND
7. Patient has good performance status.

Notes:

1. ATM gene mutations can be considered for patients using olaparib as monotherapy anticancer therapy with or without an ADT.
2. Positron emission tomography (PET) imaging results may be considered.
3. ADT is not required for patients with bilateral orchiectomy.

Renewal Criteria:

Renewal of funding will be considered in patients who have not experienced disease progression or unacceptable toxicity while on therapy

Exclusion criteria:
(Patients meeting any of the following will not be funded.)

1. Patients who have previously experienced disease progression on a PARP inhibitor (e.g. olaparib, niraparib) for prostate cancer will not be funded.
2. Combination therapy of olaparib and abiraterone with any of the following will in mCRPC will not be funded;
   i) ARI (e.g. enzalutamide)
   ii) Another PARP inhibitor
   iii) Chemotherapy (e.g. docetaxel, cabazitazel)
   iv) Another CYP-17 inhibitor

Olaparib
Brand(s): Lynparza
DOSAGE FORM/ STRENGTH: 100 mg tablets, 150 mg tablets

Approval Duration (initials and renewals): 1 year

Approved dose:

Refer to the product monograph for dosing information. Note that the 100 mg tablet can be considered for dose reduction.

Usual standard dose: Olaparib 300 mg twice daily

When used with abiraterone and prednisone: Olaparib 300 mg twice daily with abiraterone, 1000 mg daily and prednisone or prednisolone, 5 mg twice a daily.

Definitions for the purpose of the EAP funding criteria:

ADT *– A first generation androgen deprivation therapy (e.g. goserelin, leuprolide, triptorelin, buserelin, degarelix)*

ARAT*- An androgen receptor axis targeted therapy (e.g. abiraterone, apalutamide, darolutamide, enzalutamide). This terminology was used in earlier prostate cancer criteria and is equivalent to ARPI (see below). This is included for clarity and alignment with other ministry criteria.*

ARPI- *An androgen receptor pathway inhibitor (e.g. abiraterone, apalutamide, darolutamide, enzalutamide).*

ARI- *A second generation androgen receptor inhibitor (e.g. apalutamide, darolutamide, enzalutamide)*

PARP- A Polyadenosine 5-diphosphoribose polymerisation inhibitor (e.g. olaparib, niraparib)

CYP-17 inhibitor- An inhibitor of cytochrome P450 17α−hydroxy/17,20-lyase (CYP17) enzymes (e.g. abiraterone)

Olaparib
Brand(s): Lynparza
DOSAGE FORM/ STRENGTH: 100 mg tablets, 150 mg tablets

Adjuvant treatment of early breast cancer at high risk of recurrence

Initiation Criteria:

For the adjuvant treatment of adult patients with early breast cancer at high risk of recurrence meeting the following criteria;

1. Patient is 18 years of age or older; AND
2. Has documented deleterious or suspected deleterious germline *BRCA*-mutated (g*BRCA*m) breast cancer; AND
3. Has documented human epidermal growth factor receptor 2 (HER2) - negative breast cancer; AND
4. Patient's eligibility for adjuvant treatment meets one of the following clinicopathological features (Note 1);

    i) Has received surgery followed by adjuvant chemotherapy and diagnosed with triple negative breast cancer (TNBC) with axillary node-positive disease or axillary node-negative disease with a pathological tumour at least 2 cm or larger in size; OR
    ii) Has received surgery followed by adjuvant chemotherapy and diagnosed with hormone receptor (HR) positive, HER2-negative breast cancer with at least 4 or more involved pathologically confirmed positive lymph nodes; OR
    iii) Has received neoadjuvant chemotherapy followed by surgery and has TNBC with residual invasive breast cancer in the breast and/or resected lymph nodes [i.e. no pathological complete response from neoadjuvant therapy (non-PCR)]; OR
    iv) Has received neoadjuvant chemotherapy followed by surgery and with HR positive, HER2-negative breast cancer with residual invasive cancer in the breast and/or the resected lymph nodes following neoadjuvant therapy (i.e. non-pCR) and a clinical and pathological stage and estrogen-receptor status and histologic grade (CPS + EG) score equal to 3 or higher (Note 2)

5. Patient must have completed neoadjuvant or adjuvant chemotherapy containing anthracyclines, taxanes, or the combination of both (Note 3); AND

6. Olaparib should be initiated at least 2 weeks and no more than 12 weeks following completion of the last treatment, including surgery, chemotherapy, or radiation therapy depending on the situation under which they are eligible. (Note 4)

Olaparib

Brand(s): Lynparza

DOSAGE FORM/ STRENGTH: 100 mg tablets, 150 mg tablets

Exclusion criteria:

1. Patients are not eligible for funding of adjuvant olaparib if they have HER2-positive breast cancer.
2. Patients are not eligible for funding of adjuvant olaparib if they have metastatic breast cancer.
3. Patients who have received both neoadjuvant and adjuvant chemotherapy are not eligible for funding of adjuvant olaparib.

Notes:

1. Please ensure that the request application includes the objective documentation reports for germline BRCA mutations, HER 2 and hormone receptor status, and the pathology reports associated with the clinical eligibility situation.
2. The CPS + EG is a disease scoring system that includes clinical stage, estrogen receptor status, nuclear grade, and post-treatment pathologic stage. Clinicians using alternative risk-assessment tools instead of CPS + EG may be considered case-by-case upon submitting supporting clinical details of the validated alternative risk assessment tool.
3. Patients who are unable to complete at least 6 cycles of neoadjuvant or adjuvant chemotherapy (e.g. due to toxicity) may still be considered for adjuvant olaparib case-by-case if all other eligibility criteria are met.
4. For a time-limited period, patients who missed the 12 week window for initiation of olaparib may be considered case-by-case upon meeting all other eligibility criteria.
5. Renewal of funding will not be considered, however, patients who have experienced treatment interruptions may be considered for restarts on a case-by-case basis for up to a total of 12 months of adjuvant therapy as long as the treatment break was not related to disease recurrence or development of unacceptable toxicities.

Discontinuation criteria:

Olaparib in the adjuvant setting will be funded until the occurrence of any of the following, whichever occurs first:

1. Completion of a total of 1 year (i.e. 52 weeks) of treatment; OR
2. Until disease recurrence; OR
3. Until development of unacceptable toxicities from treatment with olaparib.

Olaparib
Brand(s): Lynparza
DOSAGE FORM/ STRENGTH: 100 mg tablets, 150 mg tablets

Approval duration of Initials: 52 weeks

Renewals are not considered. (See Note 5)

Recommended dose:

300 mg twice daily. Dose reductions as necessary based on the product monograph.

Osimertinib
Brand(s): Tagrisso
DOSAGE FORM/ STRENGTH: 80 mg tablets (40 mg on case-by-case)
Updated: January 10, 2020

Initiation criteria:

For the treatment of locally advanced (not amenable to curative therapies) or metastatic non-small cell lung cancer (NSCLC) in individuals meeting the following criteria:

1. Previously untreated[1] NSCLC in a patient with tumours that are documented to have Epidermal Growth Factor Receptor (EGFR) exon 19 deletions (exon 19 del) or exon 21 (L858R) substitution mutations (either alone or in combination with other EGFR mutations)
   OR
   Previously treated NSCLC in a patient who has experienced disease progression on one EGFR tyrosine kinase inhibitor (TKI) therapy (i.e. afatinib, gefitinib or erlotinib) with tumours that are documented to have EGFR T790M resistance mutations[2]; AND
2. Has a good performance status; AND

3. Osimertinib is being used as monotherapy.

Exclusion Criteria:
1. Patients with EGFR wild-type mutations
2. Patients with EGFR unknown mutations
3. Osimertinib will not be funded as a third-line TKI
4. Patients with EGFR exon 19 deletions (exon 19 del) or exon 21 (L858R) substitution mutations who receive afatinib or gefitinib in first line are not eligible for osimertinib in the 2nd line NSCLC setting.[3,4]

Osimertinib

Brand(s): Tagrisso

DOSAGE FORM/ STRENGTH: 80 mg tablets (40 mg on case-by-case)

Note:

[1] Eligible patients should be previously untreated in the locally advanced or metastatic setting.

[2] Patients with de novo EGFR 790M mutations may be considered case-by-case.

[3] Time-limited consideration will be provided for patients meeting all the above criteria who are currently on a first-, or second-generation EGFR TKI (i.e. gefitinib, afatinib, erlotinib) who have not experienced disease progression or patients who are currently on chemotherapy and are found to harbour a sensitizing or resistance mutation who wish to switch to osimertinib therapy.

[4] Patients who progress on osimertinib in the first line will not be considered for another targeted TKI therapy (i.e. gefitinib or afatinib) for NSCLC

Renewal of funding of osimertinib will be considered in patients who continue to derive benefit from treatment. (i.e. until clinically meaningful progression occurs or development of unacceptable toxicities.)

Recommended dose: 80 mg per day orally

(Note that 40mg tablets are approved on a case-by-case basis to ensure cost-effectiveness of the funded strength.)

Duration of Approval for Initial and Renewal requests: 6 months

Osimertinib

Brand(s): Tagrisso
DOSAGE FORM/ STRENGTH: 80 mg tablets (40mg on case-by-case)
Effective Date: November 15, 2022 (Adjuvant setting)

Initiation Criteria:

For use as **adjuvant therapy in patients with completely resected, EGFR mutated, non-small cell lung cancer (NSCLC)** meeting ALL the following criteria;

1. Patient is 18 years of age or older; AND
2. Has completely resected NSCLC confirmed post-operatively as being stage IB-IIIA (AJCC 7th edition, or equivalent) NSCLC; AND
3. NSCLC tumour tissue confirmed to be EGFR (exon 19 deletion and/or exon 21 L858R substitution) mutation positive; AND
4. Patients has a good performance status (e.g. Eastern Cooperative Oncology Group (ECOG) status less than or equal to 2); AND
5. Osimertinib is being initiated within 10 weeks of complete surgical resection if adjuvant chemotherapy was not used OR within 26 weeks of surgical resection if adjuvant chemotherapy (e.g. platinum-based doublet chemotherapy, maximum of 4 cycles) was administered.
6. Prescribed by a clinician experienced in the treatment and management of NSCLC.

Exclusion Criteria:

1. Patients with EGFR wild-type mutations
2. Patients with EGFR unknown mutations

Renewal Criteria:

Renewal of funding of osimertinib in this adjuvant setting will be continued until disease recurrence[1], or development of unacceptable toxicity, or until a maximum of treatment duration of 3 years is reached regardless of dose reduction and dose interruption.

[1] Patient does not have evidence of disease recurrence, based on the absence of recurrence on CT or MRI scan, pathological disease on biopsy, or both.

Recommended dose: 80 mg per day orally

Approval duration: 1 year

(Total duration of funding up to 3 years)

Palbociclib
Brand(s): Ibrance
DOSAGE FORM/ STRENGTH: 75 mg, 100 mg, 125 mg tablet or capsules
Updated December 4, 2020

Initial Criteria

For the treatment of patients with estrogen receptor(ER)-positive, human epidermal growth factor receptor 2 (HER 2)-negative; unresectable locally advanced breast cancer or metastatic breast cancer in patients who meet the following criteria;

1. Palbociclib is being used as combination therapy in one of the following treatment regimens[1];
   i) As first line therapy in combination with an aromatase inhibitor (i.e. letrozole, anastrozole, or exemestane) or fulvestrant in a patient who has not progressed on a prior systemic treatment (i.e. chemotherapy, immunotherapy, or endocrine therapy) for their unresectable locally advanced or metastatic disease; OR
   ii) As second line therapy in combination with an aromatase inhibitor (i.e. letrozole, anastrozole, or exemestane) or fulvestrant after progression on a chemotherapy for unresectable locally advanced or metastatic disease; OR

   iii) As a second or subsequent line therapy in combination with fulvestrant after progression on any number of endocrine monotherapies with the exception of progression during prior fulvestrant therapy.

   [1]Note: EAP funding will be considered for only one CDK 4/6 inhibitor regimen (i.e. Palbociclib or Ribociclib) OR Everolimus based regimen for the treatment of unresectable locally advanced or metastatic disease. No funding for sequential treatment regimens involving palbociclib or ribociclib or everolimus will be considered.

   AND

2. Patients who received anastrozole or letrozole in the neo-adjuvant or adjuvant setting, must demonstrate a minimum disease free interval of twelve (12) months after stopping therapy to qualify for funding of palbociclib in combination with anastrozole or letrozole. (Note: This does not apply to patients receiving tamoxifen or exemestane in the neoadjuvant or adjuvant setting who progress or relapse early on those treatments.)

3. Patient has good performance status defined as an Eastern Cooperative Oncology Group (ECOG) score of 0 to 2; AND

4. Patient does not have active or uncontrolled metastases to the central nervous system; AND

Palbociclib
Brand(s): Ibrance
DOSAGE FORM/ STRENGTH: 75 mg, 100 mg, 125 mg tablets or capsules

5. In the case of a Patient who is pre-menopausal or peri-menopausal, the Patient is receiving a luteinizing hormone-releasing hormone (LHRH) agonist to achieve chemically-induced menopause (Note: Women who have had an oophorectomy are considered to be post-menopausal); AND

6. The Patient has not experienced disease progression on any of the following regimens for locally advanced or metastatic breast cancer:
   (i) a palbociclib or ribociclib regimen;
   (ii) an everolimus regimen; or
   (iii) another CDK 4/6 regimen that has been publicly funded.

Renewal Criteria:

Renewals will be considered in patients who have not demonstrated evidence of disease progression or development of unacceptable toxicity requiring discontinuation while on palbociclib.

Exclusion Criteria (Note that exclusion criteria apply to both Initial eligibility criteria and renewal criteria.) Patients meeting the following criteria will not be funded.

i) Patient is using palbociclib as retreatment after disease progression on a prior palbociclib-based regimen in advanced breast cancer.
ii) Patient is using palbociclib with other drugs or in combinations other than those situations mentioned in 1 i), ii), iii) of the eligibility criteria.
iii) Patient is using palbociclib in combination with letrozole or anastrozole in the metastatic setting but has experienced progression in the neoadjuvant or adjuvant setting occurring during treatment or within 12 months of stopping treatment with letrozole or anastrozole;
iv) Patient is pre- or peri-menopausal who is not being treated with a luteinizing hormone-releasing hormone (LHRH) agonist.
v) Patient who is intending to use palbociclib with fulvestrant who has progressed on prior fulvestrant used as monotherapy or as part of another regimen.
vi) Patient whose disease has progressed during treatment with a ribociclib regimen, an everolimus regimen, or another CDK 4/6 inhibitor regimen used for advanced, metastatic breast cancer, unless that use was through a clinical trial.
vii) Patient who has active or uncontrolled central nervous system (CNS) metastases.
viii) The Patient is requesting Ibrance for use with fulvestrant and has extensive, symptomatic, potentially life-threatening visceral metastases.

Palbociclib
Brand(s): Ibrance
DOSAGE FORM/ STRENGTH: 75 mg, 100 mg, 125 mg tablets or capsules

On a time-limited basis, funding will be considered for the following on a case-by-case basis:

1. Patients who missed the opportunity to use palbociclib in the advanced setting in patients started on first-line, monotherapy with an aromatase inhibitor (AI) (e.g. letrozole, anastrozole, exemestane) AND who have not have not experienced disease progression with current AI therapy AND who meet the disease-free time requirement if anastrozole or letrozole was used previously in the adjuvant or neoadjuvant setting and the EAP request is submitted between the dates of December 4, 2020 to March 4, 2021.
2. Addition of palbociclib for patients already on fulvestrant in first, second or subsequent line who has not experienced disease progression on fulvestrant and who are CDK 4/6 inhibitor naïve and otherwise eligible for this therapy if the EAP request is submitted between the dates of December 4, 2020 to March 4, 2021.
3. A switch to palbociclib + fulvestrant at progression for patients already on endocrine/hormonal therapy other than fulvestrant and who are CDK4/6 naïve and otherwise meet the eligibility requirements for this therapy.
4. A switch to palbociclib + fulvestrant at progression for patients already on and benefitting from everolimus + exemestane, provided that the start of everolimus + exemestane was prior to December 4, 2020. Patients must be CDK 4/6 inhibitor naïve and otherwise eligible for this therapy.

Dosing:

Palbociclib (Ibrance) 125mg orally once a day for 21 consecutive days, followed by 7 days off treatment, in a combination regimen with one of the following:

- A continuous daily aromatase inhibitor or
- Fulvestrant 500mg administered intramuscularly on days 1 and 15 of cycle 1 and tehn on day 1 of each subsequent 28-day cycle.

Pazopanib
Brand(s): Votrient and generics
DOSAGE FORM/ STRENGTH: 200 mg tablet

For first-line treatment of advanced or metastatic renal cell carcinoma of clear cell histology in patients with good performance status
(ECOG* ≤ 1)

ECOG = Eastern Cooperative Oncology Group Performance Status

The approved dosage is 800 mg once daily.

Duration of Approval: 1 year

Renewals will be considered for patients who have benefited from therapy (i.e. no disease progression) and are expected to continue to do so. Exclusion criteria: Funding for Votrient will not be approved for patients who demonstrate disease progression while on sunitinib, sorafenib, temsirolimus, everolimus or other drugs approved for treatment of metastatic renal cell carcinoma.

Duration of Approval: 1 year

Pomalidomide
Brand(s): Pomalyst and generics
DOSAGE FORM/ STRENGTH: 1 mg, 2 mg, 3 mg, 4 mg capsules
Effective date: February 6, 2015
Updated: May 31, 2023

Initial criteria:

For the treatment of patients with relapsed and/or refractory multiple myeloma who meet ALL of the following criteria:

1. Patient has failed treatment on a lenalidomide-based regimen administered either alone or in combination in any prior line of treatment (Note 1); AND
2. Patient has failed treatment on a proteasome inhibitor-based regimen (e.g. bortezomib, carfilzomib) administered either alone or in combination in any prior line of treatment (Note 1); AND
3. Patient is deemed to be pomalidomide sensitive, defined as having disease that has not been refractory to a pomalidomide-based regimen, and/or has not experienced progression while on a pomalidomide-based regimen (Note 2); AND

Pomalidomide
Brand(s): Pomalyst and generics
Dosage form/Strength: 1 mg, 2 mg , 3 mg, 4 mg capsules

4. Patient is using pomalidomide in one of the following circumstances;
   a) As dual therapy in combination with dexamethasone; OR
   b) As a triple therapy regimen in combination with isatuximab and dexamethasone after two prior lines of therapy in a patient who has not been refractory to an anti-CD38 monoclonal antibody (e.g. daratumumab, isatuximab) used in another prior line of treatment (Note 3).

   AND
5. Patients must have been refractory to the last line of therapy; AND
6. Patient has good performance.

Notes:

1. Patient must be lenalidomide resistant AND bortezomib resistant or if they are not bortezomib resistant, they must have experienced disease progression on another proteasome inhibitor (PI)-based treatment regimen. If a patient is contraindicated or has unacceptable toxicities to lenalidomide and/or bortezomib, please include details in your request application for case-by-case consideration.

2. Refractory disease is defined as;

   a) Disease progression within 60 days after stopping treatment or
   b) Progression on any dose of lenalidomide or bortezomib/PI therapy including while on maintenance therapy or
   c) Non-responsive disease during therapy (either failure to achieve minimal response or disease progression).

   Relapsed / Progressive disease is defined as having one or more of the following:
   a) An increase of 25% from lowest response value in serum M-component (absolute increase must be greater than or equal to 0.5g/dL), and/or urine M-component (absolute increase must be greater than or equal to 200 mg/24 hours).
   b) An absolute increase of greater than 10mg/dL in the difference between involved and uninvolved FLC levels (if no measurable serum and urine M-protein levels).
   c) Definite development of new bone lesions or soft tissue plasmacytomas or definite increase in the size of existing bone lesions or soft tissue plasmacytomas.
   d) Development of hypercalcemia (corrected serum calcium greater than 11.5 mg/dL or 2.5 mmol/L) that can be attributed solely to the plasma cell proliferative disorder.

Pomalidomide
Brand(s): Pomalyst and generics
Dosage form/Strength: 1 mg, 2 mg , 3mg, 4 mg capsules

3. Although pomalidomide with isatuximab and dexamethasone is funded after progression on two prior lines of therapy, if a patient is resistant or refractory to first line lenalidomide and bortezomib as part of an earlier lenalidomide-bortezomib-dexamethasone regimen (RVD), the patient would be eligible for funding of second line isatuximab as part of IsaPd upon meeting other initial criteria.

4. Patients must meet the eligibility requirements for isatuximab through the New Drug Funding Program (NDFP).

5. Isatuximab can be added to pomalidomide and dexamethasone provided the patient met the eligibility criteria for isatuximab (See note 4) and has not progressed.

Exclusions:

1. Patients with primary amyloidosis

Renewal criteria:

Pomalidomide may be continued for the treatment of multiple myeloma in those who continue to respond to therapy and have not experienced refractory disease or progressive disease while on the pomalidomide-based regimen.

Dosing regimen:

Pomalidomide 4 mg on days 1–21 of each 28 day cycle

If pomalidomide is given in combination with isatuximab and dexamethasone:

Dexamethasone 40 mg oral or IV weekly (20 mg if aged ≥75 years) on days 1, 8, 15, and 22 of each cycle.

Isatuximab Dosing:
Cycle 1: Isatuximab 10 mg/kg intravenously (IV) on days 1, 8, 15, and 22
Cycle 2 and onwards: Isatuximab 10 mg/kg IV on days 1 and 15

[1 cycle = 28 days]

Approval duration of initials and renewals: 1 year

Ponatinib
Brand(s): Iclusig
DOSAGE FORM/ STRENGTH: 15 mg, 45 mg tablets

Chronic Phase CML:

a. For the treatment of patients with Philadelphia chromosome positive (Ph+) chronic myelogenous leukemia (CML) in chronic phase and documented T315i mutation; OR

b. For the treatment of patients with Philadelphia chromosome positive (Ph+) chronic myelogenous leukemia (CML) in chronic phase with documented resistance/disease progression or intolerance to at least 2 prior oral TKIs (imatinib, dasatinib or nilotinib), where ponatinib would be the third or fourth line TKI.

Duration of Approval: 1 year

Accelerated Phase CML:

- For the treatment of patients with Philadelphia chromosome positive (Ph+) chronic myelogenous leukemia (CML) in accelerated phase and documented T315i mutation; OR

- For the treatment of patients with Philadelphia chromosome positive (Ph+) chronic myelogenous leukemia (CML) in accelerated phase with documented resistance/disease progression or intolerance to at least 2 prior oral TKIs (imatinib, dasatinib or nilotinib), where ponatinib would be the third or fourth line TKI.

Duration of Approval: 1 year

Blast Phase CML:

(a) For the treatment of patients with Philadelphia chromosome positive (Ph+) chronic myelogenous leukemia (CML) in blast phase and documented T315i mutation; OR

(b) For the treatment of patients with Philadelphia chromosome positive (Ph+) chronic myelogenous leukemia (CML) in blast phase with documented resistance/disease progression or intolerance to at least 2 prior oral TKIs (imatinib and dasatinib), where ponatinib would be the third or fourth line TKI.

Ponatinib
Brand(s): Iclusig
DOSAGE FORM/ STRENGTH: 15 mg, 45 mg tablets

For Philadelphia chromosome positive acute lymphoblastic leukemia (Ph+ALL):

a. For the treatment of patients with Philadelphia chromosome positive acute lymphoblastic leukemia (Ph +ALL) and documented T315i mutation; OR

b. For the treatment of patients with Philadelphia chromosome positive acute lymphoblastic leukemia (Ph +ALL) with documented resistance/disease progression or intolerance to imatinib and dasatinib, where ponatinib would be the third line TKI.

Renewals will be considered upon confirmation from the clinician that the patient has experienced hematologic and/or cytogenic response and is expected to continue to do so.

Duration of Approval: 1 year

Regorafenib
Brand(s): Stivarga
DOSAGE FORM/ STRENGTH: 40 mg tablets
Updated November 18, 2020

For the treatment of metastatic and/or unresectable gastrointestinal stromal tumors (GIST) in patients who have had disease progression on, or intolerance to, imatinib and sunitinib

Dosage: 160 mg once daily for 3 weeks followed by 1 week of no therapy to comprise a cycle of 4 weeks.

Duration of Approval: 6 Months

Reimbursement of Stivarga will be considered as long as benefit is observed or until unacceptable toxicity occurs.

Renewals will be considered in patients who continue to derive benefit from therapy.

Duration of Approval: 6 Months

Regorafenib
Brand(s): Stivarga
DOSAGE FORM/ STRENGTH: 40 mg tablet

Initial Criteria:

For the treatment of unresectable, advanced hepatocellular carcinoma (HCC) in patients who meet ALL the following criteria prior to starting treatment with regorafenib;

- Patient is 18 years of age or older; AND
- Regorafenib will be used as monotherapy for HCC; AND
- Regorafenib will be used as second line therapy in a patient who has experienced disease progression during treatment with sorafenib or lenvatinib for HCC; AND
- If prior treatment was sorafenib, patient must have tolerated at least 400 mg a day for 20 days or more in the 28 days before stopping treatment with sorafenib; AND
- Has an Eastern Cooperative Oncology Group (ECOG) Performance status less than or equal to 1; AND
- Has a Child-Pugh class A liver function.

Exclusion Criteria: Patients meeting any of the following criteria will not be funded.

- Regorafenib will not be funded in the first line setting.
- Patients with Child-Pugh score greater than 6 (i.e. Child-Pugh class B or C) will not be funded.

Recommended Dosage: 160 mg once daily for 3 weeks followed by 1 week of no therapy to comprise a cycle of 4 weeks.

Renewal Criteria:

Renewals will be considered until disease progression (1) or until patient develops unacceptable toxicity. Please provide radiographic and/or scan results indicating no progression[2] with requests for renewal of funding.

[1] Evaluation according to modified Response Evaluation Criteria in Solid Tumors (mRECIST) or RECIST 1.1 criteria.

Approval duration for initials and renewals: 3 months

Ribociclib
Brand(s): Kisqali
DOSAGE FORM/ STRENGTH: 200 mg tablets
Updated: November 18, 2020

Initial Criteria:

For the treatment of patients with estrogen receptor(ER)-positive, human epidermal growth factor receptor 2 (HER 2)-negative; unresectable locally advanced breast cancer or metastatic breast cancer in patients who meet the following criteria;

1. Ribociclib is being used as combination therapy in one of the following treatment regimens[1];

   i) As first line therapy in combination with an aromatase inhibitor (i.e. letrozole, anastrozole, or exemestane) or fulvestrant in a patient who has not progressed on a prior systemic treatment (i.e. chemotherapy, immunotherapy, or endocrine therapy) for their unresectable locally advanced or metastatic disease; OR
   ii) As second line therapy in combination with an aromatase inhibitor (i.e. letrozole, anastrozole, or exemestane) or fulvestrant after progression on a chemotherapy for unresectable locally advanced or metastatic disease; OR
   iii) As a second or subsequent line therapy in combination with fulvestrant after progression on any number of endocrine monotherapies with the exception of progression during prior fulvestrant therapy.

   [1]Note: EAP funding will be considered for only one CDK 4/6 inhibitor regimen (i.e. Ribociclib or Palbociclib) OR Everolimus based regimen for the treatment of unresectable locally advanced or metastatic disease. No funding for sequential treatment regimens involving ribociclib or palbociclib or everolimus will be considered.

   AND

2. Patients who received anastrozole or letrozole in the neo-adjuvant or adjuvant setting, must demonstrate a minimum disease free interval of twelve (12) months after stopping therapy to qualify for funding of ribociclib in combination with anastrozole or letrozole. (Note: This does not apply to patients receiving tamoxifen or exemestane in the neoadjuvant or adjuvant setting who progress or relapse early on those treatments.)

3. Patient has good performance status defined as an Eastern Cooperative Oncology Group (ECOG) score of 0 to 2; AND

Ribociclib
Brand(s): Kisqali
DOSAGE FORM/ STRENGTH: 200 mg tablets

4. Patient does not have active or uncontrolled metastases to the central nervous system; AND
5. In the case of a Patient who is pre-menopausal or peri-menopausal, the Patient is receiving a luteinizing hormone-releasing hormone (LHRH) agonist to achieve chemically-induced menopause (Note: Women who have had an oophorectomy are considered to be post-menopausal); AND
6. The Patient has not experienced disease progression on any of the following regimens for locally advanced or metastatic breast cancer:
   i) a ribociclib or palbociclib regimen;
   ii) an everolimus regimen; or
   iii) another CDK 4/6 regimen that has been publicly funded.

Renewal Criteria:

Renewals will be considered in patients who have not demonstrated evidence of disease progression or development of unacceptable toxicity requiring discontinuation while on ribociclib

Exclusion Criteria (Note that exclusion criteria apply to both Initial eligibility criteria and renewal criteria.)

Patients meeting the following criteria will not be funded.

i) Patient is using ribociclib as retreatment after disease progression on a prior ribociclib-based regimen in advanced breast cancer.
ii) Patient is using ribociclib with other drugs or in combinations other than those situations mentioned in 1 i), ii), iii) of the eligibility criteria.
iii) Patient is using ribociclib in combination with letrozole or anastrozole in the metastatic setting but has experienced progression in the neoadjuvant or adjuvant setting occurring during treatment or within 12 months of stopping treatment with letrozole or anastrozole;
iv) Patient is pre- or peri-menopausal who is not being treated with a luteinizing hormone-releasing hormone (LHRH) agonist.
v) Patient who is intending to use ribociclib with fulvestrant who has progressed on prior fulvestrant used as monotherapy or as part of another regimen.
vi) Patient whose disease has progressed during treatment with a palbociclib regimen, an everolimus regimen, or another CDK 4/6 inhibitor regimen used for advanced, metastatic breast cancer, unless that use was through a clinical trial.
vii) Patient who has active or uncontrolled central nervous system (CNS) metastases.

Ribociclib
Brand(s): Kisqali
DOSAGE FORM/ STRENGTH: 200 mg tablets

On a time-limited basis, funding will be considered for the following on a case-by-case basis:

1. Patients who missed the opportunity to use ribociclib in the advanced setting in patients started on first-line, monotherapy with an aromatase inhibitor (AI) (e.g. letrozole, anastrozole, exemestane) AND who have not have not experienced disease progression with current AI therapy AND who meet the disease-free time requirement if anastrozole or letrozole was used previously in the adjuvant or neoadjuvant setting and the EAP request is submitted between the dates of November 18, 2020 to February 18, 2021.
2. Addition of ribociclib for patients already on fulvestrant in first, second or subsequent line who has not experienced disease progression on fulvestrant and who are CDK 4/6 inhibitor naïve and otherwise eligible for this therapy if the EAP request is submitted between the dates of November 18, 2020 to February 18, 2021.
3. A switch to ribociclib + fulvestrant at progression for patients already on endocrine/hormonal therapy other than fulvestrant and who are CDK4/6 naïve and otherwise meet the eligibility requirements for this therapy.
4. A switch to ribociclib + fulvestrant at progression for patients already on and benefitting from everolimus + exemestane, provided that the start of everolimus + exemestane was prior to November 18, 2020. Patients must be CDK 4/6 inhibitor naïve and otherwise eligible for this therapy.

Dosing:

Ribociclib (Kisqali) 600mg orally once daily for 21 consecutive days, followed by 7 days off treatment in combination with one of the following:

- A continuous daily aromatase inhibitor or
- Fulvestrant 500mg administered intramuscularly on days 1 and 15 of cycle 1 and tehn on day 1 of each subsequent 28-day cycle.

Approval duration of Initials and Renewals: 1 year

Ripretinib
Brand(s): Qinlock
DOSAGE FORM/ STRENGTH: 50 mg tablets
Effective date: August 14, 2023

Initial criteria:

For the treatment of advanced gastrointestinal stromal tumour (GIST) in adult patients who meet ALL of the following criteria:

1. Aged 18 years old or older; AND
2. Has a confirmed diagnosis of metastatic and/or unresectable GIST; AND
3. Patient has experienced disease progression on, or intolerance (Note 1) to, imatinib, sunitinib, AND regorafenib;AND
4. Has a good performance status; AND
5. Has adequate hematological and organ function; AND
6. Ripretinib is not being used in combination with other anticancer drugs for GIST; AND
7. Prescribed by a clinician experienced in the treatment of GIST.

Notes:
1. A detailed description of the experienced intolerance to each therapy must be provided with the application including the grade of toxicity where applicable. If a patient is deemed to have a contraindication to use one or more earlier lines of treatment, a description of the contraindication must be included with associated documentation and relevant comorbidities to support the request. Clinical consult notes may be included to support intolerances and contraindications to earlier treatment lines.
2. Ripretinib should not be used in patients with active central nervous system metastases.

Renewal criteria:

Renewal of reimbursement of ripretinib will be considered for patients who demonstrate a response to therapy and have not experienced unacceptable toxicity.

Approved Dose: 150 mg daily with dose adjustments as necessary based on the product monograph.

Approval duration for initials and renewals: 6 months

Ruxolitinib
Brand(s): Jakavi
DOSAGE FORM/ STRENGTH: 5 mg, 10mg, 15 mg, 20 mg tablets
Effective dates: September 20, 2013 (MF) November 20, 2017 (PV)

For the treatment of intermediate to high risk symptomatic Myelofibrosis (MF) in patients meeting the following criteria;

i) MF is assessed using the Dynamic International Prognostic Scoring System (DIPSS) Plus; or the patient has symptomatic splenomegaly
ii) Patient has an Eastern Cooperative Oncology Group (ECOG) performance status ≤ 3
iii) Patient is previously untreated or refractory to other treatment

Dosing regimen: 5 mg to 25 mg twice a day

Duration of Approval: 1 Year

Initial Renewals are considered for patients who:

- Have confirmation of either a reduction in spleen size or documented improvement of disease symptoms within 6 months of initiating therapy with Jakavi.

Second and subsequent Renewals are considered for patients who continue to benefit from therapy with Jakavi

For the treatment of patients with polycythemia vera who meet the following criteria:

a) Demonstrated resistance[1] or demonstrated intolerance[2] to hydroxyurea (HU); AND
b) Have a good performance status (ECOG ≤ 3)

[1]Resistance to Hydroxyurea as defined by:

Use of HU for at least 3 months of treatment at a dose of at least 2 grams per day (or at maximally tolerated doses if unable to take 2 grams per day) meeting one of the following:

i. Patient continues to require phlebotomy to keep hematocrit (HCT) at less than 45%; OR
ii. Patient demonstrates uncontrolled myeloproliferation (i.e. platelet count > 400 x 10^9/L and white blood cell count > 10 x 10^9/L); OR
iii. Symptomatic splenomegaly[1]Intolerance to Hydroxyurea as defined:
    - After any dose of hydroxyurea, patient demonstrates one of the following:
    - Absolute neutrophil count < 1 x 10^9/L or platelet < 100 x 10^9/L or hemoglobin < 100 g/L at the lowest dose of HU required to achieve a response; OR

Ruxolitinib
Brand(s): Jakavi
DOSAGE FORM/ STRENGTH: 5 mg, 10mg, 15 mg, 20 mg tablets

- Presence of leg ulcers or other unacceptable HU-related grade 3 or 4 non-hematological toxicities (eg. Mucocutaneous manifestations, gastrointestinal symptoms, pneumonitis, fever); OR
- If patient demonstrates non-hematological grade 2 toxicities for at least one week: OR
- If toxicity requires permanent discontinuation of HU, interruption of HU until resolution of toxicity, or requiring hospitalization as a result of HU toxicity.

Renewal:
Patient continues to respond[3] to treatment and has not experienced disease progression.

[3] Response defined by any one or more of the following;
- Hematocrit <45% without phlebotomy
- Platelet count ≤ 400 x 10^9/L
- White blood cell count ≤ 10 x 10^9/L
- Non-palpable spleen

Approval duration for initiation and renewal: 1 year

Selinexor
Brand(s): Xpovio
DOSAGE FORM/ STRENGTH: 20 mg tablet
Effective date: September 7, 2023

Initial Criteria:

For the treatment of patients with relapsed and/or refractory multiple myeloma who meet ALL of the following criteria:

1. Aged 18 years old or older; AND
2. Patient has failed treatment with at least one prior therapy for multiple myeloma; AND
3. Patient is using selinexor in combination with bortezomib and dexamethasone (SVd) (Note 1); AND
4. Patient is deemed to be sensitive to proteasome inhibitors (PIs) (Note 2), defined as having disease that has not been refractory to bortezomib or another PI, and/or has not experienced disease progression while on bortezomib or another PI (Note 3)

Notes:

1. Patients must meet the eligibility requirements for bortezomib through the New Drug Funding Program (NDFP).

2. Prior proteasome inhibitor (PI) therapy is permitted provided:
   - The patient had a PI treatment-free interval of at least 6 months before the start of SVd; AND
   - Achieved a best response of at least a partial response (PR) with prior bortezomib (at any time), and achieved a best response of at least a PR during the last PI therapy (alone or in combination); AND
   - The patient did not discontinue bortezomib due to grade 3 or higher toxicity.

3. Refractory disease is defined as:

   a. Disease progression within 60 days after stopping treatment; or
   b. Disease progression on any dose of selinexor, bortezomib or another PI; or
   c. Non-responsive disease during therapy (either failure to achieve minimal response or disease progression).

   Relapsed / Disease Progression is defined as having one or more of the following:

   a. An increase of 25% from lowest response value in serum M-component (absolute increase must be greater than or equal to 0.5g/dL), and/or urine M-component (absolute increase must be greater than or equal to 200 mg/24 hours).
   b. An absolute increase of greater than 10mg/dL in the difference between involved and uninvolved free light chain (FLC) levels (if no measurable serum and urine M-protein levels).

Selinexor
Brand(s): Xpovio
DOSAGE FORM/ STRENGTH: 20 mg tablet

c. Definite development of new bone lesions or soft tissue plasmacytomas or definite increase in the size of existing bone lesions or soft tissue plasmacytomas.
d. Development of hypercalcemia (corrected serum calcium greater than 11.5 mg/dL or 2.5 mmol/L) that can be attributed solely to the plasma cell proliferative disorder.

4. Patients with plasma cell leukemia or systemic light chain amyloidosis may be considered for funding of Selinexor (as part of SVd) provided all other eligibility criteria are met.

Exclusions:

Patients meeting any of the below criteria will not be eligible for reimbursement of selinexor:

1. Patients with multiple myeloma who have experienced disease that has been refractory to treatment with bortezomib or selinexor.
2. Patients with multiple myeloma who have experienced disease progression while on bortezomib or selinexor.
3. Patients requesting selinexor as part of a first line treatment regimen for multiple myeloma.
4. Patients requesting selinexor as monotherapy for multiple myeloma.

Renewal criteria:

Renewal of reimbursement of selinexor for use in combination with bortezomib and dexamethasone may be considered in those who continue to respond to therapy and have not experienced refractory disease, disease progression, or unacceptable toxicity.

Recommended Dose:

Selinexor 100 mg on days 1, 8, 15, 22, and 29 of each 35-day cycle

Bortezomib dosing:

Bortezomib 1.3 mg/m^2 subcutaneously (SC) or intravenously (IV) on days 1, 8, 15, and 22 in combination with selinexor and dexamethasone administered on an every 35-day cycle.

Approval duration of initials and renewals:1 year

Selpercatinib
Brand(s): Retevmo
DOSAGE FORM/ STRENGTH: 40 mg and 80 mg capsules
Effective date: July 31, 2023

Initiation Criteria for non–small cell lung cancer (NSCLC)

For the treatment of metastatic rearranged during transfection (RET) fusion-positive non–small cell lung cancer (NSCLC) **i**n adult patients meeting all the following criteria:

1. Patient is 18 years of age or older; AND
2. Has previously untreated NSCLC with documented RET-fusion positive NSCLC; OR
   Previously treated with one or more systemic therapies for NSCLC in a patient with documented RET-fusion positive NSCLC; AND
3. Has a good performance status; AND
4. Selpercatinib is administered as monotherapy; AND
5. Prescribed by a clinician with expertise in the management of lung cancer.

Exclusion Criteria:

Selpercatinib will not be funded in combination therapy with another systemic cancer treatment for NSCLC.

Renewal Criteria:

Renewals will be considered until the patient is experiencing clinically meaningful disease progression or unacceptable toxicity.

Approval Durations: Initial: 6 months **Renewals**: 1 year

Initiation Criteria for differentiated thyroid cancer (DTC)

For the treatment of rearranged during transfection (RET) fusion-positive, advanced or metastatic, differentiated thyroid cancer (DTC) in patients meeting all the following criteria;

1. Patient is 18 years of age or older; AND
2. Has differentiated thyroid cancer that is advanced or metastatic (not amenable to surgery or radioactive iodine therapy); AND
3. Patient is using selpercatinib as third or subsequent line after experiencing failure or intolerance to radioactive iodine (Note 1), and lenvatinib or sorafenib for DTC; AND
4. Has a good performance status; AND
5. Selpercatinib is administered as monotherapy; AND
6. Prescribed by a clinician with expertise in the management of thyroid cancer.

Selpercatinib
Brand(s): Retevmo
DOSAGE FORM/ STRENGTH: 40 mg and 80 mg capsules

Notes:
1. Patients with a contraindication to the use of radioactive iodine therapy are considered for funding on a case-by-case basis. Please provide details of the contraindication with your request.

Exclusion Criteria:

Selpercatinib will not be funded in combination therapy with another systemic cancer treatment for DTC.

Renewal Criteria:

Renewals will be considered until the patient is experiencing clinically meaningful disease progression or unacceptable toxicity.

Recommended dose:

Under 50kg: 120 mg orally every 12 hours.
50 kg or greater: 160 mg orally every 12 hours.

Approval Durations: Initials: 6 months **Renewals**: 1 year

Initiation Criteria for medullary thyroid cancer (MTC)

For the treatment of rearranged during transfection (RET) - mutant unresectable advanced or metastatic medullary thyroid cancer (MTC) in patients meeting all the following criteria;

1. Patient is 12 years of age or older; AND
2. Has medullary thyroid cancer that is unresectable advanced or metastatic; AND
3. Patient is using selpercatinib as second line therapy after experiencing failure or intolerance to vandetanib for MTC; AND
4. Has a good performance status; AND
5. Selpercatinib is administered as monotherapy; AND
6. Prescribed by a clinician with expertise in the management of thyroid cancer.

Notes:
1. Patients with a contraindication to the use of vandetanib are considered for funding. Please provide details of the contraindication with your request.
2. Case-by-case consideration will be provided for those who have progressed on cabozantinib (not publicly funded).

Selpercatinib
Brand(s): Retevmo
DOSAGE FORM/ STRENGTH: 40 mg and 80 mg capsules

Exclusion Criteria:

Selpercatinib will not be funded in combination therapy with another systemic cancer treatment for MTC.

Renewal Criteria:

Renewals will be considered until the patient is experiencing clinically meaningful disease progression or unacceptable toxicity.

Recommended dose:
Under 50kg: 120 mg orally every 12 hours.
50 kg or greater: 160 mg orally every 12 hours.

Approval Durations: Initials: 6 months **Renewals**: 1 year

Sorafenib
Brand(s): Nexavar
DOSAGE FORM/ STRENGTH: 200 mg tablet

For the treatment of metastatic renal cell carcinoma (MRCC) as second-line treatment for patients who have:

a) Histologically confirmed metastatic clear-cell renal-cell carcinoma; AND
b) Experienced disease progression after prior cytokine therapy within the previous 8 months; AND
c) A performance status of 0 or 1 on the basis of the Eastern Cooperative Oncology Group criteria; AND
d) Intermediate-risk or low-risk status, according to the Memorial Sloan-Kettering Cancer Center (MSKCC) prognostic score.

Duration of Approval: 1 year

Renewals will be considered with confirmation from the physician that the patient has benefited from therapy and is expected to continue to do so.

Sorafenib
Brand(s): Nexavar
DOSAGE FORM/STRENGTH: 200 mg tablet

For the treatment of advanced hepatocellular carcinoma (HCC) in patients who have:
a) Child-Pugh Class A disease; and
b) ECOG* status 0, 1 or 2; and
c) Either progressed on transarterial chemoembolization (TACE) or are not suitable for the TACE procedure (where detailed rationale is provided).

Duration of Approval: 3 months

*ECOG = Eastern Cooperative Oncology Group Performance Status

Renewal will be considered for patients with documentation of radiography and/or scan results indicating no diseases progression.

Sunitinib
Brand(s): Sutent and generics
DOSAGE FORM/ STRENGTH: 12.5 mg, 25 mg, 50 mg capsule

For the treatment of gastrointestinal stromal tumour (GIST) in patients with unresectable or metastatic/recurrent GIST where one of the following conditions is met:

- Early progression (within 6 months) while on imatinib; OR
- Progression following treatment with optimum (escalated) doses of imatinib (800mg per day); OR
- Intolerance* to imatinib (where detailed description of intolerance is provided).

*Definition of intolerance to imatinib – patient has experienced persistent grade 3 toxicity requiring discontinuation of therapy.

Duration of Approval: 6 months

Renewal will be considered for patients who are stable (no disease progression) and not experiencing intolerance to sunitinib therapy.

Note: Approval will be granted at a dose of 50mg per day (4 weeks on, 2 weeks off).

For the treatment of metastatic renal cell carcinoma (MRCC):
- First-line therapy for patients with MSK Prognostic Score of Favourable Risk or an Intermediate Risk OR
- Second-line therapy for patients where:
  - The disease is of clear cell histology AND
  - Documented failure to first-line cytokine-based therapy

Sunitinib
Brand(s): Sutent
DOSAGE FORM/ STRENGTH: 12.5 mg, 25 mg, 50 mg capsules

Duration of Approval: 1 year

Renewal will be considered for patients with documentation of radiography and/or scan results indicating no diseases progression.

Duration of Approval: 1 year
Note: The prescribed dosage should be 50 mg daily for four (4) weeks, followed by two (2) weeks off the Drug Product, in repeated six (6) week cycles.

For the treatment of progressive, unresectable, well-differentiated or moderately differentiated, locally advanced or metastatic pancreatic neuroendocrine tumors ("pNET") with good performance status (ECOG ≤ 2), until disease progression.

Exclusion criteria: Sutent will not be approved for second-line sequential therapy after everolimus failure in the first-line setting.

Dosing: 37.5 mg daily

Thalidomide
Brand(s): Thalomid
DOSAGE FORM/ STRENGTH: 50 mg capsule,100 mg capsule, 200 mg capsule

For the treatment of Multiple Myeloma in patients 65 years of age or older meeting the following criteria;

a) Thalidomide is being used in combination with melphalan and prednisone; AND
b) The patient has not previously received other treatments[1] for multiple myeloma; AND
c) The patient is deemed to be unsuitable for stem cell transplantation; AND

[1] Exception is for those meeting bortezomib criteria as described below.

It should be noted that funding of thalidomide will be considered on a case-by-case basis for patients who have developed severe (grade III/IV) thrombocytopenia during the first 1 to 2 cycles of treatment with bortezomib and who have not experienced disease progression on bortezomib.

Duration of Approval: A maximum of 12 six-week cycles

Exclusion criteria:

Funding will not be considered for patients who are using thalidomide as second-line treatment of multiple myeloma.

Trametinib
Brand(s): Mekinist
DOSAGE FORM/ STRENGTH: 0.5 mg, 2 mg tablet
Updated January 7, 2020

Initial criteria:

For the mutation-targeted treatment of patients with BRAF V600 mutation-positive unresectable melanoma or metastatic melanoma meeting the following criteria:

3. As monotherapy or as combination therapy with dabrafenib.

4. If brain metastases are present, they should be asymptomatic or stable

Exclusion Criteria:
- BRAF V600 negative, or wild type tumors, or unknown status will not be funded
- Funding will not be considered in patients who have experienced progression on a BRAF mutation targeted therapy. The Ministry will fund only one BRAF mutation targeted treatment/treatment regimen.
- May be sequenced after immunotherapies or other funded treatments, however, treatment beyond third line will not be considered for funding.

Recommended Dose as Monotherapy:

2 mg once daily until disease progression or development of unacceptable toxicity requiring discontinuation of trametinib

Recommended Dose as combination dual therapy with Dabrafenib:

Trametinib 2mg once daily and Dabrabenib 150 mg twice daily, until disease progression or development of unacceptable toxicity requiring discontinuation

Renewal criteria:

Therapy as monotherapy OR as combination dual therapy (as above) may be continued until evidence of disease progression[1] or development of unacceptable toxicity requiring discontinuation.

[1] Letter from physician outlining radiological and clinical benefit requiring continuation of the drug and verification of no disease progression must be submitted.

Approval duration (both initial and renewal requests): 6 months (patients should have their disease status assessed at least every 6 months)

Trametinib
Brand(s): Mekinist
DOSAGE FORM/ STRENGTH: 0.5 mg, 2 mg tablet

Case by case:

Requests in patients who have initiated another single-agent BRAF or MEK inhibitor therapy will be considered on a **case-by-case** basis ONLY IF there has been no disease progression.

Requests in patients who have initiated another single-agent BRAF or MEK inhibitor therapy will be considered on a case-by-case basis ONLY IF there has been no disease progression.

Exclusion Criteria:

- BRAF V600 negative, or wild type tumors, or unknown status will not be funded
- Trametinib therapy (as monotherapy or in combination with dabrafenib) will not be considered for funding in patients who have progressed on a prior BRAF inhibitor therapy used as monotherapy or in combination.

For the adjuvant treatment of resected Stage III cutaneous melanoma in patients meeting ALL the following criteria;

i) Trametinib is being used as combination therapy with Dabrafenib

ii) Patient's cutaneous melanoma met the following requirements prior to resection:
   a. Histologically confirmed stage IIIA (limited to lymph node metastases of > 1 mm), IIIB, IIIC, or IIID cutaneous melanoma [8th edition of the American Joint Committee on Cancer staging system]
   b. BRAF V600 mutated (all BRAF V600 mutations)

iii) Post-resection, clinical or radiographic confirmation of complete disease resection including absence of in-transit metastases must be provided.[1]

iv) Eastern Cooperative Oncology Group (ECOG) Performance Status 0 to 2

[1] Micrometastatic lymph node involvement detected by sentinel lymph node biopsy will be allowed.

Exclusion Criteria:
- Patients with stage IIIA cutaneous melanoma with lymph node metastases less than 1 mm.
- Monotherapy with Dabrafenib
- Combinations with other anticancer therapies

Trametinib

Brand(s): Mekinist

DOSAGE FORM/ STRENGTH: 0.5 mg, 2 mg tablet

Recommended Dose in adjuvant therapy:

Trametinib 2mg once daily and Dabrabenib 150 mg twice daily

Notes: Treatment administered post-resection until disease recurrence or unacceptable toxicity to a maximum of 12 months of treatment in total.

(Note: 12 months refers to duration of adjuvant treatment accessed through all sources of funding (i.e. private and public).

Approval duration: Maximum of 12 months. Renewals are not considered.

Additional notes:

1. The Ministry will reimburse for provincially funded treatments for use in the adjuvant setting in patients with cutaneous melanoma for a total duration of up to 12 months. Overall access to adjuvant therapy will be limited to 12 months in total and combines the duration of use of all treatments administered in the adjuvant setting.

2. Funding will not be granted for dabrafenif-trametinib in patients who have used another treatment in the adjuvant setting for cutaneous melanoma for a duration of 3 months or longer.

3. A one-time switch to dabrafenif-trametinib in the adjuvant cutaneous melanoma setting will be permitted for BRAF-mutated patients who switch from another adjuvant treatment that has been used for less than 3 months and upon meeting the above funding criteria.

4. Patients who experience disease progression within 6 months of completion of adjuvant BRAF therapy will not be funded for another BRAF targeted therapy.

5. Switching to cobimetinib-vemurafenib from dabrafenib-trametinib will not be permitted in BRAF-positive patients.

Trifluridine/Tipiracil
Brand(s): Lonsurf
DOSAGE FORM/ STRENGTH: 15 mg/6.14 mg tablet, 20 mg/8.19 mg tablet
Effective date: March 25, 2021 Updated: November 1, 2024 (MCC)

Metastatic gastric cancer or adenocarcinoma of the gastroesophageal junction

Initiation Criteria:

In combination with best supportive care (BSC) for the treatment of metastatic gastric cancer (mGC) or adenocarcinoma of the gastroesophageal junction (GEJ) in adult patients who meet ALL of the following criteria;

1. Patient has histologically confirmed non-resectable, metastatic, gastric adenocarcinoma (including GEJ) as defined by the American Joint Committee of Cancer (AJCC) staging classification; AND
2. Patient has experienced disease progression[1] and/or clinically relevant intolerances or allergies with at least two (2) prior lines of chemotherapy including a fluoropyrimidine, a platinum, and either a taxane or irinotecan-containing regimen;
   OR
   Patient has HER2 positive disease and has experienced disease progression[1] and/or clinically relevant intolerances or allergies with at least two (2) prior lines of chemotherapy including a fluoropyrimidine, a platinum, and either a taxane or irinotecan-containing regimen, and at least one HER2/neu-targeted therapy;

AND

3. Patient has Eastern Cooperative Oncology Group (ECOG) status 0 or 1.

[1] As confirmed via imaging during/within 3 months of previously completed line(s) of therapy

Note: If patients have experienced intolerances with the prior lines of therapy, please provide a description of the intolerance including grade of toxicity which required the drug regimen to be stopped.

Renewal Criteria:
Renewals will be considered until radiographic evidence of disease progression or development of unacceptable toxicities.

Renewals should include radiographic reports and will be evaluated according to modified Response Evaluation Criteria in Solid Tumors (mRECIST) or RECIST 1.1 criteria.

Approval duration of initial and renewals: 6 months.

Recommended dose:
35 mg/m^2/dose twice daily on days 1 to 5 and days 8 to 12 of each 28-day cycle.
Dose adjustments based on individual safety and tolerability.

Trifluridine / Tipiracil
Brand(s): Lonsurf
DOSAGE FORM/ STRENGTH: 15 mg/6.14 mg , 20 mg/8.19 mg tablet

Metastatic colorectal cancer as combination therapy with bevacizumab

Initiation Criteria:

For the treatment of patients with previously treated metastatic colorectal cancer (mCRC) as combination therapy with bevacizumab in patients meeting ALL the following criteria:

1. 18 years of age or older; AND
2. Histologically confirmed adenocarcinoma with either unresectable or metastatic disease; AND
3. Disease progression or demonstrated intolerance to a maximum of 2 prior chemotherapy regimens for the treatment of advanced colorectal cancer that must include a fluoropyrimidine-, oxaliplatin-, and irinotecan-based chemotherapy, anti-VEGF monoclonal antibody and/or an anti-EGFR monoclonal antibody for RAS wild-type disease. (Note 1, 2 and 3); AND
4. Trifluridine-tipiracil must be used in combination with bevacizumab and the regimen should not be used with other systemic therapy for the treatment of mCRC; AND
5. Patient should have good performance status; AND
6. Prescribed by a clinician with expertise in the diagnosis and treatment of colorectal cancer.

Notes:

1. Patients who had received adjuvant/neoadjuvant chemotherapy and had recurrence during or within 6 months of completion could count the adjuvant/ neoadjuvant therapy as ONE of the maximum of 2 required prior chemotherapy regimens to qualify.
2. Patients who have experienced intolerances with the prior lines of therapy must provide a description of the intolerance including grade of toxicity which required the drug regimen to be stopped. Those who are not deemed to be a candidate for a required prior line of therapy must include the contraindication with the request.
3. Trifluridine-tipiracil used in combination with bevacizumab may be considered after third line treatment for mCRC on a case-by-case basis.
4. Patients may be eligible for trifluridine-tipiracil in combination with bevacizumab regardless of prior bevacizumab exposure.

Trifluridine / Tipiracil
Brand(s): Lonsurf
DOSAGE FORM/ STRENGTH: 15 mg/6.14 mg , 20 mg/8.19 mg tablet

5. Patients who were unable to receive bevacizumab in a prior line of therapy due to a contraindication may be eligible for trifluridine-tipiracil in combination with bevacizumab.
6. Patients with metastatic small bowel adenocarcinoma or appendiceal adenocarcinoma who meet all other funding criteria may be considered for trifluridine-tipiracil in combination with bevacizumab.
7. Patients meeting eligibility criteria for trifluridine and tipiracil who are microsatellite instability high/mismatch repair deficient and/or those with a BRAF V600E mutation would be considered eligible for treatment with trifluridine-tipiracil in combination with bevacizumab if all other lines of therapy have been used.
8. If bevacizumab is discontinued for reasons other than disease progression, trifluridine-tipiracil could be continued. If trifluridine-tipiracil are discontinued, then bevacizumab is to be discontinued.

Exclusion criteria:
Patients meeting any ONE of the following will not be funded.

1. Funding is not provided in patients with symptomatic, unstable central nervous system (CNS) metastases.

2. Funding is not provided in those requiring increasing doses of steroid to control CNS disease.

Renewal Criteria:

Combination therapy with bevacizumab may be continued until evidence of disease progression based on RECIST criteria as determined by radiographic scans or development of unacceptable toxicity.

Approved dose:

Recommended starting dose is 35 mg/m^2/dose administered orally with water, twice daily on Days 1 to 5 and Days 8 to 12 of each 28-day cycle. This treatment cycle is repeated every 4 weeks.

Doses may be adjusted to manage adverse effects as aligned with the product monograph.

Approval duration: 1 year

Tucatinib
Brand(s): Tukysa
DOSAGE FORM/ STRENGTH: 50 mg, 150 mg tablet
Effective date: February 21, 2023 Updated: October 24, 2023

Initial criteria:

For the treatment of adult patients with HER-2 positive locally advanced or metastatic breast cancer in patients meeting ALL the following criteria;

1. Patient is at least 18 years old; AND

2. HER2-positive status is confirmed using a validated test; AND

3. Has received at least ONE prior systemic treatment for HER-2 positive locally advanced/metastatic breast cancer; AND

4. Has received prior treatment separately, or in combination with, trastuzumab, pertuzumab, and either trastuzumab emtansine (T-DM1) or trastuzumab deruxtecan; AND

5. Has Eastern Cooperative Oncology Group (ECOG) Performance Status 0 to 2 and have adequate blood counts and organ function; AND

6. Tucatinib is not being used as monotherapy and must be used in combination with trastuzumab and/or capecitabine unless the patient must discontinue for therapeutic reasons either trastuzumab or capecitabine, but not both. (see note 1).

Exclusion criteria:

Patients who have experienced disease progression on capecitabine used in a prior line of therapy.

Notes:

1. Treatment with tucatinib can continue if discontinuation is required for either capecitabine or trastuzumab due to toxicity. If trastuzumab and capecitabine are both discontinued, tucatinib must also be discontinued as it is not funded as monotherapy.
2. Patients with brain metastases are eligible for funding of tucatinib upon meeting all the criteria.
3. Patients currently or previously treated with lapatinib can be considered for tucatinib-capecitabine-trastuzumab combination therapy as long as the lapatinib therapy is stopped.

Tucatinib
Brand(s): Tukysa
Dosage Form/Strength: 50 mg and 150 mg tablets

4. Patients currently on capecitabine monotherapy may add tucatinib and trastuzumab to the treatment regimen as long as disease progression on capecitabine has not occurred.
5. Patients who have not experienced disease progression on their current systemic therapy may consider switching to a tucatinib-trastuzumab-capecitabine regimen if the tucatinib criteria are otherwise met.

Renewal Criteria:

Renewals will be considered in patients who have not demonstrated evidence of disease progression or development of unacceptable toxicity requiring discontinuation of tucatinib or discontinuation of both capecitabine and trastuzumab (see Note 1)

Recommended dose:

Tucatinib 300 mg orally twice daily

Tucatinib is funded in combination with capecitabine and trastuzumab at the recommended doses as follows:

Capecitabine 1000 mg/m^2 orally twice daily on days 1 to 14 of every 21-day cycle.

Trastuzumab 8 mg/kg as a loading dose intravenously (IV) on day 1 of the first cycle, followed by 6 mg/kg IV every 21 days until disease progression or unacceptable toxicity, whichever comes first. (Note: Other dosing options may be administered. Please refer to Ontario Health Cancer Care Ontario)

Approval Duration (Initials): 6 months

Approval Duration of first renewal: 6 months

Approval Duration of renewals: 1 year

Vandetanib
Brand(s): Caprelsa
DOSAGE FORM/ STRENGTH: 100 mg, 300mg tablet
Effective date: September 13, 2018

Caprelsa (Vandetanib) is funded for the treatment of symptomatic and/or progressive[1] medullary thyroid cancer (MTC) in patients who meet the following criteria;

(a) Patient has unresectable locally advanced or metastatic disease; AND

(b) Vandetanib is being used as monotherapy for MTC; AND

(c) ECOG less than or equal to 2[2]; AND

(d) Prescribed by or in consultation with an oncologist or internist experienced with the treatment of MTC.

Exclusion Criteria:

(a) Patients with QT interval prolongation/abnormalities (e.g. QTc that is unmeasurable or greater than or the same as 480ms) or who are taking medications that prolong QT interval prolongation.

(b) Patients with indolent, asymptomatic, or slowly progressive disease.

(c) Vandetanib is not funded as combination therapy

Renewal Criteria:

Renewal of funding will be provided until disease progression or development of unacceptable toxicity[3].

[1] As confirmed by radiological reports.

[2] Patients with an ECOG greater than 2 will be considered case-by-case upon submission of information regarding the risk of toxicity.

[3] At the time of renewal, prescriber should address whether there have been any significant cardiac events or concerns regarding cardiovascular toxicities.

Duration of approval for initial and renewal criteria: 1 year

Note: Prescribers and dispensing pharmacies are presumed to be in compliance with the requirements of the Caprelsa Restricted Distribution Program which is administered through the manufacturer.

Venetoclax

Brand(s): Venclexta
DOSAGE FORM/ STRENGTH: 10 mg, 50 mg, 100 mg, tablet; Starter Pk (10mg/50mg/100mg)
Effective date: May 13, 2019 (CLL), Updated: March 16 (CLL); 2020; May 6, 2022 (first line ven-obi); August 19, 2022 (AML)

Chronic lymphocytic leukemia

Initiation Criteria:

For the treatment of adult patients with chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL) who requires treatment according to the International Workshop on Chronic Lymphoma Leukemia criteria and meeting the following criteria;

1. Patient has good performance status with ECOG equal to or less than 2; AND
2. Venetoclax is being used in one of the following situations;

i) Venetoclax will be used in combination with obinutuzumab as first line therapy in a patient with previously untreated CLL or SLL and who is deemed to be unfit for a fludarabine-based regimen (Note 1); OR

ii) Venetoclax will be used in the relapsed refractory setting in combination with rituximab as second or subsequent line of therapy in a patient who has experienced treatment failure or unacceptable toxicities to ONE or more of the following regimens:

a. a fludarabine-based regimen
b. a Bruton's Tyrosine Kinase (BTK) inhibitor (i.e. acalabrutinib or ibrutinib) OR a combination therapy with idelalisib and rituximab
c. relapsed after a progression-free remission of more than 6 months in duration following chlorambucil-obinutuzumab in first line or a rituximab-based chemoimmunotherapy regimen in first or subsequent lines
d. relapsed after a progression-free remission of more than 12 months following a combination regimen of venetoclax and obinutuzumab used as first line;

OR

iii) Venetoclax will be used as monotherapy in the relapsed refractory setting as second or subsequent line of therapy in a patient who has experienced treatment failure or unacceptable toxicities to at least one prior line of therapy which may include;

a. a fludarabine-based regimen or a rituximab-based chemoimmunotherapy regimen
b. a Bruton's Tyrosine Kinase (BTK) inhibitor (i.e. acalabrutinib or ibrutinib) or a combination therapy with idelalisib and rituximab
c. chlorambucil-obinutuzumab in first line

Venetoclax
Brand(s): Venclexta
Dosage Form/Strength: 10 mg, 50 mg,100 mg, Starter Pack (4 week supply)

d. relapsed after a progression-free remission of more than 12 months following a combination regimen of venetoclax and obinutuzumab used as first line or a venetoclax and rituximab combination used in second or subsequent lines.

Notes:

1. A patient who is deemed to be unfit for a fludarabine-based regimen may be indicated by a Cumulative Illness Rating Scale (CIRS) score greater than 6 OR creatine clearance (CrCl) that is less than 70 mL per minute.

2. Provincially funded chemotherapy and immunotherapy combination regimens for CLL can be considered based on the patient's fitness/frailty and tolerability to targeted options. Patients must have met the provincial funding criteria for the prior lines of therapy. (For example, a patient using a BTK inhibitor as first line must have high risk cytogenic markers in accordance with the published EAP reimbursement criteria.)

   Refer to a list of funded chemoimmunotherapy regimens on the Ontario Health - Cancer Care Ontario (OH-CCO) website at https://www.cancercareontario.ca/en/search?nav-search=CLL&sort_by=search_api_relevance&=Apply

3. Retreatment with venetoclax in combination with rituximab therapy may be considered at the time of relapse for patients who were able to tolerate and complete 12 months of venetoclax and obinutuzumab and/or 24 months of a combination venetoclax and rituximab regimen and who have demonstrated a progression-free remission of at least 12 months in duration after stopping therapy.

4. Patients with severe intolerances to treatments required in prior lines of therapy will be considered case-by-case. Please provide details of the grade of toxicity experienced and/or clinical details to justify the contraindication to treatment options.

5. Venetoclax as monotherapy or as combination therapy with rituximab will not be funded in fifth line or beyond, except case-by-case consideration will be provided for a venetoclax and rituximab combination therapy if the request meets the retreatment criteria in Note 3.

Venetoclax
Brand(s): Venclexta
Dosage Form/Strength: 10 mg, 50 mg,100 mg, Starter Pack (4 week supply)

Renewal Criteria:

Renewals for venetoclax monotherapy will be considered until disease progression or development of unacceptable toxicity.

Renewals for venetoclax in combination with rituximab will be considered until disease progression or development of unacceptable toxicity up to a maximum of two years, whichever comes first.

Renewals for venetoclax in combination with Obinutuzumab will not be considered.

Exclusion Criteria (The following situations will not be funded.)

1. Patients who have experienced disease progression while on venetoclax.
2. Retreatment with venetoclax in a combination with obinutuzumab for relapsed disease.
3. Patient who has experienced a relapse of CLL or SLL within 6 months of stopping/completing a rituximab-containing regimen or an obinutuzumab-containing regimen for CLL will not be reimbursed for a venetoclax combination regimen with rituximab in a subsequent line.
4. Patient who has had an allogenic stem cell transplant in the 12 months preceding the request for EAP coverage for venetoclax as monotherapy or as combination therapy with rituximab.
5. Patients with active or uncontrolled autoimmune cytopenias.
6. Patients with a history of central nervous system (CNS) lymphoma, CNS leukemia, CNS prolymphocytic leukemia, or Richter syndrome will not be reimbursed for venetoclax in combination with obinutuzumab.

Dosing Regimen of Venetoclax monotherapy:

Using the venetoclax (Venclexta) “starter pack” for the ramp up phase, dose at 20 mg once daily for 7 days, followed by 50 mg once daily for 7 days, followed by 100 mg once daily for 7 days, followed by 200 mg once daily for 7 days, followed by 400 mg once daily until disease progression or unacceptable toxicity.

Approved Duration for venetoclax monotherapy Initiation and renewals: 1 year

Dosing Regimen for venetoclax and obinutuzumab (VEN-OBI) combination regimen:

Venetoclax:

Using the venetoclax (Venclexta) “starter pack” for the ramp up phase starting on day 22 of Cycle 1, dose at 20 mg once daily for 7 days (week 1), 50 mg once daily for 7 days (week 2), 100mg once daily for 7 days (week 3), followed by 200 mg once daily for 7 days

(week 4), followed by 400mg once daily until disease progression or unacceptable toxicity up to a maximum of 12 Cycles (i.e. 48 weeks) whichever comes first.

Obinutuzumab:
Cycle 1 - 100 mg Intravenously (IV) on Day 1 followed by 900 mg on day 2 (or 1000 mg on day 1), followed by 1000 mg IV on days 8 and 15, in combination with venetoclax.

Cycle 2 to 6 - 1000 mg IV on day 1 in combination with venetoclax

Treatment should be given for a total of 12 months as a finite treatment (i.e., six 28-day cycles of obinutuzumab in combination with venetoclax, followed by six additional cycles of single agent venetoclax)

Approved Duration for venetoclax (used in a regimen with Obinutuzumab): 1 year

Dosing Regimen for venetoclax and rituximab (VEN-RITUX) combination regimen:

Venetoclax: Using the venetoclax (Venclexta) “starter pack” for the ramp up phase, dose at 20 mg once daily for 7 days (week 1), 50mg once daily for 7 days (week 2), 100 mg once daily for 7 days (week 3), followed by 200mg once daily for 7 days (week 4), followed by 400 mg once daily until disease progression or unacceptable toxicity up to a maximum of two years (24 months from Cycle 1 Day 2 of rituximab) whichever comes first.

Rituximab:

Cycle 1 - 375 mg/metre^2 Intravenously (IV) on Day 1 (to be initiated after the patient has completed 5 weeks of ramp-up schedule with venetoclax and having received the 400 mg dose of venetoclax for 7 days)

Cycle 2 to 6 – 500 mg/m^2 IV on Day 1, for a total of 6 infusions of rituximab.

The use of rituximab subcutaneous may be considered in patients who are able to tolerate at least one full dose of intravenous infusion of rituximab during the first cycle. If a patient is unable to receive the full IV rituximab dose, continue subsequent cycles with rituximab IV until a full IV dose can be successfully given.

Approved Duration for venetoclax (used in a regimen with rituximab) - 1 year

A total treatment duration of 2 years will be funded from the date of addition of rituximab to the treatment regimen

Exclusion Criteria:

- Patients who are NOT CD20 antibody sensitive (i.e. an individual who has experienced a relapse of CLL within 12 months of stopping/completing a rituximab-containing regimen or an obinutuzumab-containing regimen for CLL) will not be reimbursed for a venetoclax combination regimen with rituximab.

Venetoclax
Brand(s): Venclexta
Dosage Form/Strength: 10 mg, 50 mg,100 mg, Starter Pack (4 week supply)

Exclusion Criteria (Continued):

- Patient who has had an allogenic stem cell transplant in the 12 months preceding the request for EAP coverage for venetoclax as monotherapy or as combination therapy with rituximab.
- Patients with active or uncontrolled autoimmune cytopenias.

Dosing Regimen of Venetoclax monotherapy:

Using the venetoclax (Venclexta) “starter pack” for the ramp up phase, dose at 20 mg once daily for 7 days, followed by 50mg once daily for 7 days, followed by 100mg once daily for 7 days, followed by 200mg once daily for 7 days, followed by 400mg once daily until disease progression or unacceptable toxicity.

Approved Duration for venetoclax monotherapy initiation and renewals: 1 year

Dosing Regimen for Venetoclax within a rituximab combination regimen:

Using the venetoclax (Venclexta) “starter pack” for the ramp up phase, dose at 20mg once daily for 7 days (week 1), 50mg once daily for 7 days (week 2), 100mg once daily for 7 days (week 3), followed by 200mg once daily for 7 days (week 4), followed by 400mg once daily until disease progression or unacceptable toxicity up to a maximum of two years (24 months from Cycle 1 Day 2 of rituximab) whichever comes first.

Dosing Regimen for Rituximab within a venetoclax combination regimen:

375 mg/metre^2 Intravenously[1] on Day 1 of Cycle 1 (to be initiated after the patient has completed 5 weeks of ramp-up schedule with venetoclax and having received the 400 mg dose of venetoclax for 7 days), followed by 500mg/m^2 on Day 1 of Cycles 2 to 6, for a total of 6 infusions[1] of rituximab.

Approved Duration for venetoclax within a combination regimen with rituximab - Initiation: 1 year

Renewal duration for venetoclax within a combination regimen with rituximab:1 year (total treatment duration funded is a maximum of 2 years from the date of addition of rituximab to the treatment regimen.)

Venetoclax
Brand(s): Venclexta
DOSAGE FORM/ STRENGTH: 50 mg, 100 mg tablet
Effective: August 19, 2022

Acute myeloid leukemia

Initial Criteria:

For the treatment of adult patients with newly diagnosed acute myeloid leukemia (AML) who meet the following criteria:

1. Venetoclax is used in combination with azacitidine; AND

2. Patient has not received prior treatment with venetoclax, a hypomethylating agent (e.g. azacitidine), and/or chemotherapy for myelodysplastic syndrome (MDS); AND

3. Patient is considered to be ineliglble for standard intensive induction chemotherapy for AML as a result of one of the following circumstances:

   i) Patient is 75 years of age or older and has an Eastern Cooperative Oncology Group (ECOG) performance status less than or equal to 2*
   OR
   ii) Patient is 18 to 74 years of age with at least ONE of the following comorbidities below;

      a. ECOG performance status of 2 to 3
      b. History of congestive heart failure requiring treatment
      c. Ejection fraction less than or equal to 50%
      d. Chronic stable angina
      e. Diffusing capacity of the lungs for carbon monoxide (DLCO) levels less than or equal to 65%
      f. Forced Expiry Volume in 1 second (FEV_1) less than or equal to 65%
      g. Creatinine clearance between 30 mL/min to less than 45 mL/min
      h. Moderate hepatic impairment with total bilirubin greater than 1.5 to less than or the same as 3 times the Upper limit of normal (ULN)

   *Case by case consideration may be provided for ECOG >2 if the worsened performance status is the result of AML.

4. Prescribed by clinicians with expertise in the diagnosis, treatment, and management of patients with AML.

Venetoclax
Brand(s): Venclexta
Dosage Form/Strength: 50 mg,100 mg tablets

Renewal Criteria

Renewals of funding of venetoclax in combination with azacitidine will be considered for patients who continue to derive clinical benefit and do not have documented disease progression or unacceptable toxicities from treatment.

Notes:

1. Patients without unacceptable toxicity, are recommended to be treated for a minimum of 6 cycles.
2. If a patient stops treatment with the azacitidine component as a result of toxicities or intolerances (i.e. reasons other than disease progression), venetoclax should also be discontinued.

Funded Dose and Duration:

Cycle 1:

Azacitidine 75 mg/m2 subcutaneously (SC) once daily for 6 or 7 doses (starting on day 1) in combination with oral venetoclax 100 mg once daily on day 1, 200 mg once daily on day 2, then 400 mg once daily on days 3 to 28.

Cycle 2 and onwards:

Azacitidine 75 mg/m2 SC once daily for 6 or 7 doses (starting on day 1) in combination with oral venetoclax 400 mg once daily on days 1 to 28
[repeated every 28 days; 1 cycle = every 28 days]

Renewal Duration of initials and renewals: 1 year

Vemurafenib
Brand(s): Zelboraf
DOSAGE FORM/ STRENGTH: 240 mg tablet

Initiation requests:

For the treatment of patients with BRAF V600 mutation-positive unresectable stage III or stage IV melanoma.

- As monotherapy or as combination therapy with cobimetinib
- If brain metastases are present, they should be asymptomatic or stable

Exclusion Criteria:

- BRAF V600 negative, or wild type tumors, or unknown status will not be funded
- The Ministry will fund only one BRAF mutation targeted treatment/treatment regimen.
- May be sequenced after immunotherapies or other funded treatments, however, treatment beyond third line will not be considered for funding.

Renewal requests:

Therapy as monotherapy OR as combination dual therapy (as above) may be continued until evidence of disease progression[1] or development of unacceptable toxicity requiring discontinuation.

[1] Letter from physician outlining radiological and clinical benefit requiring continuation of the drug and verification of no disease progression or development of unacceptable toxicity must be submitted.

Approval duration (both initial and renewal requests): 6 months (patients should have their disease status assessed at least every 6 months)

Case by case: Requests in patients who have initiated another BRAF and/or MEK inhibitor as monotherapy or combination therapy will be considered on a **case-by-case** basis ONLY IF there has been no disease progression.

Recommended Dose as Monotherapy:

960 mg twice daily until disease progression or development of unacceptable toxicity requiring discontinuation of vemurafenib.

Recommended Dose as combination dual therapy with Cobimetinib:

Cobimetinib 60mg once daily for 21 days, followed by seven days off treatment; AND

Vemurafenib 960mg twice daily for 28 days. Both drugs are given until disease progression or unacceptable toxicity.

Vismodegib
Brand(s): Erivedge
DOSAGE FORM/ STRENGTH: 150 mg tablet

For the treatment of metastatic basal cell carcinoma (BCC) or locally advanced BCC (including patients with basal cell nevus syndrome, i.e. Gorlin syndrome) in patients who meet the following criteria;

- Patient must have measurable metastatic disease or locally advanced disease; AND
- Patient's disease must be considered inoperable or inappropriate for surgery[1]; AND
- Patient's disease must be considered inappropriate for radiotherapy[2]; AND
- Patient is 18 years or age or older; AND
- Patient has an ECOG ≤ 2

Dose: 150 mg orally once daily taken until disease progression or unacceptable toxicity.
Requests must include the following information:

Duration of Approval: 1 Year

Physicians must provide rationale for why surgery AND radiation cannot be considered

- The request must include a surgical consult note that provides a preoperative/surgical evaluation why surgery is not appropriate for the patient; AND
- A consult note as to why radiation therapy is not appropriate for the patient; AND
- Both of the above evaluations must come from a physician who is not the requesting physician; AND
- The request must include confirmation that the patient has been discussed at a multi-disciplinary cancer conference (MCC) or equivalent.

[1] Considered inoperable or inappropriate for surgery for at least ONE of the following reasons:
- Technically not possible to perform surgery due to size/location/invasiveness of BCC (either lesion too large or can be several small lesions making surgery not feasible); OR
- Recurrence of BCC after two or more surgical procedures and curative resection unlikely; OR
- Substantial deformity and/or morbidity anticipated from surgery.

[2] Considered inappropriate for radiation for at least ONE of the following reasons:
- Contraindication to radiation (e.g. Gorlin syndrome); OR
- Prior radiation to lesion; OR
- Suboptimal outcomes expected due to size/location/invasiveness of BCC.

Vismodegib
Brand(s): Erivedge
DOSAGE FORM/ STRENGTH: 150 mg tablet

Note: Patient preference for oral therapy will not be considered

Renewals will be considered where the physician has confirmed that the patient has not experienced disease progression while on Erivedge therapy.

Duration of Approval: 1 Year

Zanubrutinib
Brand(s): Brukinsa
DOSAGE FORM/ STRENGTH: 80 mg capsule
Effective date: March 9, 2023 (WM) Updated January 12, 2024 (added CLL)

Zanubrutinib for Waldenstrom Macroglobulinemia

Initiation Criteria:

For the treatment of Relapsed or Refractory Waldenstrom Macroglobulinemia (WM) in patients meeting ALL the following criteria:

1. Confirmed diagnosis of WM from a prescriber with expertise in the management and diagnosis of WM; AND
2. At the time of initial diagnosis of WM, the patient met at least one criterion for treatment of active, symptomatic WM according to the International Workshops for Waldenström Macroglobulinaemia (IWWM) consensus panel; AND
3. Has relapsed or is refractory to at least one prior line of treatment for WM; AND
4. Has a good performance status of ECOG less than or equal to 2; AND
5. Zanubrutinib will be used as monotherapy.

Exclusion Criteria:

1. Patients who have experienced disease progression on another BTK inhibitor for WM.

2. Patients who have experienced disease transformation to another form of cancer.

Notes:

1. Blood work should be performed monthly at the beginning of treatment and then can be performed less frequently at the discretion of the treating physician.
2. Baseline imaging should be completed. For patients with extramedullary disease, imaging should be at the discretion of the treating physician.

Renewal Criteria:

Renewals will be considered in patients until disease progression or development of unacceptable toxicity.

Response to therapy should be evaluated in accordance with IWWM response criteria.

Approved dose:

320 mg orally daily or 160 mg twice a day.

Initial and renewal approval period: 1 year

Zanubrutinib
Brand(s): Brukinsa
DOSAGE FORM/ STRENGTH: 80 mg capsule

Zanubrutinib for chronic lymphocytic leukemia

Initiation Criteria:

For the treatment of adult patients with chronic lymphocytic leukemia (CLL) who meet the following criteria:

1. Diagnosed with active disease according to one or more of the criteria from the International Workshop on Chronic Lymphocytic Leukemia (iwCLL) criteria;

   AND

2. Meets one of the following circumstances of use:

   i) First line use in a previously untreated patient who presents with one or more of the following cytogenic markers:
      - chromosome 17p deletion; OR
      - TP53 mutation, OR
      - unmutated immunoglobulin heavy chain variable region (IgHV);

      OR

   ii) Patient with relapsed or refractory CLL who has experienced disease progression on atleast one prior systemic therapy/regimen for CLL.*

   *A prior line of therapy should include a fludarabine-based regimen in fit patients.

   AND

3. Zanubrutinib will be used as monotherapy; AND

4. Patient has good ECOG performance status; AND

5. Prescribed by a clinician with expertise and experience in the treatment and management of CLL.

Renewal Criteria:

Renewals will be considered in patients until disease progression (as defined based on published iwCLL [2018] or a more recent iwCLL) or unacceptable toxicity.

Zanubrutinib
Brand(s): Brukinsa
DOSAGE FORM/ STRENGTH: 80 mg capsule

Exclusion Criteria:
(Patients meeting the below will not be funded)

1. Patients who have experienced disease progression while being treated with another Bruton's tyrosine kinase (BTK) inhibitor (e.g. ibrutinib, acalabrutinib) for the treatment of CLL.
2. Patients with prolymphocytic leukemia.
3. Patients with current or history of Richter's syndrome.
4. Patients with central nervous system (CNS) lymphoma or leukemia.

Notes:

1. The Ministry will not fund idelalisib following progression on a BTK inhibitor.
2. Patients may switch to zanubrutinib from another BTK inhibitor (e.g. ibrutinib, acalabrutinib) as long as they have not experienced disease progression on another BTK inhibitor. Please include the reasons for requesting the switch with the application (e.g. intolerances, contraindications, etc.).
3. Zanibrutinib may be considered in patients diagnosed with small lymphocytic lymphoma (SLL) on a case-by-case basis upon meeting the above treatment eligibility criteria for CLL.

Approved Dosage for Initials and Renewals:

320 mg orally daily or 160 mg twice daily with dose adjustments as necessary based on the product monograph.

Duration for Approval of Initials and Renewals: 1 year

ONCOLOGY – SUPPORTIVE MANAGEMENT

Aprepitant
Brand(s): Emend
DOSAGE FORM/ STRENGTH: 80 mg,125 mg capsule,Tri-pack

Effective September 25, 2014, Emend transitioned to the ODB formulary for reimbursement in patients who meet the Limited Use criteria. Dosage regimens not meeting the LU criteria may be submitted to the EAP for consideration of reimbursement.

Denosumab
Brand(s): Xgeva
DOSAGE FORM/ STRENGTH: 120 mg per vial for subcutaneous injection
Updated September 11. 2024

Originator Xgeva will only be considered in patients who are established on Xgeva therapy who meet a medically necessary exemption.

For the treatment of bony metastases in patients with hormone refractory prostate cancer.

Xgeva is considered through CCO for those receiving prostate cancer treatment from a cancer clinic.

Hormone refractory prostate cancer is determined using the following criteria:

i) Patient has an elevated PSA level or evidence of progressive bony disease[1], despite castrate serum testosterone levels (Less than 1.7 nmol/L or less than 50 ng/dL)[2].

[1] Progressive bony disease is defined as progressive changes in radionucleotide bone scan or clinical signs of disease profession, such as pathologic fracture or increasing bone pain.

[2] Note: Patients who have undergone orchidectomy do not need to provide a serum testosterone level in the request submission.

Approved Dosing. 120 mg subcutaneously every four (4) weeks

Duration of Approval: 1 Year

Renewals will be considered for patient responding to treatment with Xgeva and who still requires treatment.

Duration of Approval: 1 Year

Filgrastim [Granulocyte colony stimulating factor (G-CSF)]
Brand(s): Neupogen
DOSAGE FORM/ STRENGTH: 300 mcg/mL, 480 mcg /1.6 mL

Effective August 30, 2017, Exceptional Access Program (EAP) requests for Neupogen (filgrastim) will no longer be accepted for any indication.

Patients who have an existing EAP approval for Neupogen can continue to receive Neupogen for the duration of the EAP approval period.

Neupogen and Grastofil are not interchangeable products. As of August 30, 2017, new prescriptions for filgrastim for ODB eligible patients will be dispensed Grastofil, unless it specifies Neupogen with the appropriate LU code. Refer to the Ministry's e-formulary for a listing of Limited Use (LU) criteria for Neupogen.

Effective **December 22, 2016,** the subsequent entry biologic (SEB) filgrastim as Grastofil® is funded under the Ontario Drug Benefit (ODB) Program as a general benefit (GB).

Please refer to the e-formulary for funded strengths.

Ruxolitinib
Brand(s): Jakavi
DOSAGE FORM/ STRENGTH: 5 mg, 10 mg, 15 mg, 20 mg tablets
Effective date: July 5, 2023

For the treatment of Acute Graft versus host disease (aGvHD) in patients meeting the following criteria;

1. Aged 12 years of age or older; AND

2. Confirmed diagnosis* of aGvHD clinically defined as grade II to IV aGvHD according to the National Institutes of Health (NIH) criteria (Harris et al. [2016]);

*Prescribers to provide the etiology (i.e. allogeneic stem cell or bone marrow transplant or other transplant type that led to aGvHD), approximate date of diagnosis, stage and clinical details to support the diagnosis and baseline presentation including affected organs or systems. The baseline information is important for discontinuation and renewal criteria.

AND

3. Patients have a confirmed diagnosis of corticosteroid-refractory or corticosteroid-dependent aGvHD;

   i) Corticosteroid refractory is defined by one or more of the following criteria:

   - **Progressing** based on an organ assessment after at least 3 days compared to organ stage at the time of initiation of high-dose systemic corticosteroid ± calcineurin inhibitor for the treatment of Grade II-IV aGVHD; AND/OR

   - **Failure** to achieve at **a minimum partial response** based on organ assessment after 7 days compared to organ stage at the time of initiation of high-dose systemic corticosteroid ± calcineurin inhibitor for the treatment of Grade II-IV aGvHD; AND/OR

   - Patients who **fail corticosteroid taper** defined as fulfilling either one of the following criteria:
     - Requirement for an increase in the corticosteroid dose to methylprednisolone ≥2 mg/kg/day (or equivalent prednisone dose ≥2.5 mg/kg/day)
     - Failure to taper the methylprednisolone dose to <0.5 mg/kg/day (or equivalent prednisone dose <0.6 mg/kg/day) for a minimum 7 days.

Ruxolitinib
Brand(s): Jakavi
DOSAGE FORM/ STRENGTH: 5 mg, 10 mg, 15 mg, 20 mg tablets

ii) Corticosteroid dependence is defined as the inability to taper prednisone under 2 mg/kg/day after an initially successful treatment of at least 7 days or as the recurrence of aGvHD activity during steroid taper.

AND

4. Prescribed by a clinician who has experience in the diagnosis and management of patients with GvHD.

Notes:

1. The definition of corticosteroid refractory aGvHD is defined based on criteria in the EBMT-NIH-CIBMTR Task Force position statement, irrespective of the concomitant use of a calcineurin inhibitor.

2. Treatment with ruxolitinib must not be added to patients' concurrent treatment of systemic therapies for the treatment of aGvHD other than steroids ± calcineurin inhibitors

Exclusions:

Treatment with ruxolitinib must not be used with' concurrent treatment of systemic therapies for aGvHD other than steroids ± calcineurin inhibitors

Discontinuation Criteria:

Ruxolitinib should be discontinued upon the occurrence of any of the following:

1. Progression of aGvHD, defined as worsening of aGvHD symptoms or occurrence of new aGvHD symptoms

2. Patient is experiencing unacceptable toxicity to ruxolitinib.

3. Patient must use additional systemic therapies (other than calcineurin inhibitors) for aGvHD after day 28.

4. Recurrence or relapse of underlying hematological malignancy.

Ruxolitinib
Brand(s): Jakavi
DOSAGE FORM/ STRENGTH: 5 mg, 10 mg, 15 mg, 20 mg tablets

Renewal:

Renewal of funding of ruxolitinib for aGvHD will be considered for patients who met the initiation criteria and who do not meet the discontinuation criteria AND who have achieved an overall response (i.e., Complete response (CR), Very good partial response (VGPR), Partial Response (PR), or stable disease with significant reduction in steroid doses), according to standard NIH criteria at day 28 (approximately 4 weeks).

For subsequent renewals, patients should be assessed for treatment response every 2 to 3 months, until the occurrence of any of the discontinuation criteria.

Approval duration of initials: 2 months

Approval duration of renewals: 6 months

Ruxolitinib
Brand(s): Jakavi
DOSAGE FORM/ STRENGTH: 5 mg, 10 mg, 15 mg, 20 mg tablets
Effective date: July 5, 2023

Initiation Criteria:

For the treatment of Chronic Graft versus host disease (cGvHD) in patients meeting the following criteria;

1. Aged 12 years of age or older; AND

2. Confirmed diagnosis* of cGvHD defined as having moderate to severe cGVHD based on National Institutes of Health (NIH) consensus criteria (Prescribers to provide the stage and clinical details to support the diagnosis and baseline presentation.)

   *Prescribers to provide the etiology (i.e. allogeneic stem cell or bone marrow transplant or other transplant type that caused cGvHD), approximate date of diagnosis, stage and clinical details to support the diagnosis and baseline presentation including affected organs or systems. The baseline information is important for discontinuation and renewal criteria.

   AND

Ruxolitinib
Brand(s): Jakavi
DOSAGE FORM/ STRENGTH: 5 mg, 10 mg, 15 mg, 20 mg tablets

3. Inadequate response to corticosteroids or systemic therapies as defined by meeting at least one of the below circumstances with prednisone or an equivalent corticosteroid therapy;

- A lack of response or disease progression after administration of minimum prednisone 1 mg/kg/day for at least one week (or equivalent); OR

- Disease persistence without improvement despite continued treatment with prednisone at greater than 0.5 mg/kg/day or 1 mg/kg/every other day for at least four (4) weeks (or equivalent); OR

- Increase prednisone dose to greater than 0.25 mg/kg/day after two unsuccessful attempts to taper the dose (or equivalent).

4. Prescribed by a clinician who has experience in the diagnosis and management of patients with GvHD.

Notes:

1. The definition of corticosteroid refractory cGvHD is defined according to the NIH consensus criteria, irrespective of the concomitant use of a calcineurin inhibitor.

2. Treatment with ruxolitinib must not be added to patients' concurrent treatment of systemic therapies for the treatment of cGvHD other than steroids ± calcineurin inhibitors.

3. Request applications must include the clinical baseline presentations, details of the dose, duration, and timelines of corticosteroid treatments used to treat the patient's GvHD, the doses and relevant other therapies used including calcineurin treatments

Exclusions:

Treatment with ruxolitinib must not be used with concurrent treatment of systemic therapies for cGvHD other than steroids ± calcineurin inhibitors

Ruxolitinib
Brand(s): Jakavi
DOSAGE FORM/ STRENGTH: 5 mg, 10 mg, 15 mg, 20 mg tablets

Discontinuation Criteria:

Ruxolitinib should be discontinued upon the occurrence of any of the following:

1. Progression of cGvHD, defined as worsening of cGvHD symptoms or occurrence of new cGvHD symptoms

2. Recurrence or relapse of underlying hematological malignancy.

3. Patient is experiencing unacceptable toxicity to ruxolitinib.

Renewal:

Treatment with ruxolitinib for cGvHD should be renewed for patients who met the initiation criteria and who do not meet any of the discontinuation criteria AND who have achieved an overall response (i.e., Complete Response (CR) or Partial Response (PR), or stable disease with significant reduction in steroid doses), according to NIH criteria, after 24 weeks of therapy (approximately 6 months)

Approval duration of initials: 6 months

Approval duration of initial renewal: 6 months

Approval duration of 2nd and subsequent renewal: 1 year

Zoledronic Acid
Brand(s): Zometa Concentrate
DOSAGE FORM/ STRENGTH: 4 mg/ 5 mL Vial

Zoledronic acid as Zometa Concentrate will only be considered **for the treatment of bony metastases in those with hormone refractory prostate cancer as well as other cancers** through the Exceptional Access Program (EAP) **in those receiving outpatient care** who cannot obtain Zometa through the Systemic Treatment-Quality Based Procedure (STQBP).

Zometa is considered through STQBP CCO for those receiving prostate cancer treatment from a cancer clinic.

https://www.cancercareontario.ca/en/cancer-treatments/chemotherapy/funding-reimbursement/systemic-treatment-quality-based-procedure

Duration of Approval: 6 Months

For the treatment of bony metastases for patients with hormone refractory prostate cancer as determined by an elevated PSA level, or evidence of progressive bony disease[1], despite castrate serum testosterone levels (<50 ng/dL).

[1]Progressive bony disease should be demonstrated by: progressive changes in radionucleotide bone scan or clinical signs of disease progression (e.g., via radionucleotide scanning, pathologic fracture or increasing bone pain).

Requests for patients who have undergone orchidectomy do not need to provide a serum testosterone level.

- For the prevention of skeletal related events in patients who have not experienced previous skeletal related events[2] and who have bony metastases secondary to:
- Solid tumours (e.g. renal, small cell lung, pancreatic cancers) who have good performance status [3] **OR**
- Breast cancer or multiple myeloma who are intolerant to pamidronate.
- [2] A skeletal related event is defined as: pathologic fracture, spinal cord compression, radiation therapy to bone or surgery to bone.
- [3] Good performance status is defined as patients that are ambulatory, capable of self care and up and about more than 50 per cent of waking hours.
- For the treatment of patients with symptoms due to bony metastases secondary to breast cancer or multiple myeloma who have failed or are intolerant to pamidronate.
- Consideration for patients who are symptomatic due to bony metastases secondary to other types of solid tumours or cancers will be considered on a case-by-case basis. The physician is asked to include information describing the patient's bone pain and use of other therapies including the use of bisphosphonates. The use of other non-pharmacologic treatment modalities such as surgery or radiation that have been tried should be provided in the request.

Zoledronic Acid
Brand(s): Zometa Concentrate
DOSAGE FORM/ STRENGTH: 4 mg/ 5 mL Vial

Duration of Approval: 6 Months

Renewals will be considered for patients who are responding to therapy and is still deemed to require treatment.

Duration of Approval: 6 Months

OSTEOPOROSIS

Romosozumab
Brand(s): Evenity
DOSAGE FORM/ STRENGTH: 90 mg/mL pre-filled syringe
Effective date: October 11, 2023

For the treatment of osteoporosis in postmenopausal women meeting ALL the following criteria:

1. History of osteoporotic fracture; AND

2. Is at a high risk for future fracture, defined as a 10-year fracture risk greater than or equal to 20% as defined by the Fracture Risk Assessment (FRAX) Tool; AND

3. Treatment naive to osteoporosis medications, except for calcium and/or vitamin D.

Exclusion criteria:

Romosozumab will not be funded as combination therapy with other osteoporosis medications, except for calcium and/or vitamin D.

Recommended dose:

210 mg subcutaneously once every month for 12 doses

Approval duration: 12 months (A maximum of 12 monthly doses will be reimbursed.)

Renewals will not be considered.

Note: Requesting prescriber must include a copy of the FRAX assessment.

Teriparatide
Brand(s): Forteo and generics
DOSAGE FORM/ STRENGTH: Please refer to the ODB Formulary for a list of funded products

Effective with the May 31, 2024 Ontario Drug Benefit Formulary/ Comparative Drug Index update, Teriparatide as Forteo has transitioned to the ODB formulary with its generic versions. Also, please note that the Teriparatide biosimilar (Osnuvo) is also publicly funded as a limited use benefit on the Ontario Drug Benefit formulary effective on September 29, 2022. Refer to the ODB formulary for the Limited Use Criteria for all teriparatide products.

PAIN MANAGEMENT

Cannabidiol and delta-9-tetrahydro-cannabinol
Brand(s): Sativex
DOSAGE FORM/ STRENGTH: 25 mg/27 mg per mL buccal spray

For the treatment of neuropathic pain related to multiple sclerosis in patients who have:

- Ineffective response or intolerable side effects / contraindications to adequate trials* of a tricyclic antidepressant and gabapentin and pregabalin; and
- Ineffective response or intolerable side effects / contraindications to adequate trials* of Cesamet (nabilone) and Marinol (delta-9-tetrahydrocannabinol); and
- No contraindications to Sativex therapy.

* Adequate trial is defined as 2 months unless intolerable side effect(s) occur.

Duration of Approval: 1 Year

Note: Side effects and contraindications must be described in detail. Side effects should be deemed serious by the physician such that no further therapy with the agent would be warranted.

Renewal will be considered for patients responding to Sativex therapy as demonstrated by decreased pain and other pain-related symptoms; no initiation of new analgesics; and no increase in doses of any analgesics.

Duration of Approval: Renewal is lifetime.

Sativex is also reimbursed for the treatment of refractory pain in palliative cancer patients according to specified criteria.

Duration of Approval: 6 Months

Methadone
Brand(s): Metadol
DOSAGE FORM/ STRENGTH: 1 mg, 5 mg, 10 mg, 25 mg tablets, 1 mg/mL oral solution, 10 mg/mL oral concentrate solution

For the treatment of cancer and non-cancer pain in patients who cannot tolerate, or have failed treatment with a listed long-acting opioid.

The CED noted that there is a potential for drug interactions with the use of methadone resulting from inhibition of drug metabolism (via CYP 3A4 inhibition; e.g. QT prolongation with certain antibiotics). The requesting physician is asked to ensure that this issue is addressed with the patient.

Duration of Approval 1 Year

Renewals will be considered on a case-by-case basis.

For renewals, the requesting physician is asked to provide details of the patient's clinical response to therapy and additional information pertaining to the current medications and addition or stoppage of other pain medications in the prior year of methadone use. Please specify the dosages and dosing frequency of current medications and provide reasons for any changes in the medication regimen.

Oxycodone Controlled Release Tablet
Brand(s): OxyNeo
DOSAGE FORM/ STRENGTH: 10 mg CR,15 mg CR, 20 mg CR, 30 mg CR, 40 mg CR

For the treatment of chronic pain in patients who have experienced intolerance or have failed an adequate trial (for example, three months) of at least one other listed long-acting opioid product.

Note: Physicians should consider best practice guidelines for the safe and effective use of opioids in chronic non-cancer pain, such as the Canadian Guideline for Safe and Effective Use of Opioids for Chronic Non-Cancer Pain.

Please include the following information in your request:

i) The diagnosis for which the pain management is required must be documented.

ii) All concomitant pain medication therapy must be documented.

iii) Other medications with potential for abuse or interaction with opioid therapy should be documented.

Duration of Approval: 1 Year

Oxycodone Controlled Release Tablet

Brand(s): OxyNeo

DOSAGE FORM/ STRENGTH: 10 mg CR,15 mg CR, 20 mg CR, 30 mg CR, 40 mg CR

Renewals will be considered if treatment continues to be appropriate for the management of the patient's chronic pain. Please include the following information on your renewal request:

Duration of Approval: 1 Year

i) All concomitant pain medication therapy must be documented.

ii) Other medications with potential for abuse or interaction with opioid therapy should be documented.

Note: OxyNEO 60mg and 80mg tablets are not funded.

Note: Physicians registered on the Ontario Medical Association's Palliative Care Facilitated Access List and Nurse Practitioners registered on the PCFA list through the Registered Nurses Association of Ontario or the Nurse Practitioner Association of Ontario can access OxyNeo for chronic pain management of their palliative care patient for an initial duration of one year without approval through the Exceptional Access Program.

PARKINSON'S DISEASE TREATMENTS

Foslevodopa/foscarbidopa

Brand(s): Vyalev
DOSAGE FORM/ STRENGTH: 240 mg/mL/12 mg/mL Solution for Infusion
Effective date: September 5, 2024

For the treatment of advanced levodopa-responsive Parkinson's disease (PD) in patients who meet all of the following criteria:

1. 18 years of age and older; AND

2. Has not been able to achieve satisfactory control of severe, debilitating motor fluctuations and hyper-/dyskinesia despite optimized treatment with available combinations of PD treatments[1] including all the following:

    - Maximally tolerated doses of levodopa in combination with carbidopa (Note: the patient must have demonstrated an initial clinical response to an adequate trial of maximally tolerated doses of levodopa to be eligible for Vyalev); AND
    - A catechol-O-methyltransferase (COMT) inhibitor, if not contraindicated[2]; AND
    - A dopamine agonist, if not contraindicated[2]; AND
    - A monoamine oxidase-B (MAO-B) inhibitor, if not contraindicated[2]; AND
    - Amantadine, if not contraindicated[2];

    AND

3. Has severe disability associated with at least 25% of the waking day in the off state and/or ongoing, bothersome levodopa-induced dyskinesias, despite having tried frequent dosing of levodopa (at least five doses per day)[3]; AND

4. Patient or caregiver must demonstrate correct understanding and use of the Vyalev delivery system; AND

5. Prescribed by neurologists who are movement disorder subspecialists, or who have expertise in managing advanced PD.

Notes

1. Clinical details pertaining to the severity of the patient's disability while in the off-state as well as a complete history of all previous and current medications (e.g., name, start date and duration of therapy, doses used, side effects, and response) must be included.

Foslevodopa/foscarbidopa
Brand(s): Vyalev
DOSAGE FORM/ STRENGTH: 240 mg/mL/12 mg/mL solution for Infusion

2. If a contraindication is deemed to be applicable to the patient, the requesting physician must state the contraindication and provide the rationale why it is considered a contraindication for the patient.

3. Patients on levodopa/carbidopa intestinal gel may be considered for a switch to Vyalev on a case-by-case basis.

Exclusion criteria:
Patients meeting one or more of the following clinical circumstances will NOT be considered.

i) Patient with severe psychosis.
ii) Patient with severe dementia.
iii) Combination therapy with levodopa/carbidopa intestinal gel.

Renewal Criteria:

Renewal of reimbursement will be considered in patients who continue to benefit from treatment, including a significant reduction in the time spent in the off state and an improvement in the severity of the disability in the off state.

At the time of renewal, please confirm the average daily dose.

Recommended dose:

Administer dose as a continuous subcutaneous infusion over 24 hours with doses calculated based on levodopa equivalents. Refer to the Vyalev product monograph for dosing guidelines.

Duration of Approval of Initials and Renewals: 1 Year

Levodopa 20 mg/mL and Carbidopa 5 mg/mL Intestinal gel
Brand(s): Duodopa
DOSAGE FORM/ STRENGTH: Intestinal Gel containing Levodopa 20 mg/mL – Carbidopa 5 mg/mL (100 mL cassette)

For the treatment of Parkinson's disease in patients who meet the following criteria;

- Experiences at least 25% of the waking day in the off state; **AND**
- Has severe disability while in the off-state as assessed by a Movement Disorder Specialist; **AND**
- Has received an adequate trial of maximally tolerated doses of levodopa, with demonstrated clinical response; **AND**
- Has failed adequate trials of other adjunctive medications (entacapone, dopamine agonists, monoamine oxidase-B [MAO-B] inhibitors) if not contraindicated. Note that if a contraindication is deemed to be applicable to the patient, the requesting physician must state the contraindication and provide the rationale why it is considered a contraindication for the patient).

Clinical details pertaining to the severity of the patient's disability while in the off-state as well as a complete history of all previous and current medications (e.g., name, start date and duration of therapy, doses used, side effects, and response) must be included.

Requests for treatment initiation will be limited to the physicians practicing in the following specialized movement disorder clinics: Ottawa, London, Toronto Western, Kingston, Baycrest and Hamilton. (Note: An Ontario specialized movement disorder clinic listed on the website of the Canadian Movement Disorder Group http://www.cmdg.org/AcrossCanada/acrosscanada.htm#que is acceptable)

Exclusion criteria: Patients meeting ANY of the following criteria will NOT be considered.
- Patients who have a contraindication to insertion of a percutaneous endoscopic gastrostomy (PEG) tube
- Severe psychosis or dementia

Duration of Approval of Initials: 1 Year

Renewals will be considered in patients who continue to benefit from treatment. The patient should continue to demonstrate a significant reduction in the time spent in the off state and an improvement in the severity of the disability in the off state.

Duration of Approval of Renewals: 1 Year

Rasagiline
Brand(s): Azilect
DOSAGE FORM/ STRENGTH: 0.5 mg, 1 mg tablet

For the treatment of patients with Parkinson's disease who experience about 25% of the waking day in the off-state despite maximally tolerated doses of levodopa.

Duration of Approval of Initials and Renewals: 5 Years

PSORIATIC ARTHRITIS TREATMENTS

Adalimumab – See Formulary for funded biosimilars
Brand(s): Humira (Only for those approved for biosimilar exemption)
DOSAGE FORM/ STRENGTH: 40 mg/0.8 mL prefilled syringe, 40 mg/0.8mL and 20 mg/0.2 mL prefilled pens for subcutaneous injection

Certolizumab
Brand(s): Cimzia
DOSAGE FORM/ STRENGTH: 200 mg/mL prefilled syringe and autoinjector

Etanercept – see Formulary for funded biosimilars
Brand(s): Enbrel (Only for those approved for biosimilar exemption)
DOSAGE FORM/ STRENGTH: 25 mg/vial and 50 mg prefilled syringe or pens for subcutaneous injection per formulary listed options

Golimumab
Brand(s): Simponi
DOSAGE FORM/ STRENGTH: 50 mg/0.5 ml prefilled syringe and autoinjector

Guselkumab
Brand(s): Tremfya
DOSAGE FORM/ STRENGTH: 100 mg/mL prefilled syringe and Patient controlled injector (AI) Effective date: November 27, 2023

Refer to the Executive Officer Communications on the Ministry website for the Ministry's Biosimilar Policy including frequently asked questions and updates for the biosimilar policy updates. http://www.health.gov.on.ca/en/pro/programs/drugs/opdp_eo/eo_communiq.aspx

Effective March 31, 2023, the ODB program will start transitioning coverage for Copaxone®, Enbrel®, Humalog®, Humira®, Lantus®, NovoRapid®, Remicade®, and Rituxan® to their biosimilar versions.

Effective December 29, 2023, coverage for these originator biologic drugs through the ODB program will not be available for patients and the ODB program will only provide coverage for the biosimilar version of these drugs for all ODB program recipients, with limited exemptions. In general, for ODB program recipients who are already on these biologic drugs, there is up to a 9-month transition period (see the biosimilar switch policy described on page 6 to 8 of this document).

It should be noted that after the date when a biosimilar becomes publicly funded for an approved indication, patients initiated on an originator biologic for this same provincially funded indication through support from a manufacturer's patient support program, will be

expected to be provided ongoing access of the originator biologic through the patient's original payer mechanism (e.g. manufacturer's patient support program) or to switch to an ODB funded biosimilar version upon meeting specified criteria. The Ministry will no longer consider funding of originator biologics that are part of the biosimilar policy with limited exemptions on or after December 29, 2023.

Psoriatic Arthritis

Initiation Criteria:

For the treatment of psoriatic arthritis in patients who have:

Severe active disease (≥ 5 swollen joints and radiographic evidence of psoriatic arthritis) despite treatment with methotrexate (20 mg/week) for at least 3 months and one of leflunomide (20mg/day) or sulfasalazine (1g twice daily) for at least 3 months.

If the patient has documented contraindications or intolerances to methotrexate, then only one of leflunomide (20 mg/day) or sulfasalazine (1 g twice daily) for at least 3 months is required. Details of contraindications and intolerances must also be provided.

Duration of Approval of initials: 1 Year

Renewal will be considered for patients with objective evidence of at least a 20% reduction in swollen joint count and a minimum of improvement in 2 swollen joints over the previous year. For renewals beyond the second year, objective evidence of preservation of treatment effect must be provided.

Duration of Approval of first renewal: 1 Year

The planned dosing regimen for the requested biologic should be provided. The recommended doses for the treatment of psoriatic arthritis are as follows:

- Adalimumab 40mg every two weeks
- Certolizumab 400 mg at week 0, 2, 4 then maintenance doses of 200 mg every 2 weeks or 400 mg every 4weeks
- Etanercept 25 mg twice weekly or 50 mg once weekly
- Golimumab 50 mg once a month
- Guselkumab 100 mg subcutaneously at week 0 and 4, then maintenance dose of 100 mg every 8 weeks thereafter.

  Guselkumab may be used alone or in combination with a conventional DMARD (e.g., methotrexate).

Duration of Approval of second and subsequent renewals: 5 years

Ixekizumab
Brand(s): Taltz
DOSAGE FORM/ STRENGTH: 80 mg/mL Autoinjector or **80 mg/mL** Syringe for subcutaneous injection
Effective date: March 4, 2019

Secukinumab
Brand(s): Cosentyx
DOSAGE FORM/ STRENGTH: 150 mg/mL prefilled syringe and 150 mg/mL prefilled pen
Effective date: March 6, 2018

Psoriatic Arthritis

Initiation Criteria:

For the treatment of psoriatic arthritis (PsA) in patients who have:

Severe active disease (≥ 5 swollen joints and radiographic evidence of psoriatic arthritis) despite treatment with methotrexate (20 mg/week) for at least 3 months and one of leflunomide (20mg/day) or sulfasalazine (1g twice daily) for at least 3 months.

If the patient has documented contraindications or intolerances to methotrexate, then only one of leflunomide (20 mg/day) or sulfasalazine (1 g twice daily) for at least 3 months is required. Details of contraindications and intolerances must also be provided.

Duration of Approval: 1 Year

Renewals will be considered for patients with objective evidence of at least a 20% reduction in swollen joint count and a minimum of improvement in 2 swollen joints over the previous year.

For renewals beyond the second year, objective evidence of preservation of treatment effect must be provided.

Duration of Approval of first renewal: 1 Year

Duration of Approval: Second and subsequent renewals are 2 years

Recommended Dose:

The planned dosing regimen for the requested biologic should be provided.

Ixekizumab:

Ixekizumab for the treatment of psoriatic arthritis (PsA) patients or those with PsA and coexistent mild plaque psoriasis: 160 mg (two 80 mg injections) sc at Week 0, followed by 80 mg every 4 weeks.

For psoriatic arthritis patients with coexistent moderate-to severe plaque psoriasis, you may wish to refer to the ODB formulary for access upon meeting the Limited Use Criteria for Plaque psoriasis. (EAP authorization would not be required).

Dose recommended for such patients is 160 mg by subcutaneous injection (two 80 mg injections) at Week 0, followed by 80 mg every 2 weeks for 6 doses (i.e. weeks 2, 4, 6, 8, 10, and 12), then 80 mg every 4 weeks thereafter.

Ixekizumab may be used alone or in combination with a conventional DMARD (e.g. methotrexate)

Secukinumab:

Secukinumab for the treatment of psoriatic arthritis 150mg sc at weeks 0, 1, 2, and 3 followed by monthly maintenance dosing starting at week 4. If a patient is an anti-TNF alpha inadequate responder and continues to have active psoriatic arthritis, consider using the 300 mg sc dose.

For psoriatic arthritis patients with coexistent moderate to severe plaque psoriasis, use the dosing and administration recommendations for plaque psoriasis (i.e. 300 mg sc at weeks 0, 1, 2, and 3, followed by monthly maintenance dosing starting at week 4)

Upadacitinib
Brand(s): Rinvoq
DOSAGE FORM/ STRENGTH: 15 mg Extended Release tablet
Effective date:
November 16, 2022 (PsA)

Upadacitinib for Psoriatic Arthritis

Initiation criteria

For the treatment of psoriatic arthritis (PsA) in patients who have:

- Severe active disease (Greater than or equal to 5 swollen joints and radiographic evidence of psoriatic arthritis) despite treatment with methotrexate (20 mg/week) for at least 3 months and one of leflunomide (20 mg/day) or sulfasalazine (1 g twice daily) for at least 3 months.

If the patient has documented contraindications or intolerances to methotrexate, then only one of leflunomide (20 mg/day) or sulfasalazine (1 g twice daily) for at least 3 months is required. Details of contraindications and intolerances must also be provided.

Renewal Criteria:

Renewals will be considered for patients with objective evidence of at least a 20% reduction in swollen joint count and a minimum of improvement in 2 swollen joints over the previous year. For renewals beyond the second year, objective evidence of preservation of treatment effect must be provided.

Exclusion Criteria:

Upadacitinib will not be reimbursed when used in combination with other Janus Kinase (JAK) inhibitor treatments for psoriatic arthritis or other biologic disease-modifying antirheumatic drugs (DMARDs) for psoriatic arthritis.

Recommended Dose: 15 mg once daily.

Approval durations:

Initials: 1 year
First renewal: 1 year
Second and subsequent renewals: 5 years

PULMONARY ARTERIAL HYPERTENSION

Drugs for Pulmonary Arterial Hypertension (PAH) under EAP

i) Phosphodiesterase (PDE)-5 inhibitor: sildenafil (Revatio), tadalafil (Adcirca)

ii) Endothelin receptor antagonists (ERAs): ambrisentan (Volibris), bosentan (Tracleer), macitentan (Opsumit)

iii) Prostanoids: epoprostenol (Flolan, Caripul), treprostinil (Remodulin), selexipag (Uptravi)

Sildenafil
Brand(s): Revatio
DOSAGE FORM/ STRENGTH: 20 mg tablet

Tadalafil
Brand(s): Adcirca
DOSAGE FORM/ STRENGTH: 20 mg tablet

All requests (initial, renewal, monotherapy, combination therapy) for a PAH drug must come from one of the following recognized PAH referral centres.

- **Pulmonary Hypertension Centre**
  Hamilton Health Sciences – General Hospital
- **The Firestone Institute Pulmonary Hypertension Program**
  St. Joseph's Healthcare Hamilton and McMaster University
- **Pulmonary Hypertension Clinic**
  Hotel Dieu Hospital/Kingston General Hospital
- **Pulmonary Hypertension Program**
  London Health Science Centre – Victoria Hospital
- **Ottawa Pulmonary Hypertension Clinic**
  University of Ottawa Heart Institute and the Ottawa Hospital
- **University Health Network Pulmonary Hypertension Program**
  Toronto General Hospital

Sildenafil
Brand(s): Revatio
DOSAGE FORM/ STRENGTH: 20 mg tablet

Tadalafil
Brand(s): Adcirca
DOSAGE FORM/ STRENGTH: 20 mg tablet

Requests from other physicians/centres must include a recent (less than or equal to 3 months old) consult note/recommendation from a recognized PAH referral centre that supports the request;

Out-of-province referral centre consults (e.g., from Winnipeg for patients in Northern Ontario) will also be considered on a case-by-case basis

i) **Sildenafil (Revatio, generics), Tadalafil (Adcirca, generics)**

Initial Criteria:

For the treatment of patients with pulmonary arterial hypertension (PAH) [WHO Group 1 Pulmonary hypertension] who meet all the following criteria;

- PAH defined as a resting mean pulmonary artery pressure (mPAP) of **≥ 25 mmHg** at rest AND normal pulmonary capillary wedge pressure (PCWP) **≤ 15 mmHg** on right heart catheterization[1]; AND
- The drug request meets one of the following circumstances of use:
    - Drug is being used as monotherapy in a patient with WHO-functional class II (Note that a PDE-5 inhibitor must be used as first line monotherapy for WHO-FC II (unless contraindicated or demonstrated intolerance), III, or IV; OR
    - Drug is being used as sequential dual therapy in combination with a funded ERA (i.e. ambrisentan, bosentan, macitentan) or a funded prostanoid (i.e. epoprostenol, treprostinil) in a patient who has had an inadequate response with monotherapy (i.e., failure to achieve WHO-FC I or II; or 6MWD >440 metres; or no/mild RV failure); OR
    - Drug is being used as up-front dual therapy in combination with a funded ERA (i.e. ambrisentan, bosentan, macitentan) or a funded prostanoid (i.e. epoprostenol, treprostinil) in a patient with advanced disease (i.e. WHO-functional class III or IV, 6MWD <380 metres; OR evidence of RV failure.)

[1] Note: Left ventricular end-diastolic pressure ≤ **15 mmHg** is also acceptable.

Ambrisentan
Brand(s): Volibris
DOSAGE FORM/ STRENGTH: 5 mg, 10 mg tablet

Bosentan
Brand(s): Tracleer, Generics (Co-, Mylan-. PMS-, Sandoz-)
DOSAGE FORM/ STRENGTH: 62.5 mg, 125 mg tablet

Macitentan
Brand(s): Opsumit
DOSAGE FORM/ STRENGTH: 10 mg tablet

Updated April 20, 2021

All requests (initial, renewal, monotherapy, combination therapy) for a PAH drug must come from one of the following recognized PAH referral centres.

- **Pulmonary Hypertension Centre**
  Hamilton Health Sciences – General Hospital
- **The Firestone Institute Pulmonary Hypertension Program**
  St. Joseph's Healthcare Hamilton and McMaster University
- **Pulmonary Hypertension Clinic**
  Hotel Dieu Hospital/Kingston General Hospital
- **Pulmonary Hypertension Program**
  London Health Science Centre – Victoria Hospital
- **Ottawa Pulmonary Hypertension Clinic**
  University of Ottawa Heart Institute and the Ottawa Hospital
- **University Health Network Pulmonary Hypertension Program**
  Toronto General Hospital

Requests from other physicians/centres must include a recent (less than or equal to 3 months old) consult note/recommendation from a recognized PAH referral centre that supports the request;

Out-of-province referral centre consults (e.g., from Winnipeg for patients in Northern Ontario) will also be considered on a case-by-case basis

Initial Criteria:

For the treatment of patients with pulmonary arterial hypertension (PAH) [WHO Group 1 Pulmonary hypertension] who meet all the following criteria;

Ambrisentan
Brand(s): Volibris
DOSAGE FORM/ STRENGTH: 5 mg, 10 mg tablet

Bosentan
Brand(s): Tracleer, Generics (Co-, Mylan-. PMS-, Sandoz-)
DOSAGE FORM/ STRENGTH: 62.5 mg, 125 mg tablet

Macitentan
Brand(s): Opsumit
DOSAGE FORM/ STRENGTH: 10 mg tablet
Updated: April 20, 2021

- PAH defined as a resting mean pulmonary artery pressure (mPAP) of **≥ 25 mmHg** at rest AND normal pulmonary capillary wedge pressure (PCWP) ≤ **15 mmHg** on right heart catheterization[1]; AND
- The drug request meets one of the following circumstances of use:
    - Drug is being used as monotherapy in a patient with WHO-functional class III or IV; OR
    - Drug is being used as monotherapy in a patient with WHO-functional class II who has contraindication or has intolerance to a PDE-5 inhibitor; OR
    - Drug is being used as sequential dual therapy in combination with a funded PDE-5 (i.e. sildenafil, tadalafil) or a funded prostanoid (i.e. epoprostenol, treprostinil) in a patient who has had an inadequate response with monotherapy (i.e., failure to achieve WHO-FC I or II; or 6MWD >440 metres; or no/mild RV failure); OR
    - Drug is being used as up-front dual therapy in combination with a funded PDE-5 (i.e. sildenafil, tadalafil) or a funded prostanoid (i.e. epoprostenol, treprostinil) in a patient with advanced disease (i.e. WHO-functional class III or IV; OR 6MWD <380 metres; OR evidence of RV failure.)

[1] Note: Left ventricular end-diastolic pressure ≤**15 mmHg** is also acceptable.

Treprostinil
Brand(s): Remodulin
DOSAGE FORM/ STRENGTH: 1 mg/mL, 2.5 mg/mL, 5 mg/mL and 10 mg/mL vials

Epoprostenol
Brand(s): Flolan
DOSAGE FORM/ STRENGTH: 0.5 mg and 1mg vial

Epoprostenol
Brand(s): Caripul
DOSAGE FORM/ STRENGTH: 0.5 mg and 1.5 mg vial

<u>All</u> requests (initial, renewal, monotherapy, combination therapy) for a PAH drug must come from one of the following recognized PAH referral centres.

- **Pulmonary Hypertension Centre**
  Hamilton Health Sciences – General Hospital
- **The Firestone Institute Pulmonary Hypertension Program**
  St. Joseph's Healthcare Hamilton and McMaster University
- **Pulmonary Hypertension Clinic**
  Hotel Dieu Hospital/Kingston General Hospital
- **Pulmonary Hypertension Program**
  London Health Science Centre – Victoria Hospital
- **Ottawa Pulmonary Hypertension Clinic**
  University of Ottawa Heart Institute and the Ottawa Hospital
- **University Health Network Pulmonary Hypertension Program**
  Toronto General Hospital

Requests from other physicians/centres must include a recent (less than or equal to 3 months old) consult note/recommendation from a recognized PAH referral centre that supports the request;

Out-of-province referral centre consults (e.g., from Winnipeg for patients in Northern Ontario) will also be considered on a case-by-case basis

Treprostinil
Brand(s): Remodulin
DOSAGE FORM/ STRENGTH: 1 mg/mL, 2.5 mg/mL, 5 mg/mL and 10 mg/mL vials

Epoprostenol
Brand(s): Flolan
DOSAGE FORM/ STRENGTH: 0.5 mg and 1mg vial

Epoprostenol
Brand(s): Caripul
DOSAGE FORM/ STRENGTH: 0.5 mg and 1.5 mg vial

Epoprostenol (Flolan, Caripul), Treprostinil (Remodulin)

Initial Criteria:

For the treatment of patients with pulmonary arterial hypertension (PAH) [WHO Group 1 Pulmonary hypertension] who meet all the following criteria;

- PAH defined as a resting mean pulmonary artery pressure (mPAP) of **≥ 25 mmHg** at rest AND normal pulmonary capillary wedge pressure (PCWP) **≤ 15 mmHg** on right heart catheterization[1]; AND

- The drug request meets one of the following circumstances of use:

    - Drug is being used as monotherapy in a patient with WHO-functional class III or IV; OR

    - Drug is being used as sequential dual therapy in combination with a funded PDE-5 (i.e. sildenafil, tadalafil) or with a funded ERA (i.e. ambrisentan, bosentan, macitentan) in a patient who fails to meet treatment targets (i.e. failure to achieve WHO-FC I or II; or 6MWD >440 metres; or no/mild RV failure) with monotherapy; OR

    - Drug is being used as up-front dual therapy in combination with a funded PDE-5 (i.e. sildenafil, tadalafil) or with a funded ERA (i.e. ambrisentan, bosentan, macitentan) in a patient with advanced disease (i.e. WHO-functional class III or IV; OR 6MWD <380 metres; OR evidence of RV failure.)

[1] Note: Left ventricular end-diastolic pressure **≤ 15 mmHg** is also acceptable.

Treprostinil
Brand(s): Remodulin
DOSAGE FORM/ STRENGTH: 1 mg/mL, 2.5 mg/mL, 5 mg/mL and 10 mg/mL vials

Epoprostenol
Brand(s): Flolan
DOSAGE FORM/ STRENGTH: 0.5 mg and 1mg vial

Epoprostenol
Brand(s): Caripul
DOSAGE FORM/ STRENGTH: 0.5 mg and 1.5 mg vial

For all funded PAH Drugs, case-by-case consideration may be provided for the following;

- Requests for triple therapy (Including patients awaiting lung transplant.)
- Patients who may have mixed co-morbidities that include ILD, COPD or LV failure.(i.e. patients with mixed WHO Group 1 and Group 3 pulmonary hypertension OR mixed WHO Group 1 and Group 2 pulmonary hypertension)

Exclusion Criteria:

Combinations of drugs targeting similar pathways will not be funded.(i.e. combination regimen may only include one agent from each drug class -- phosphodiesterase type 5 [PDE-5] inhibitors, endothelin receptor antagonists (ERA), and/or prostanoids)

Renewal criteria for funded PAH Drugs:

Renewals will be provided for patients who remain under the care of a physician from a recognized PAH Centre (see list above) and who continue to benefit from therapy.

Approval Durations:

Duration of Approval for Initial Requests: 1 year

Duration on triple therapy regimens awaiting lung transplantation: 1 year

Duration of first renewal: 1 Year

Duration of subsequent renewals: 5 Years

Selexipag
Brand(s): Uptravi
DOSAGE FORM/ STRENGTH: 200mcg, 400mcg, 600mcg, 800mcg, 1000mcg, 1200mcg, 1400mcg, 1600mcg Tablets

All requests (initial, renewal, monotherapy, combination therapy) for a PAH drug must come from one of the following recognized PAH referral centres.

- **Pulmonary Hypertension Centre**
  Hamilton Health Sciences – General Hospital
- **The Firestone Institute Pulmonary Hypertension Program**
  St. Joseph's Healthcare Hamilton and McMaster University
- **Pulmonary Hypertension Clinic**
  Hotel Dieu Hospital/Kingston General Hospital
- **Pulmonary Hypertension Program**
  London Health Science Centre – Victoria Hospital
- **Ottawa Pulmonary Hypertension Clinic**
  University of Ottawa Heart Institute and the Ottawa Hospital
- **University Health Network Pulmonary Hypertension Program**
  Toronto General Hospital

Initial Criteria:

For the treatment of patients with pulmonary arterial hypertension (PAH) [WHO Group 1 Pulmonary hypertension] who meet all the following criteria:

- PAH defined as a resting mean pulmonary artery pressure (mPAP) of ≥ 25 mmHg at rest AND normal pulmonary capillary wedge pressure (PCWP) ≤ 15 mmHg on right heart catheterization[1]; AND
- Patient with World Health Organization (WHO) functional class II to IV; AND
- Selexipag is being used in a patient experiencing inadequate control[2] with a Phosphodiesterase (PDE)-5 inhibitor (i.e. tadalafil or sildenafil) AND an endothelin receptor antagonist (ERA) (i.e. bosentan, ambrisentan, or macitentan)

Notes:

1. Left ventricular end-diastolic pressure ≤ 15 mmHg is also acceptable.
2. Unable to meet treatment targets (i.e. failure to achieve WHO-FC I or II; or 6MWD >440 metres; or no/mild RV failure)

Case-by-case consideration may be provided for the following;

- Requests for Selexipag in patients who demonstrate intolerance or have a contraindication to either PDE-5 inhibitors (i.e. both sildenafil and tadalafil) or ERAs (i.e. each of bosentan, ambrisentan, macitentan)

Selexipag
Brand(s): Uptravi
DOSAGE FORM/ STRENGTH: 200mcg, 400mcg, 600mcg, 800mcg, 1000mcg, 1200mcg, 1400mcg, 1600mcg Tablets

- Patients who may have mixed co-morbidities that include ILD, COPD or LV failure. (i.e. patients with mixed WHO Group 1 and Group 3 pulmonary hypertension OR mixed WHO Group 1 and Group 2 pulmonary hypertension)

Exclusion Criteria:

Combination therapy with prostacyclin or prostacyclin analog therapies and Selexipag will not be covered.

Renewal criteria:

Renewals will be provided for patients who remain under the care of a physician from a recognized PAH Centre (see list above) and who continue to benefit from therapy.

Approval Durations:

Duration of Approval for Initial Requests: 1 year

Duration on triple therapy regimens awaiting lung transplantation: 1 year

Duration of first renewal: 1 Year

Duration of subsequent renewals: 5 Years

Riociguat
Brand(s): Adempas
DOSAGE FORM/ STRENGTH: 0.5 mg, 1 mg, 1.5 mg, 2 mg, 2.5 mg tablet

For the treatment of chronic thromboembolic pulmonary hypertension (CTEPH) in patients who meet the following criteria;

- the physician making the request is a clinician with experience in the diagnosis and treatment of CTEPH[1]; AND

- the patient is diagnosed with inoperable CTEPH (World Health Organization [WHO] Group 4); OR persistent or recurrent CTEPH after surgical treatment in adult patients (18 years of age or older) with WHO Functional Class (FC) II or III pulmonary hypertension.

[1] Request should come from a clinician from a Pulmonary Hypertension referral centre (See Pulmonary Arterial Hypertension referral clinics above).

Duration of Approval: 1 Year

Renewal of funding will be considered for patients who continue to respond to therapy with riociguat. When submitting a request for renewal of funding, the physician should submit clinical information to support that the patient is deriving benefit from the treatment compared to before they started the treatment. The physician should provide confirmation of improvement of any ONE or more reasonable clinical parameters which supports the response of the patient's CTEPH to riociguat.

Duration of Approval: 1 Year

Requests for subsequent funding renewals (i.e. beyond the first two years of treatment) will be considered when a physician provides written confirmation that the patient continues to respond to therapy with riociguat. The physician should provide confirmation of improvement of any ONE or more reasonable clinical parameters which supports the response of the patient's CTEPH to riociguat compared to baseline or that supports that the patient's condition is stable while on riociguat.

Duration of Approval: Subsequent Renewals - 5 Years

RESPIROLOGY THERAPIES

Elexacaftor/Tezacaftor/Ivacaftor and Ivacaftor

Brand(s): Trikafta
DOSAGE FORM/ STRENGTH: 100 mg / 50 mg/ 75 mg & 150mg tablets;
50 mg/25 mg/37.5 mg & 75mg tablets; 100mg/50mg/75mg & 75 mg granules;
80 mg/40 mg/60 mg & 59.5 mg granules
Original Effective date: September 22, 2021 Updated: July 8, 2022
Updated: December 21, 2023; Updated November 5, 2024

INITIATION CRITERIA

For the treatment of cystic fibrosis (CF) in patients who meet all of the following criteria:

1. 2 years of age and older; **AND**

2. Patient has a confirmed diagnoses of CF through a validated test documenting one of the following mutational results in the cystic fibrosis transmembrane conductance regulator (CFTR) gene;

   a. Has at least one F508del mutation
   OR
   b. Has at least one N1303K mutation
   OR
   c. Has at least one mutation in the CFTR gene that is responsive to Trikafta listed in Table 1 below;

   AND

3. Patient has been optimized on best supportive care for their CF prior to starting Trikafta; **AND**
4. Prescribed by a clinical specialist affiliated with a Canadian cystic fibrosis centre.

*The following measurements **must be completed prior to initiating treatment with Trikafta** and will serve as the "baseline" measures upon which renewal of funding will be compared.*
For patients 2 to less than 6 years of age:

1. Number of days treated with oral and/or intravenous (IV) antibiotics for pulmonary exacerbations in the 6 months preceding* the request OR number of pulmonary exacerbations requiring oral and/or IV antibiotics in the 6 months preceding* the request; **AND**

Elexacaftor/Tezacaftor/Ivacaftor and Ivacaftor

Brand(s): Trikafta
DOSAGE FORM/ STRENGTH: 100 mg/50 mg/75 mg &150 mg tablets;
50 mg/25 mg/37.5 mg a& 75 mg tablets; 100 mg/50 mg/75 mg & 75 mg granules;
80 mg/40 mg/60 mg & 59.5 mg granules

2. Number of CF-related hospitalizations in the 6 months preceding* the request (if patient has not required any hospitalizations, no hospitalizations can be stated on the request); **AND**
3. Weight, height, and body mass index (BMI) and/or BMI z-score

For patients 6 years of and older:

1. Baseline spirometry measurements of forced expiratory volume in 1 second (FEV_1) in litres and percent predicted ($ppFEV_1$) taken within the 3 months preceding* the request; **AND**
2. Either the number of days treated with oral and/or intravenous (IV) antibiotics for pulmonary exacerbations in the 6 months preceding* the request OR the number of pulmonary exacerbations requiring oral and/or IV antibiotics in the 6 months preceding the request; **AND**
3. Number of CF-related hospitalizations in the 6 months preceding* the request; **AND**
4. Weight, height, and body mass index (BMI) or BMI z-score in children; **AND**
5. A score from an age-appropriate Cystic Fibrosis Questionnaire as follows:
   i) Cystic Fibrosis Questionnaire Child (CFQ-C) and Cystic Fibrosis Questionnaire-Parent (CFQ-P) if the patient is 6 to 13 years of age inclusive;

   OR
   ii) Cystic Fibrosis Questionnaire Revised (CFQ-R teen/adult) Respiratory Domain score it the patient is 14 years of age or older.

* Note that where it states “preceding the request”, this is intended to refer to the baseline measure taken before the initiation of Trikafta at the time the request is first submitted for funding consideration.

Elexacaftor/Tezacaftor/Ivacaftor and Ivacaftor

Brand(s): Trikafta
DOSAGE FORM/ STRENGTH: 100 mg/50 mg/75 mg &150 mg tablets;
50 mg/25 mg/37.5 mg a& 75 mg tablets; 100 mg/50 mg/75 mg & 75 mg granules;
80 mg/40 mg/60 mg & 59.5 mg granules

Notes:

1. Pediatric patients who start therapy when they are 5 years of age or younger can provide the additional measures below at the time of renewal after turning 6 years old;

    i) Baseline spirometry measurements of forced expiratory volume in 1 second (FEV_1) in litres and percent predicted ($ppFEV_1$)
    ii) CFQ questionnaires at the time of renewal of funding when they become 6 years old.

2. Case-by-case consideration will be provided for patients with mutations not listed in Table 1 below but where the mutation has been listed on the Health Canada product monograph for Trikafta or as supported by submitted in-vitro or in-vivo evidence aligned with the national review by Canada's Drug Agency.

Exclusion criteria:
(Patients meeting any of the following will not be funded)

1. Patient has undergone lung transplantation;
2. Patient is using Trikafta as combination therapy with another cystic fibrosis transmembrane conductance regulator (CFTR) modulator.

Initial approval duration for 2 to 5 years (i.e. Less than 6 years old) : 1 year

Initial approval duration for 6 years and older : 7 months

Elexacaftor/Tezacaftor/Ivacaftor and Ivacaftor

Brand(s): Trikafta
DOSAGE FORM/ STRENGTH: 100 mg/50 mg/75 mg &150 mg tablets;
50 mg/25 mg/37.5 mg a& 75 mg tablets; 100 mg/50 mg/75 mg & 75 mg granules;
80 mg/40 mg/60 mg & 59.5 mg granules

RENEWAL CRITERIA

Initial Renewal Criteria:

2 to 5 years:

Renewal of funding for patients 2 to 5 years of age will be considered in patients who are 2 to less than 6 years of age at the time the request is submitted where the prescriber confirms that the patient meets the following criteria:

1. The patient continues to demonstrate continuing benefit from treatment with Trikafta; AND
2. The patient has demonstrated **at least ONE** of the following within six months of the renewal request:

   i) A decrease in the total number of days on which the patient received treatment with oral and/or IV antibiotics for pulmonary exacerbations OR a decrease in the total number of pulmonary exacerbations requiring oral and/or IV antibiotics compared to the baseline measure

   ii) A decreased number of cystic fibrosis related hospitalizations

   iii) No decline in BMI using an age-appropriate measure compared with the baseline BMI measurement (i.e. BMI z-score)

6 years and older:

Renewal of funding for patients 6 years of age and older will be considered in patients demonstrating **at least ONE** of the following improvements after 6 months of treatment with Trikafta;

1. In those providing a baseline lung function test, improvement of percent predicted FEV_1 by 5% or more above the baseline measurement or improvement above the baseline of the associated age-appropriate lung function test used by the CF clinic to evaluate a pediatric patient;
2. A decrease in the total number of days for which the patient received treatment with oral and/or IV antibiotics for pulmonary exacerbations compared with the 6-month period prior to initiating treatment OR a decrease in the total number of pulmonary exacerbations requiring oral and/or IV antibiotics compared with the 6-month period prior to initiating treatment;
3. A decreased number of CF-related hospitalizations compared to the 6-month period prior to initiating Trikafta;

Elexacaftor/Tezacaftor/Ivacaftor and Ivacaftor

Brand(s): Trikafta
DOSAGE FORM/ STRENGTH: 100 mg/50 mg/75 mg &150 mg tablets;
50 mg/25 mg/37.5 mg a& 75 mg tablets; 100 mg/50 mg/75 mg & 75 mg granules;
80 mg/40 mg/60 mg & 59.5 mg granules

4. No decline in BMI using an age-appropriate measure compared with the baseline BMI measurement;
5. If the patient is 6 to 13 years of age inclusive, an improved or sustained quality of life through the scores of the age-appropriate questionnaires using the CFQ-C and CFQ-P compared to the baseline, scores using these questionnaires;
6. If the patient is 14 years of age or older, an improvement by 4 points or more in the CFQ-R Respiratory Domain scale compared to baseline scores.

Subsequent renewal criteria:

For patients who have met the initiation criteria and initial renewal criteria.

1. Ongoing renewal of funding will be provided for those who are continuing to benefit from therapy with Trikafta and who do not meet any of the exclusion criteria.
2. At the time of renewal of funding, include the patient's most recent ppFEV$_1$ if the patient is 6 years of age or older and also include a clinical update to confirm the treatment benefits or response to trikafta that has been experienced by the patient.

Exclusion criteria for Initial and Renewal criteria:
(Patients meeting any of the following will not be funded)

1. Patient has undergone lung transplantation;
2. Patient is using Trikafta as combination therapy with another cystic fibrosis transmembrane conductance regulator (CFTR) modulator.

Approval Duration of first and subsequent renewals: 1 year

Table 1: Additional CFTR Mutations

CFTR mutations with significant clinical evidence of efficacy for trikafta, independent of the mutation on the second allele, are bolded and highlighted

* Complex/compound mutations where a single allele of the CFTR gene has multiple mutations; these exist independent of the presence of mutations on the other allele. † CFTR mutations for which an in vitro response was also demonstrated for ivacaftor alone

3141del9	*E588V*	*H139R*	*P574H*	*S341P*
546insCTA	*E822K*†	*H199Y*	*Q98R*	*S364P*
711+3A→G†	*F191V*	*H1054D*	*Q237E*†	*S492F*
2789+5G→A†	*F311del*†	*H1085P*	*Q237H*†	*S549N*†
3272-26A→G†	*F311L*†	*H1085R*	*Q359R*†	*S549R*†
3849+10kbC→T†	*F508C; S1251N**†	*H1375P*†	*Q1291R*†	*S737F*†
A46D	***F508del***	*I336K*	*R74Q*	*S912L*
A120T†	*F575Y*	*I502T*	*R74W*†	*S945L*†
A234D†	*F1016S*	*I601F*	*R74W;D1270N*	*S977F*†
A349V†	*F1052V*†	*I618T*	*R74W;V201M**	*S1159F*†
A455E	*F1074L*†	*I980K*	*R74W;V201M;*	*S1159P*†
A554E	*F1099L*	*I1269N*	*R117C*†	*S1251N*†
A1006E	*G27R*	*I1366N*	*R117G*†	*S1255P*†
A1067T†	***G85E***	*L15P*	*R117H*†	*T338I*†
D110E†	*G126D*	*L165S*	*R117L*†	*T1036N*
D110H†	*G178R*†	***L206W***	*R117P*†	*V201M*
D192G†	*G194R*†	*L346P*	*R258G*	*V232D*†
D443Y	*G194V*	*L453S*	*R334L*	*V456A*
D443Y;G576A;	*G314E*†	*L967S*†	*R334Q*	*V456F*
D579G†	*G463V*	*L1077P*	*R347H*†	*V1153E*
D614G	*G480C*	*L1324P*	*R347L*†	*V1240G*

D924N†	*G551D*†	*L1335P*	***R347P***	*W361R*
D979V	*G551S*†	*L1480P*†	*R352Q*†	*W1098C*
D1152H†	*G622D*	*M265R*	*R352W*	*W1282R*†
D1270N†	*G628R*	*M952I*†	*R933G*†	*Y109N*
E56K	*G970D*†	*M952T*†	***R1066H***	*Y161D*
E60K	*G1061R*	***M1101K***	*R1070Q*†	*Y161S*
E92K	*G1069R*†	***N1303K***	*R1070W*†	*Y563N*
E116K	*G1244E*†	*P5L*	*R1283M*†	*Y1032C*†
E193K†	*G1249R*†	*P67L*	*R1283S*	
E474K	*G1349D*†	*P205S*	*S13F*	

Approved doses fo Trikafta:

(Refer to the product monograph for dose adjustments when used concomitantly with CYP3A inhibitors.)

Patients 2 to less than 6 years weighing less than 14 kg:

One packet (containing elexacaftor 80 mg, tezacaftor 40 mg and ivacaftor 60 mg granules) in the morning and one packet (ivacaftor 59.5 mg granules) in the evening.

Patients 2 to less than 6 years weighing 14 kg or more: One packet (containing elexacaftor 100 mg, tezacaftor 50 mg and ivacaftor 75 mg granules) in the morning and one packet (ivacaftor 75 mg granules) in the evening.

6 to less than 12 years of age (weighing less than 30 kg): 2 tablets (each containing elexacaftor 50mg/tezacaftor 25mg/ivacaftor 37.5mg) taken in the morning & one tablet (ivacaftor 75mg) taken in the evening approximately 12 hours apart.

6 to less than 12 years of age (weighing 30 kg or more) OR 12 years of age and older: 2 tablets (each containing elexacaftor 100mg/ tezacaftor 50mg/ ivacaftor 75mg) taken in the morning & one tablet (ivacaftor 150mg) taken in the evening approximately 12 hours apart. The following measurements must be completed prior to initiating treatment with Trikafta:

Ivacaftor
Brand(s): Kalydeco
DOSAGE FORM/ STRENGTH: 150 mg tablets
Effective date: June 20, 2014, Updated December 20, 2019

For the treatment of cystic fibrosis in Patients meeting the following criteria;

(i) the Patient is at least 6 years old and has one of the following mutations in the Cystic Fibrosis Transmembrane conductance Regulator (CFTR) gene: G551D, G1244E, G1349D, G178R, G551S, S1251N, S1255P, S549N or S549R;
OR
the Patient is at least 18 years old with an R117H mutation in the CFTR gene.

Initial approval period: 1 year

Initial renewal criteria:

Documented response to treatment (after at least 6 months of therapy), as evidenced by the following:

(a) In cases where the patient's sweat chloride levels prior to commencing therapy were above 60mmol/litre:
- the Patient's sweat chloride level fell below 60mmol/litre; or
- the Patient's sweat chloride level is 30% lower than the level reported in a previous test;

(b) In cases where the patient's sweat chloride levels prior to commencing therapy were below 60mmol/litre:
- the Patient's sweat chloride level is 30% lower than the level reported in a previous test; or
- the patient demonstrates a sustained absolute improvement in FEV1 of at least 5% when compared to the FEV1 test conducted prior to the commencement of therapy.

Duration of approval: 1 year

Subsequent renewal criteria:The Patient is continuing to benefit from therapy with Kalydeco.

[1] It should be noted that, while baseline sweat chloride levels and FEV1 are not required to meet initial approval criteria for Kalydeco, these parameters are used to evaluate the effect of Kalydeco at the time of renewal. To avoid delays, the prescriber should submit a copy of the mutation report, recent baseline sweat chloride levels before starting Kalydeco, and recent baseline FEV1 with the initial request for funding of Kalydeco. These baseline values will be used to evaluate the patient's response to therapy at the time of renewal and would be logistically difficult to obtain once treatment is initiated.

Duration of Approval: 1 Year

Ivacaftor/Lumacaftor

Brand(s): Orkambi
DOSAGE FORM/ STRENGTH: 100 mg / 125 mg tablets; 200 mg/ 125 mg tablets
Effective date: February 20, 2019 Updated: June 25, 2021 and July 8, 2022

Initiation Criteria:

1. Patient is 2 years of age or older: AND
2. Has a confirmed diagnosis of cystic fibrosis and homozygous for F508del mutation in the cystic fibrosis transmembrane conductance regulator gene; AND
3. The patient has demonstrated adherence to their prescribed cystic fibrosis therapeutic regimen; AND
4. Prescribed by a clinical specialist affiliated with a Canadian cystic fibrosis centre: AND
5. Patient must meet one of the following criteria:

    i) Patient is 2 years of age or older and has experienced 1 or more pulmonary exacerbation(s) per year requiring therapy with IV antibiotics OR 3 or more pulmonary exacerbations per year requiring therapy with oral antibiotics.
    ii) Patient is 6 to 11 years of age and has an absolute decline in FEV1 percent predicted equal to or greater than 5% within a 12 month period, sustained over at least 4 months, in spite of optimized medical therapies (For example drop from 90% to 85% predicted)
    iii) Patient is 12 years of age or older and has a baseline FEV1 equal to or less than 70% predicted, who have an absolute decline in FEV1 of ≥5%, within a 12 month period, sustained over at least 4 months, in spite of optimized medical therapies, (For example, FEV1 decline from 60% predicted to 55% predicted in the last 6 months)
    iv) Patient is 12 years of age and older and has a baseline FEV1 of greater than 70% predicted who have an absolute decline in FEV1 of ≥10% predicted within a 12 month period, sustained over at least 4 months, in spite of optimized medical therapies (For example, FEV1 decline from 80% predicted to 70% predicted in the last 6 months)

Exclusion criteria:
(Patients meeting the following will not be funded)

- Patient is currently receiving invasive mechanical ventilation via endotracheal tube or tracheostomy tube; OR
- Patient is the previous recipient of a double lung transplant; OR
- Patient receiving concomitant therapy with another cystic fibrosis transmembrane conductance regulator (CFTR) modulator.

Ivacaftor/Lumacaftor
Brand(s): Orkambi
DOSAGE FORM/ STRENGTH: 100 mg/125 mg tablets; 200 mg/125 mg tablets

.
Notes:

The following assessments should be made prior to initiating treatment:

- Weight, height, and BMI;
- Number of CF related hospitalizations in the previous 6 months;
- Number of days treated with oral and IV antibiotics for pulmonary exacerbations in the previous 6 months (OR number of pulmonary exacerbations requiring oral and IV antibiotics in previous 6 months);

Additionally, for patients 6 years of age and older all the following MUST be provided:

- Baseline measurement of FEV1 in litres and % predicted taken within 3 months of planned initiation of treatment or prior to commencing treatment;
- Change in FEV1 demonstrating decline in FEV1 % predicted prior to starting therapy (as defined in initiation criteria);
- Cystic Fibrosis Questionnaire Child (CFQ-C) and Cystic Fibrosis Questionnaire-Parent (CFQ-P) for those 6 to 13 years old OR Cystic Fibrosis Questionnaire Respiratory (CFQ-R) Domain score for those 14 years and older.

Approval duration of initials: 7 months

Initial Renewal Criteria:

Renewal of funding will be considered in individuals meeting the following:

1. The patient continues to demonstrate adherence to their prescribed cystic fibrosis therapeutic regimen; AND
2. The patient has demonstrated at least ONE of the following after six months of treatment:

    i) A decrease in the total number of days for which the patient received treatment with oral and/or IV antibiotics for pulmonary exacerbations compared with the six month period prior to initiating treatment OR a decrease in the total number of pulmonary exacerbations requiring oral and IV antibiotics compared with the six month period prior to initiating treatment; OR
    ii) Decreased number of CF related hospitalizations at 6 months compared with the six month period prior to initiating Orkambi treatment; OR
    iii) No decline in BMI at six months compared with the baseline BMI assessment (those 2 to 5 years old may also use BMI percentile); OR

Ivacaftor/Lumacaftor
Brand(s): Orkambi
DOSAGE FORM/ STRENGTH: 100 mg/125 mg tablets; 200 mg/125 mg tablets

iv) No decline in FEV1 at six months compared with the baseline FEV1 assessment (as applicable to initiation criteria);

3. If the patient is 6 years of age or older, they must demonstrate improved or sustained quality of life through an age appropriate test (i.e. CFQ-C and CFQ-P scores for those 6 to 13 years old and CFQ-R Respiratory Domain score if the patient is 14 years or older)

Subsequent renewal criteria:

For patients who have met the initiation criteria and initial renewal criteria.

Ongoing renewal of funding will be provided for those who are continuing to benefit from therapy with Orkambi.

Approval Duration of renewals: 1 year

Approved doses:

Patients 2 to 5 years old weighing less than 14kg: 1 packet of granules (containing lumacaftor 100 mg and ivacaftor 125* mg) every 12 hours*.

2 to 5 years old weighing more than 14 kg: 1 packet of granules (containing lumacaftor 150 mg and ivacaftor 188* mg) every 12 hours*.

6-11 years old: 200 mg/250mg lumacaftor/ivacaftor every 12 hours.

12 years and older: 400 mg/250mg lumacaftor/ivacaftor every 12 hours.

*Sachets may be considered case-by-case to accommodate dosing requirements.

Nintedanib
Brand(s): Ofev
DOSAGE FORM/ STRENGTH: 100 mg,150 mg capsules
Updated: April 29, 2022

Initial approval criteria:

For the treatment of adult patients with a diagnosis of **mild to moderate idiopathic pulmonary fibrosis (IPF):**

- Diagnosis confirmed by a respirologist and a high-resolution CT scan.
- All other causes of restrictive lung disease (e.g. collagen vascular disorder or hypersensitivity pneumonitis) should be excluded.
- Mild to moderate IPF is defined as forced vital capacity (FVC) greater than or equal to 50% of predicted.
- Patient is under the care of a physician with experience in IPF.

Initial approval period: 7 months (allow 4 weeks for repeat pulmonary function tests)

Initial renewal criteria (at 6 months):

Patients must NOT demonstrate progression of disease defined as an absolute decline in percent predicted FVC of ≥10% from initiation of therapy until renewal (initial 6 month treatment period). If a patient has experienced progression as defined above, then the results should be validated with a confirmatory pulmonary function test conducted 4 weeks later.

Initial Renewal Duration: 6 Months

Second and subsequent renewals (at 12 months and thereafter):

Patients must NOT demonstrate progression of disease defined as an absolute decline in percent predicted FVC of ≥10% within any 12 month period. If a patient has experienced progression as defined above, then the results should be validated with a confirmatory pulmonary function test conducted 4 weeks later.

Approval period: 12 months

Documentation/information required:

- *If high-resolution CT scan is not available, lung biopsy may be provided to support the diagnosis of IPF as applicable and available*
- *Full pulmonary function test results.*

Second Renewal Duration: 12 Months

Exclusion Criteria:
Combination use of Ofev (nintedanib) and Esbriet (pirfenidone) will not be funded.

Nintedanib
Brand(s): Ofev
DOSAGE FORM/ STRENGTH: 100 mg, 150 mg capsules

Initiation Criteria

For the treatment of **chronic fibrosing interstitial lung disease with a progressive phenotype (PF-ILD)** in patients meeting all of the following criteria:

- Has a confirmed diagnosis by a specialist in interstitial lung diseases. Provide a copy of the consultation note.
- Has a forced vital capacity (FVC) greater than or equal to 45% of predicted.
- Requests must come from or in consultation with a specialist with experience in managing interstitial lung diseases.

Initial requests should contain the following information:
- Pulmonary function test results.
- A high-resolution computed tomography (HRCT) scan, if available.
- A consultation note from a specialist in interstitial lung diseases.

Exclusion Criteria:

- Nintedanib will not be funded as combination therapy with pirfenidone.

Renewal Criteria:

Renewals will be considered in patients who have not experienced an absolute decline in percent predicted forced vital capacity of greater than or equal to 10% over the preceding year of treatment with nintedanib.

Duration of approval of initials and renewal: 12 months

Approved Dosage: up to 150 mg orally every 12 hours

Pirfenidone
Brand(s): Esbriet and generics (see formulary for OFIs)
DOSAGE FORM/ STRENGTH: 267 mg capsule, 267 mg tablet, 801 mg tablet

Initial approval criteria:

For the treatment of adult patients with a diagnosis of **mild to moderate idiopathic pulmonary fibrosis (IPF):**

- Diagnosis confirmed by a respirologist and a high-resolution CT scan.
- All other causes of restrictive lung disease (e.g. collagen vascular disorder or hypersensitivity pneumonitis) should be excluded.
- Mild to moderate IPF is defined as forced vital capacity (FVC) greater than or equal to 50% of predicted.
- Patient is under the care of a physician with experience in IPF.

Initial approval period: 7 months (allow 4 weeks for repeat pulmonary function tests)

Initial renewal criteria (at 6 months):

Patients must NOT demonstrate progression of disease defined as an absolute decline in percent predicted FVC of ≥10% from initiation of therapy until renewal (initial 6 month treatment period). If a patient has experienced progression as defined above, then the results should be validated with a confirmatory pulmonary function test conducted 4 weeks later.

Approval period: 6 months

Second and subsequent renewals (at 12 months and thereafter):

Patients must NOT demonstrate progression of disease defined as an absolute decline in percent predicted FVC of ≥10% within any 12 month period. If a patient has experienced progression as defined above, then the results should be validated with a confirmatory pulmonary function test conducted 4 weeks later.

Approval period: 12 months

Documentation/information required:

- *If high-resolution CT scan is not available, lung biopsy may be provided to support the diagnosis of IPF as applicable and available*
- *Full pulmonary function test results.*

Exclusion Criteria:
Combination use of Esbriet (pirfenidone) and Ofev (nintedanib) will not be funded.

POLYARTICULAR JUVENILE IDIOPATHIC ARTHRITIS

Etanercept – see Formulary for funded biosimilars
Brand(s): Enbrel
DOSAGE FORM/ STRENGTH: 25 mg/vial, 25 mg and 50 mg prefilled syringe or pens for subcutaneous injection per formulary listed options

Adalimumab – see Formulary for funded biosimilars
Brand(s): Humira and formulary listed biosimilars
DOSAGE FORM/ STRENGTH: 40 mg/0.8mL prefilled syringe, 40 mg/0.8mL and and 20 mg/0.2 mL prefilled pens for subcutaneous injection

Tociluzumab
Brand(s): Actemra
DOSAGE FORM/ STRENGTH: 80 mg/4 mL Vial, 200 mg/10 mL Vial, 400 mg/20 mL Vial, 162mg/0.9mL Inj (Prefilled syringe), 162mg/0.9mL Auto Injector

Rituximab
Brand(s): Riximyo, Ruxience, and Truxima (biosimilar); Rituxan (biologic originator for those meeting biosimilar exemption)
DOSAGE FORM/ STRENGTH: 10 mg/mL intravenous injection

Refer to the Executive Officer Communications on the Ministry website for the Ministry's Biosimilar Policy including frequently asked questions and updates for the biosimilar policy updates. http://www.health.gov.on.ca/en/pro/programs/drugs/opdp_eo/eo_communiq.aspx

Effective March 31, 2023, the ODB program will start transitioning coverage for Copaxone®, Enbrel®, Humalog®, Humira®, Lantus®, NovoRapid®, Remicade®, and Rituxan® to their biosimilar versions.

Effective December 29, 2023, coverage for these originator biologic drugs through the ODB program will not be available for patients and the ODB program will only provide coverage for the biosimilar version of these drugs for all ODB program recipients, with limited exemptions. In general, for ODB program recipients who are already on these biologic drugs, there is up to a 9-month transition period (see the biosimilar switch policy described on page 6 to 8 of this document).

It should be noted that after the date when a biosimilar becomes publicly funded for an approved indication, patients initiated on an originator biologic for this same provincially funded indication through support from a manufacturer's patient support program, will be expected to be provided ongoing access of the originator biologic through the patient's original payer mechanism (e.g. manufacturer's patient support program) or to switch to an ODB funded biosimilar version upon meeting specified criteria. The Ministry will no longer

consider funding of originator biologics that are part of the biosimilar policy with limited exemptions on or after December 29, 2023.

For the first-line treatment of polyarticular-course juvenile idiopathic arthritis in patients meeting the following criteria:

- Patient has active disease (≥ 3 swollen joints and ≥ 5 active joints) despite a trial of optimal dose of subcutaneously administered methotrexate (i.e. 15 mg/m^2 per week) for at least 3 months. If the patient is unable to tolerate or has a contraindication to subcutaneous methotrexate, the nature of the intolerance or contraindication must be described in detail.

Duration of Approval: 1 Year

Renewal will be considered for patients with objective evidence of at least a 20% reduction in swollen joint count and a minimum of improvement in 2 swollen joints over the previous year. For renewals beyond the second year, objective evidence of preservation of treatment effect must be provided.

Duration of Approval: 5 Year

Dosing for Etanercept:

The planned dosing regimen should be provided. The maximum recommended dose is 50mg once weekly.

Recommended Dosing for Adalimumab:

a) 24 mg/m^2 (maximum 40 mg) every two weeks; OR
b) 20 mg every 2 weeks, if the Patient weighs less than 30 kg; OR
c) 40 mg every 2 weeks, if the Patient weighs more than 30 kg.

Recommended dosing for tocilizumab in combination with methotrexate:

IV dosing regimen:
a) 10 mg/kg every 4 weeks, if the Patient weighs less than 30kg; OR
b) 8 mg/kg every 4 weeks, if the Patient weighs more than or equal to 30kg.

SC dosing regimen:

a) 162 mg once every 3 weeks if the Patient weighs less than 30kg
b) 162 mg once every 2 weeks if the Patient weighs 30kg or more

Abatacept
Brand(s): Orencia
DOSAGE FORM/ STRENGTH: 250 mg/15 mL vial (Note that the sc injection is not approved for this indication)

Infliximab - See formulary for funded biosimilars
Brand(s): Avsola, Inflectra, Renflexis Biosimilars); Remicade (Only for those approved for biosimilar exemption)
DOSAGE FORM/ STRENGTH: 100 mg/vial

Rituximab -See formulary for funded biosimilars
Brand(s): Riximyo, Ruxience, and Truxima (biosimilar); Rituxan (Only for those approved for biosimilar exemption)
DOSAGE FORM/ STRENGTH: 10 mg/mL intravenous injection

Refer to the Executive Officer Communications on the Ministry website for the Ministry's Biosimilar Policy including frequently asked questions and updates for the biosimilar policy updates. http://www.health.gov.on.ca/en/pro/programs/drugs/opdp_eo/eo_communiq.aspx

Effective March 31, 2023, the ODB program will start transitioning coverage for Copaxone®, Enbrel®, Humalog®, Humira®, Lantus®, NovoRapid®, Remicade®, and Rituxan® to their biosimilar versions.

Effective December 29, 2023, coverage for these originator biologic drugs through the ODB program will not be available for patients and the ODB program will only provide coverage for the biosimilar version of these drugs for all ODB program recipients, with limited exemptions. In general, for ODB program recipients who are already on these biologic drugs, there is up to a 9-month transition period (see the biosimilar switch policy described on page 6 to 8 of this document).

It should be noted that after the date when a biosimilar becomes publicly funded for an approved indication, patients initiated on an originator biologic for this same provincially funded indication through support from a manufacturer's patient support program, will be expected to be provided ongoing access of the originator biologic through the patient's original payer mechanism (e.g. manufacturer's patient support program) or to switch to an ODB funded biosimilar version upon meeting specified criteria. The Ministry will no longer consider funding of originator biologics that are part of the biosimilar policy with limited exemptions on or after December 29, 2023.

For the treatment of polyarticular-course juvenile idiopathic arthritis in patients meeting the following criteria;

- Patient has active disease (a minimum of 3 (three) swollen joints and a total of 5 active joints); AND

- Patient has had an inadequate response to a three month course of methotrexate administered subcutaneously at a dosage of at least 15 mg/m^2 per week for at least 3 months. If the patient is unable to tolerate or has a contraindication to subcutaneous methotrexate the nature of the intolerance or contraindication must be described in detail.; AND

- Patient has had an inadequate response to a three month course of etanercept OR adalimumab OR tociluzumab. If the patient is unable to tolerate or has a contraindication to etanercept OR adalimumab OR tociluzumab, the nature of the intolerance or contraindication must be described in detail.

Duration of Approval: 1 Year

Renewals will be considered for patients with objective evidence of at least a 20% reduction in swollen joint count. For renewals beyond the second year, objective evidence of preservation of treatment effect should be provided. (i.e. the current joint count should be compared to the count prior to initiating treatment with the biologic agent)

Duration of Approval: 5 Year

Approved Dose:

Abatacept refer to the Orencia product monograph for dosing information

Infliximab dose up to 6mg/kg/dose at 0, 2 and 6 weeks followed by maintenance of up to 6mg/kg/dose every 8 weeks

RHEUMATOID ARTHRITIS

Abatacept
Brand(s): Orencia
DOSAGE FORM/ STRENGTH: 250 mg/15 mL intravenous injection,125 mg/mL pre-filled syringe for subcutaneous injection

For the treatment of adult patients with severe active rheumatoid arthritis who meet the following criteria:

The Patient has severe active disease as demonstrated by;

- ≥ 5 swollen joints; AND
- rheumatoid factor positive; AND/OR
- having radiographic evidence of rheumatoid arthritis

Despite the optimal* use of various disease-modifying anti-rheumatic drugs (“DMARDs”).

* For the purpose of the criteria, the optimal use of DMARDs is defined as;

- use of methotrexate (dosed at 20 mg per week) for at least 3 months; AND
- use of leflunomide (dosed at 20 mg per day) for at least 3 months; AND
- an adequate trial (3 months) of at least one combination of DMARDs;

  OR

- use of methotrexate (dosed at 20 mg per week) for at least 3 months; AND
- leflunomide in combination with methotrexate for at least 3 months.

Note: If the patient cannot be treated with adequate trial(s) of methotrexate and/ or leflunomide due to contraindication(s) or intolerance(s), the nature of the contraindication(s) or intolerance(s) must be provided along with details of trials of other DMARDs or clear rationale why other DMARDs cannot be considered.

For patients who have failed treatment with an anti-TNF therapy due to lack of efficacy or toxicity, prescribers should consider use of a biologic with a different mechanism of action.

Abatacept
Brand(s): Orencia
DOSAGE FORM/ STRENGTH: 250 mg/15 mL intravenous injection,125 mg/mL pre-filled syringe for subcutaneous injection

Approved Dosing:

IV use: The initial dose is administered at 0, 2, and 4 weeks then every 4 weeks thereafter. Note that funding for higher doses will not be considered.

Body weight of patient	Dose
< 60 kg	500 mg
60-100 kg	750 mg
>100 kg	1 gram

SC use: 125 mg SC weekly. Note that an IV loading dose of 750 mg may be given prior to initiating the weekly SC dosing. (Please refer to the Orencia product monograph for further details.)

Duration of Approval: First Renewal – 1 Year, Subsequent Renewals – 5 Years

Renewals will be considered in patients with objective evidence of at least a twenty percent (20%) reduction in swollen joint count and a minimum of improvement in two (2) swollen joints over the previous year.

For renewals beyond the second year, objective evidence of the preservation of treatment effect must be provided by the requesting physician.

Note that Orencia SC (abatacept) 125mg/mL PFS – 1mL Pk (BQU) – Effective Date: June 28, 2024

This product (PIN 09858343) is funded under the EAP on a temporary basis for the treatment of rheumatoid arthritis to manage a drug shortage of Orencia DIN 02402475. This temporary PIN is expected to end date by April 1, 2025 which provides 3 months of time from the expected return to stock date for the Canadian Orencia injection DIN 02402475.

Adalimumab – see Formulary for funded biosimilars
Brand(s): Humira (Only for those approved for biosimilar exemption)
DOSAGE FORM/ STRENGTH: 40 mg/0.8mL prefilled syringe, 40 mg/0.8mL and 20 mg/0.2 mL prefilled pens for subcutaneous injection

Anakinra
Brand(s): Kineret
DOSAGE FORM/ STRENGTH: 100 mg /0.67 mL subcutaneous injection

Certolizumab pegol
Brand(s): Cimzia
DOSAGE FORM/ STRENGTH: 200 mg/mL prefilled syringe and autoinjector

Etanercept – see Formulary for funded biosimilars
Brand(s): Enbrel (Only for those approved for biosimilar exemption)
DOSAGE FORM/ STRENGTH: 25 mg and/or 50 mg prefilled syringe or pens for subcutaneous injection per formulary listed options

Golimumab
Brand(s): Simponi
DOSAGE FORM/ STRENGTH: 50 mg/0.5 mL prefilled syringe and autoinjector

Infliximab – see Formulary for funded biosimilars
Brand(s): Remicade (Only for those approved for biosimilar exemption)
DOSAGE FORM/ STRENGTH: 100 mg/vial intravenous infusion

Refer to the Executive Officer Communications on the Ministry website for the Ministry's Biosimilar Policy including frequently asked questions and updates for the biosimilar policy updates. http://www.health.gov.on.ca/en/pro/programs/drugs/opdp_eo/eo_communiq.aspx

Effective March 31, 2023, the ODB program will start transitioning coverage for Copaxone®, Enbrel®, Humalog®, Humira®, Lantus®, NovoRapid®, Remicade®, and Rituxan® to their biosimilar versions.

Effective December 29, 2023, coverage for these originator biologic drugs through the ODB program will not be available for patients and the ODB program will only provide coverage for the biosimilar version of these drugs for all ODB program recipients, with limited exemptions. In general, for ODB program recipients who are already on these biologic drugs, there is up to a 9-month transition period (see the biosimilar switch policy described on page 6 to 8 of this document).

It should be noted that after the date when a biosimilar becomes publicly funded for an approved indication, patients initiated on an originator biologic for this same provincially

funded indication through support from a manufacturer's patient support program, will be expected to be provided ongoing access of the originator biologic through the patient's original payer mechanism (e.g. manufacturer's patient support program) or to switch to an ODB funded biosimilar version upon meeting specified criteria. The Ministry will no longer consider funding of originator biologics that are part of the biosimilar policy with limited exemptions on or after December 29, 2023.

For the treatment of rheumatoid arthritis in patients who have:

- Severe active disease (≥ 5 swollen joints and rheumatoid factor positive and/or, anti-CCP positive, and/or radiographic evidence of rheumatoid arthritis) despite the optimal use of various formulary disease-modifying anti-rheumatic drugs (DMARDs)*.

* Optimal use of DMARDs include:

- Methotrexate (20 mg/week) for at least 3 months and leflunomide (20 mg/day) for at least 3 months in addition to an adequate trial (3 months) of at least one combination of DMARDs; or
- Methotrexate (20 mg/week) for at least 3 months and leflunomide in combination with methotrexate for at least 3 months.
- If the patient could not receive adequate trial(s) of methotrexate and/or leflunomide due to contraindication(s) or intolerance(s), the nature of contraindication(s) or intolerance(s) must be provided along with details of trials of other DMARDs or clear rationale why other DMARDs cannot be considered.

OR

- Methotrexate (20mg/week), sulfasalazine (2 GM/day) and hydroxychloroquine (400mg/day)* for at least 3 months. If the patient could not receive an adequate trial of methotrexate, sulfasalazine and hydroxychloroquine due to intolerance, then the above DMARD trial criteria must be met.

Hydroxychloroquine is based by weight up to 400 mg per day

Duration of Approval: 1 Year

Renewal will be considered for patients with objective evidence of at least a 20% reduction in swollen joint count and a minimum of improvement in 2 swollen joints over the previous year. For renewals beyond the second year, objective evidence of preservation of treatment effect must be provided.

The planned dosing regimen for the requested biologic should be provided. The recommended doses for the treatment of rheumatoid arthritis are as follows:

- Adalimumab 40mg every two weeks
- Anakinra 100mg per day

- Certolizumab pegol 400mg at 0, 2 and 4 weeks followed by maintenance therapy of 200 mg every 2 weeks. For maintenance dosing, 400mg every 4 weeks may be considered
- Etanercept 25mg twice weekly or 50mg once weekly
- Golimumab 50mg once a month
- Infliximab 3mg/kg/dose at 0, 2 and 6 weeks followed by maintenance therapy of 3mg/kg/dose every 8 weeks up to a maximum of six maintenance doses per year

Duration of Approval:

First Renewal: 1 Year
Subsequent Renewals: 5 Years

Rituximab – See Formulary for funded biosimilars

Brand(s): Riximyo, Ruxience, Truxima (Biosimilar); Rituxan (Only for those approved for biosimilar exemption)
DOSAGE FORM/ STRENGTH: 10 mg/mL intravenous injection

Refer to the Executive Officer Communications on the Ministry website for the Ministry's Biosimilar Policy including frequently asked questions and updates for the biosimilar policy updates. http://www.health.gov.on.ca/en/pro/programs/drugs/opdp_eo/eo_communiq.aspx

Effective March 31, 2023, the ODB program will start transitioning coverage for Copaxone®, Enbrel®, Humalog®, Humira®, Lantus®, NovoRapid®, Remicade®, and Rituxan® to their biosimilar versions.

Effective December 29, 2023, coverage for these originator biologic drugs through the ODB program will not be available for patients and the ODB program will only provide coverage for the biosimilar version of these drugs for all ODB program recipients, with limited exemptions. In general, for ODB program recipients who are already on these biologic drugs, there is up to a 9-month transition period (see the biosimilar switch policy described on page 6 to 8 of this document).

It should be noted that after the date when a biosimilar becomes publicly funded for an approved indication, patients initiated on an originator biologic for this same provincially funded indication through support from a manufacturer's patient support program, will be expected to be provided ongoing access of the originator biologic through the patient's original payer mechanism (e.g. manufacturer's patient support program) or to switch to an ODB funded biosimilar version upon meeting specified criteria. The Ministry will no longer consider funding of originator biologics that are part of the biosimilar policy with limited exemptions on or after December 29, 2023.

Rituximab (See formulary for funded biosimilars)

Brand(s): Riximyo, Ruxience, Truxima, Rituxan (Only for those approved for biosimilar exemption)
DOSAGE FORM/ STRENGTH: 10 mg/mL Intravenous injection

First course of Rituximab for the treatment of rheumatoid arthritis in adult patients with:

- Severe active disease (≥ 5 swollen joints and rheumatoid factor positive and/or radiographic evidence of rheumatoid arthritis); **AND**
- Failure to respond to optimal use of DMARDs or documented intolerance or contraindications to DMARDs (per current EAP reimbursement criteria for anti-TNF agents); **AND**
- Failure to respond to, or the patient has intolerance or contraindications to, an adequate trial of at least ONE anti-TNF agent (e.g., adalimumab, etanercept, infliximab, golimumab, certolizumab pegol)

Initial approval: One year: One course of treatment is 1000 mg followed two weeks later by the second 1000mg dose. Two courses will be approved each year (courses should be at least 6 months apart with second course being given only AFTER loss of effect as noted in the re-treatment guidelines below). Second course is not approved for “maintenance” therapy.

Renewal criteria: A joint count at 3-4 months indicating at least a 20% reduction in swollen joint count and a minimum of improvement in 2 swollen joints, should be recorded to indicate a response, and then re-treatment can be given after an interval of at least 6 months AND after a loss of effect. Details of all courses given and the subsequent response should be provided in the renewal request.

Renewal approval: 1 year (2 courses). One course of treatment is 1000 mg followed two weeks later by the second 1000mg dose. Repeated courses are not approved for maintenance therapy.

Note: Rituximab should not be used concomitantly with other anti-TNF agents.

Sarilumab
Brand(s): Kevzara
DOSAGE FORM/ STRENGTH: 150mg/1.14mL, 200mg/1.14mL Pre-filled Pen and Pre-filled Syringe

For the treatment of rheumatoid arthritis in adult patients meeting the following criteria:

a) Sarilumab is being used as monotherapy or in combination with methotrexate or other non-biologic disease-modifying antirheumatic drugs (DMARDs); AND
b) Patient is 18 years of age or older; AND
c) Has severe active disease (≥ 5 swollen joints and rheumatoid factor positive ***and/or anti-CCP positive*** and/or radiographic evidence of rheumatoid arthritis) despite the optimal use of various formulary disease-modifying anti-rheumatic drugs (DMARDs); AND
d) Has one of the following:
    i) fails to respond to Optimal use[1] of DMARDs (e.g.hydroxychloroquine, methotrexate, sulfasalazine, leflunomide, cyclosporine, azathioprine, penicillamine, chloroquine and gold compounds).

        [1]Optimal use of DMARDs is defined as one of the below::
        a) methotrexate (20 mg/week) for at least 3 months and leflunomide (20 mg/day) for at least 3 months, in addition to an adequate trial (3 months) of at least one combination of DMARDs;
        b) methotrexate (20 mg/week) for at least 3 months and leflunomide in combination with methotrexate for at least 3 months; or
        c) methotrexate (20 mg/week), sulfasalazine (2 G/day) and hydroxychloroquine (based on weight and up to 400 mg/day) for at least 3 months.
    ii) has a documented intolerance or contraindication to DMARDs in which case the nature of the contraindication(s) or intolerance(s) must be provided with the request, along with details of trials of other DMARDs or clear rationale as to why other DMARDs cannot be considered

Approval duration of Initials: 1 year

Objective evidence of at least a 20% reduction in swollen joint count and a minimum of improvement in 2 swollen joints over the previous year.

Approval duration of first renewal: 1 year

For renewals beyond the second year, objective evidence of preservation of treatment effect must be provided.

Subsequent Renewal Criteria: Approval duration 5 years

Recommended Dose:

The recommended dose of KEVZARA is 200 mg once every 2 weeks given as a subcutaneous injection.

A reduced dose of 150 mg once every two weeks is recommended for patients with neutropenia, thrombocytopenia, or with elevated liver enzymes.

Tocilizumab
Brand(s): Actemra
DOSAGE FORM/ STRENGTH: 80 mg/4 mL Vial, 200 mg/10 mL Vial, 400 mg/20 mL Vial, 162mg/0.9mL Inj (Prefilled syringe), 162mg/0.9mL Auto Injector

For the treatment of rheumatoid arthritis in adult patients with;

- Severe active disease (≥ 5 swollen joints and rheumatoid factor positive and/or anti-CCP positive and/or has radiographic evidence of rheumatoid arthritis); **AND**

- Failure to respond to optimal use[1] of DMARDs or with documented intolerance to DMARDs (per current EAP reimbursement criteria for anti-TNF agents).

Optimal use of DMARDs (hydroxychloroquine, methotrexate, sulfasalazine, leflunomide, cyclosporine, azathioprine, penicillamine, chloroquine and gold compounds) defined as:

a) Methotrexate (20 mg/week) for at least 3 months AND

b) Leflunomide (20 mg/day) for at least 3 months, in addition to an adequate trial (3 months) of at least one combination of DMARDs; **OR**

c) Methotrexate (20 mg/week) for at least 3 months AND leflunomide in combination with methotrexate for at least 3 months; **OR**

[1] Note: If the patient could not receive adequate trial(s) of methotrexate and/or leflunomide due to contraindication(s) or intolerance(s), the nature of the contraindication(s) or intolerance(s) must be provided along with details of trials of other DMARDs or clear rationale as to why other DMARDs cannot be considered.

d) Methotrexate (20 mg/week), sulfasalazine (2 G/day) and hydroxychloroquine (400 mg/day)[2] for at least 3 months. If the patient could not receive an adequate trial of methotrexate, sulfasalazine and hydroxychloroquine due to intolerance, then the above DMARD trial criteria must be met.

[2] Hydroxychloroquine is based by weight up to 400 mg per day

The requesting physician is required to provide the planned dosing regimen on the request.

Tocilizumab

Brand(s): Actemra

DOSAGE FORM/ STRENGTH: 80 mg / 4 mL Vial, 200 mg /10 mL Vial, 400 mg/ 20 mL Vial, 162 mg/0.9 mL solution for injection, 162 mg/0.9 mL Autoinjector

The following are the recommended doses for tocilizumab (Actemra) IV and SC for rheumatoid arthritis:

IV recommended dose:

Approval for 4mg/kg/dose once every 4 weeks followed by an increase to 8mg/kg/dose based on clinical response; even for individuals whose body weight is more than 100kg, doses exceeding 800mg per infusion are not recommended

SC recommended dose:

For patients < 100 kg weight, starting dose of 162 mg every other week, followed by an increase to every week based on clinical response. For patients at or above 100 kg weight, 162 mg every week.

Duration of Approval: 1 Year

Renewal will be considered for patients with objective evidence

of at least a 20% reduction in swollen joint count and a minimum

of improvement in 2 joints over the previous year.

For renewals beyond the second year, objective evidence of preservation of treatment effect must be provided.

Duration of Approval of first Renewal – 1 Year

Duration of Second and Subsequent Renewals – 5 Years

SUBSTANCE DEPENDENCE

Methadone Compounded Solution
Brand(s):
DOSAGE FORM/ STRENGTH:

Effective September 1, 2014

Reimbursement of Compounded Methadone solution for the treatment of opioid dependence will be considered for patients who meet the following criteria;

Patient has demonstrated that they have experienced a true allergy to both commercially available Methadose formulations (i.e., Methadose 10 mg/mL oral cherry flavoured concentrate AND Methadose 10 mg/mL dye-free, sugar-free, unflavoured oral concentrate).

The request must be accompanied by a completed Health Canada adverse drug reaction form (Canada Vigilance Adverse Reaction Reporting Form) and include a detailed description of the allergic reaction to each Methadose product, a description of the circumstances in which the reactions occurred, and demonstration that the allergy is unlikely to be related to any diluent in which Methadose was mixed, but rather, that it was caused by the excipients within the Methadose formulation.

SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS

Anakinra
Brand(s): Kineret
DOSAGE FORM/ STRENGTH: 100mg/0.67Ml pre-filled syringe

For the treatment of systemic juvenile idiopathic arthritis in patients who meet the following criteria;

a) Patient must have a diagnosis of sJIA with fever (>38 degrees Celsius) for at least 2 weeks AND at least ONE of the following:

- o rash of systemic JIA
- o serositis (e.g. pericarditis , pleuritis, or peritonitis)
- o lymphadenopathy (e.g. cervical, axillary, inguinal)
- o hepatomegaly
- o splenomegaly

b) The physician making the request has ruled out other potential etiologies (e.g. malignancies, serious clinical infections, and other inflammatory or connective tissue diseases); AND

c) Age of disease onset is younger than 16 years of age. (Note: the physician must specify age of disease onset in the request); AND

d) Systemic corticosteroids cannot be used for at least ONE of the following reasons (please specify name and current dose of corticosteroid, if applicable):

- o The patient is unresponsive and/or refractory to systemic corticosteroids; OR
- o The patient has experienced a systemic reaction (e.g. fever, rash of sJIA, serositis, lymphadenopathy, hepatomegaly or splenomegaly) while on tapering doses of systemic corticosteroids (i.e. the patient is corticosteroid dependent); OR
- o The patient has experienced an adverse drug reaction to a systemic corticosteroid; OR
- o The use of systemic corticosteroids is contraindicated in this patient.

Anakinra
Brand(s): Kineret
DOSAGE FORM/ STRENGTH: 100mg/0.67Ml pre-filled syringe

Note: The following requests will undergo external review on a case-by-case basis:

- Patients with Macrophage Activation Syndrome
- Patients who meet initial sJIA criteria and are currently 16 years of age or older
- Patients who meet initial sJIA criteria and are requesting higher dosing regimens (Please provide rationale for the higher dosing regimen with your request)

Dosing: 1-2 mg/kg subcutaneously once daily.

Duration of Approval: 1 Year

Renewal will be considered for patients demonstrating at least a 50% reduction in corticosteroid dose (unless contraindicated, not tolerated, unresponsive or refractory at the time of initial request) and no evidence of active systemic disease. For renewals beyond the second year, objective evidence of preservation of treatment effect must be provided.

The following renewal requests will undergo external review:

- Evidence of active systemic disease
- Requests for higher dosing regimens (Please provide rationale for the higher dosing regimen with your request)
- Patient is currently 16 years of age or older

Duration of Approval: 1 Year

Tocilizumab
Brand(s): Actemra
DOSAGE FORM/ STRENGTH: 80 mg / 4 mL, 200 mg / 10 mL, 400 mg / 20 mL, 162 mg sc inj (Prefilled Syringe), 162 mg Auto Injector

For the treatment of systemic juvenile idiopathic arthritis in patients who meet the following criteria;

- Patient must have a diagnosis of sJIA with fever (>38 degrees Celsius) for at least 2 weeks AND at least ONE of the following:
    - rash of systemic JIA
    - serositis (e.g. pericarditis , pleuritis, or peritonitis)
    - lymphadenopathy (e.g. cervical, axillary, inguinal)
    - hepatomegaly
    - splenomegaly
- The physician has ruled out other potential etiologies (e.g. malignancies, serious clinical infections, and other inflammatory or connective tissue diseases); AND
- Age of disease onset is younger than 16 years of age. (Note: the physician must specify age of disease onset in the request); AND
- Systemic corticosteroids cannot be used for at least ONE of the following reasons (please specify name and current dose of corticosteroid, if applicable):
    - The patient is unresponsive and/or refractory to systemic corticosteroids; OR
    - The patient has experienced a systemic reaction (e.g. fever, rash of sJIA, serositis, lymphadenopathy, hepatomegaly or splenomegaly) while on tapering doses of systemic cortico-steroids (i.e. the patient is corticosteroid dependent); OR
    - The patient has experienced an adverse drug reaction to a systemic corticosteroid; OR
    - The use of systemic corticosteroids is contraindicated in this patient.

Note: The following requests will undergo external review on a case-by-case basis:

- Patients with Macrophage Activation Syndrome
- Patients who meet initial sJIA criteria and are currently 16 years of age or older
- Patients who meet initial sJIA criteria and are requesting higher dosing regimens (Please provide rationale for the higher dosing regimen with your request)

Tocilizumab

Brand(s): Actemra
DOSAGE FORM/ STRENGTH: 80 mg / 4 mL, 200 mg / 10 mL, 400 mg / 20 mL, 162 mg sc inj (Prefilled Syringe), 162 mg Autoinjector

Dosing: For those less than 30 kg,12 mg/kg IV every 2 weeks
For those greater than or the same as 30 kg, 8 mg/kg IV every 2 weeks

Note: Recommended maximum adult dose is 800 mg.

SC dosing regimen:

a) 162 mg once every 2 weeks if the Patient weighs less than 30kg
b) 162 mg once every week if the Patient weighs 30 kg or more

Duration of Approval: 1 Year

Renewal will be considered for patients demonstrating at least a 50% reduction in corticosteroid dose (unless contraindicated, not tolerated, unresponsive or refractory at the time of initial request) and no evidence of active systemic disease. For renewals beyond the second year, objective evidence of preservation of treatment effect must be provided.

The following renewal requests will undergo external review:

- Evidence of active systemic disease
- Requests for higher dosing regimens (Please provide rationale for the higher dosing regimen with your request)

Patient is currently 16 years of age or older

Duration of Approval: 1 Year

JUVENILE SPONDYLOARTHRITIS OR ENTHESITIS-RELATED ARTHRITIS

Adalimumab – see Formulary for funded biosimilars

Brand(s): Humira (Only for those approved for biosimilar exemptions)
DOSAGE FORM/ STRENGTH: 40mg/0.8mL prefilled syringe, 40mg/0.8mL and 20 mg/0.2 mL prefilled pens for subcutaneous injection

Etanercept – see Formulary for funded biosimilars

Brand(s): Enbrel (Only for those approved for biosimilar exemptions)
DOSAGE FORM/ STRENGTH: 25mg/vial, 50 mg prefilled syringe for subcutaneous injection

Infliximab – see Formulary for funded biosimilars

Brand(s): Remicade (Only for those approved for biosimilar exemptions)DOSAGE FORM/ STRENGTH: 100 mg/vial

Updated: March 29, 2021

Refer to the Executive Officer Communications on the Ministry website for the Ministry's Biosimilar Policy including frequently asked questions and updates for the biosimilar policy updates. http://www.health.gov.on.ca/en/pro/programs/drugs/opdp_eo/eo_communiq.aspx

Effective March 31, 2023, the ODB program will start transitioning coverage for Copaxone®, Enbrel®, Humalog®, Humira®, Lantus®, NovoRapid®, Remicade®, and Rituxan® to their biosimilar versions.

Effective December 29, 2023, coverage for these originator biologic drugs through the ODB program will not be available for patients and the ODB program will only provide coverage for the biosimilar version of these drugs for all ODB program recipients, with limited exemptions. In general, for ODB program recipients who are already on these biologic drugs, there is up to a 9-month transition period (see the biosimilar switch policy described on page 6 to 8 of this document).

It should be noted that after the date when a biosimilar becomes publicly funded for an approved indication, patients initiated on an originator biologic for this same provincially funded indication through support from a manufacturer's patient support program, will be expected to be provided ongoing access of the originator biologic through the patient's original payer mechanism (e.g. manufacturer's patient support program) or to switch to an ODB funded biosimilar version upon meeting specified criteria. The Ministry will no longer consider funding of originator biologics that are part of the biosimilar policy with limited exemptions on or after December 29, 2023.

For the treatment of juvenile spondyloarthritis (JSpA) or enthesitis-related arthritis (ERA) in patients who meet the following criteria for either axial or peripheral disease:

Axial Disease

- Age of disease onset ≤ 16 years; AND
- Low back pain and stiffness for > 3 months that improve with exercise and not relieved by rest; AND
- Failure to respond to or documented intolerance to adequate trials of 2 nonsteroidal anti-inflammatory drugs (NSAIDs) for at least 4 weeks each; AND
- BASDAI score of ≥ 4 after at least 4 weeks of standard NSAID therapy; AND
- Imaging evidence of severe active disease by X-ray, CT scan or MRI

The details of imaging reports for severe active disease must provide the following;

- X-ray or CT scan report stating the presence of “SI joint fusion” or “SI joint erosion” OR
- MRI report stating the presence of “inflammation” or “edema” or “erosion” of the SI joint.

Actual imaging reports must be submitted with the request. If the imaging reports do not specify the above findings, the request will be reviewed by external medical experts. The imaging interpretation report from the radiologist or rheumatologist may be submitted along with radiographic report.

Adalimumab – see Formulary for funded biosimilars
Brand(s): Humira (Only for those approved for biosimilar exemptions)
DOSAGE FORM/ STRENGTH: 40 mg/0.8 mL prefilled syringe, 40mg/0.8mL and 20 mg/0.2 mL prefilled pen for subcutaneous injection

Etanercept – see Formulary for funded biosimilars
Brand(s): Enbrel (Only for those approved for biosimilar exemptions)
DOSAGE FORM/ STRENGTH: 25mg/vial, 50 mg prefilled syringe for subcutaneous injection

Infliximab – see Formulary for funded biosimilars
Brand(s): Remicade (Only for those approved for biosimilar exemptions)
DOSAGE FORM/ STRENGTH: 100 mg/vial

Renewal will be considered for patients with objective evidence of at least a 50% reduction in BASDAI score or ≥ 2 absolute point reduction in BASDAI score.

For renewals beyond the second year, objective evidence of preservation of treatment effect must be provided.

Peripheral Disease

- Age of disease onset ≤ 16 years; AND
- ≥ 5 active sites of inflammation attained by a combination of swollen/active joints and/or enthesitis sites (tenderness or swelling at entheseal insertion)
- Failure or intolerance to at least one DMARD (sulfasalazine 50 mg/kg/day-maximum 2 grams, or methotrexate 15 mg/m^2/week-maximum 25 mg per week) for at least 3 months.

Renewals will be considered for patients with objective evidence of at least a 20% reduction in active sites over the previous year. There should also be an improvement in number of enthesitis sites.

For renewals beyond the second year, objective evidence of preservation of treatment effect must be provided. Requests that do not meet these criteria will undergo external review.

The planned dosing regimen for the requested biologic should be provided.

The recommended dose for the treatment of JSpA/ERA is as follows:

i) Etanercept 0.4mg/kg (max 25 mg) twice weekly or 0.8mg/kg (max 50 mg) once weekly

ii) Infliximab: 5mg/kg/dose at 0, 2 and 6 weeks followed by maintenance therapy of up to 5mg/kg/dose every 6-8 weeks

iii) Adalimumab:
   a. If Less than 30 kg: 20 mg SC q 2 weeks
   b. If Greater than or equal to 30 kg: 40 mg SC every 2 weeks

Requests for higher doses will be considered on a case-by-case basis.

Duration of Approval of Initials and Renewals: 1 Year

SPASTICITY TREATMENTS

Tizanidine
Brand(s): Zanaflex
DOSAGE FORM/ STRENGTH: 4 mg tablet

For the treatment of spasticity in patients who have failed and/or cannot tolerate at least two of the following available alternatives: baclofen, diazepam and dantrolene.

- Submission must describe the intolerance experienced.

Duration of Approval: Lifetime

URINARY ANTISPASMODICS

Oxybutynin Transdermal System
Brand(s): Oxytrol
DOSAGE FORM/ STRENGTH: 36 mg transdermal patch (3.9 mg/day system)

The treatment of urinary frequency, urgency or urge incontinence in patients who are unable to take oral treatments (e.g. inability to swallow or who are unable to absorb (e.g. short gut syndrome).

Adverse effects to oral therapy (e.g. dizziness) are not acceptable.

Duration of Approval: 5 Years

EXCEPTIONAL ACCESS PROGRAM

TELEPHONE REQUEST SERVICE (TRS)

REIMBURSEMENT CRITERIA FOR SELECTED TRS DRUGS

INTRODUCTION

The Ontario Public Drug Programs has developed these reimbursement criteria to provide physicians with information about selected drug products that may be considered for funding through the Exceptional Access Program's Telephone Request Service (TRS). The TRS offers prescribers (i.e. physicians and nurse practitioners) another way to submit EAP requests for a group of selected drugs. This document provides a list of the drugs and their funding criteria that are considered through the TRS. In most cases, the request will be assessed during the call and a funding decision provided to the caller by the end of the call. In general, approvals will be processed within one business day turnaround.

Prescribers (or their delegates) are encouraged to review the reimbursement criteria for the drug being requested before calling the service to ensure that all of the necessary information is available during the call. Callers who wish to submit a request for drug products and indications not currently available through TRS will be asked to fax the request to EAP. If your request is approved, the prescriber will receive a response letter notifying him/her of the funding decision.

The EAP response letter will list the specific drug, drug identification number (DIN) or product identification number (PIN), strength and dosage form that is considered for funding. Prescribers and pharmacists are responsible to ensure that funded products are provided to avoid unnecessary out-of-pocket costs to the patient. Note that not all generic brands are funded or interchangeable (on-formulary or off-formulary). You can also refer to the formulary for a list of the most updated interchangeable drugs products.

The Ministry reserves the right to change the list of drug products at its sole discretion. If you have any questions or concerns regarding the TRS, please contact us at:

Exceptional Access Program – Telephone Request Service 3rd Floor, 5700 Yonge St. North York, ON M2M 4K5 Phone: 1-866-811-9893 or 416-327-8109 Fax: 1-866-811-9908 or 416-327-7526

E-mail: EAPFeedbackLine@ontario.ca

Anti-Infectives

Cefazolin
Brand(s): Many Generic Brands
DOSAGE FORM/ STRENGTH: 1 g/vial Injection

For treatment of infections susceptible to cefazolin.

Standard Approval Duration: As requested up to 5 years

Daptomycin
Brand(s): Cubicin RF, daptomycin generics (refer to formulary for funded drugs)
DOSAGE FORM/ STRENGTH: 500 mg/10mL injection
Effective date: October 11, 2011 Updated October 21, 2014; July 30, 2021 (VRE)

For the treatment of patients with one or more of the following condition(s):

1. Osteomyelitis caused by methicillin-resistant staphylococcus aureus (MRSA)
2. Device-related osteoarticular or prosthetic joint infections caused by methicillin resistant staphylococcus aureus (MRSA);
3. Diabetic foot infections caused by methicillin-resistant staphylococcus aureus (MRSA);AND/OR
4. Staphyloccoccus aureus bloodstream (SAB) infection including right-sided Staphylococcus aureus infective endocarditis (SARIE) infection caused by methicillin-resistant Staphylococcus aureus (MRSA)

Additionally, the patient must have failed to adequately respond to, be intolerant* to, or have a contraindication to vancomycin.

*Requests involving red-man-syndrome with vancomycin must provide details of the intolerance including the rate of infusion and the use of antihistamines and other histamine blockers prior to therapy.

Standard Approval Duration: Up to maximum of 56 days

Exclusion Criteria: Daptomycin is not funded for patients with:
a) MRSA-related pneumonia;
b) skin/skin structure infections other than diabetic foot infections caused by MRSA.

Daptomycin

Brand(s): Cubicin RF, generic daptomycin (refer to the formulary for funded list)
DOSAGE FORM/ STRENGTH: 500 mg/10 mL powder for injection

For the treatment of invasive infections[1] caused by vancomycin-resistant enterococcus (VRE) in patients who meet the following criteria:

1. VRE infection is confirmed by blood or tissue culture and sensitivity report
2. Patient is unable to use linezolid as a result of at least ONE of the following reasons:
   i) has developed resistance to linezolid as confirmed by the microbiology sensitivity report
   ii) has experienced intolerance[2] to linezolid (for example: severe gastric symptoms, myelosuppression, peripheral neuropathy requiring medical intervention, lactic acidosis)
   iii) has a contraindication[2] to linezolid

   OR

   Prescribed by an infectious disease expert for a patient who is able to use linezolid but where the bacteriostatic effect of linezolid may not be deemed to be clinically optimal due to other patient factors or comorbidities (e.g., immunocompromised, neutropenic).

[1] Not approved for colonization (e.g., nares, skin, stool)

[2] Intolerances and contraindications to linezolid must be fully described in the EAP application.

Recommended dose: 8 to 12 mg/kg daily for VRE with adjustments based on renal function

Duration of approval:

Note that the below are examples of durations for reimbursement of some common VRE infections. This is not an all-inclusive list.

Urinary tract infections: up to 10 days

Bacteremia: up to 14 days

Endocarditis: up to 6 weeks

Osteomyelitis: up to 8 weeks

Requests for longer durations of funding will be considered case-by-case through external review and must be accompanied by a recent microbiology sensitivity report to confirm sensitivity to daptomycin.

Fidaxomicin
Brand(s): Dificid
DOSAGE FORM/ STRENGTH: 200 mg tablet
Effective date: December 16, 2013

For the treatment of Clostridium difficile infection (CDI) in patients who meet the EAP criteria for vancomycin use, but where the patient:

- has experienced a third or subsequent episode within 6 months of treatment with vancomycin for prior episode(s), with no previous trial of fidaxomicin; OR
- has experienced treatment failure* with oral vancomycin for the current CDI episode; OR
- has had a documented allergy (immune-mediated reaction) to oral vancomycin; OR
- has experienced a severe adverse reaction or intolerance** to oral vancomycin treatment that resulted in the discontinuation of vancomycin therapy.

**Treatment failure is defined as 7 days of vancomycin therapy without acceptable clinical improvement.*

***Details of severe adverse reaction or intolerance must be provided and should be clinically related to oral administration of vancomycin.*

Re-treatment criteria:

- Re-treatment with fidaxomicin will only be considered for an early relapse occurring within 30 days of the completion of the most recent fidaxomicin course.
- Relapse/ recurrence occurring beyond 30 days after the completion of the most recent fidaxomicin course will require a trial with vancomycin, unless there is a documented allergy, severe adverse reaction or intolerance to prior oral vancomycin use.

Note: Fecal biotherapy ("stool transplantation"), if available, should be encouraged for this patient population.

Approved dose and duration: 200 mg twice a day for 10 days

Gentamycin
Brand(s): Many Generic Brands
DOSAGE FORM/ STRENGTH: 40 mg/mL injection

For treatment of infections susceptible to gentamycin.

Standard Approval Duration: As requested up to 5 years

Posaconazole
Brand(s): Posanol
DOSAGE FORM/ STRENGTH: 40 mg/mL Suspension, 100 mg tablets

1. For the prophylaxis of Aspergillus and Candida infections in patients who have recently (within the past 3 months) undergone an allogeneic bone marrow transplant.

2. For the prophylaxis of invasive fungal infections in patients who have previously (3 months or longer) undergone an allogeneic stem cell transplant and are experiencing moderate to severe graft-versus-host-disease (GVHD) will be considered on a case-by-case basis.

   Renewals will be considered on a case-by-case basis for patients who continue to experience ongoing symptoms of moderate to severe GVHD. Please provide information regarding infections that were experienced while on therapy (as applicable) including the names of medications and treatments being used to manage GVHD.

3. For the treatment of invasive aspergillosis* in patients who are refractory or intolerant to voriconazole OR who have documented contraindication to voriconazole.

   *Invasive aspergillosis should be confirmed by fungal culture.

   Note: Requests without a positive fungal culture must be accompanied by a consultation note from an infectious disease expert with details of how the diagnosis was made and will be considered on a case-by-case basis.

   Renewals will be considered on a case-by-case basis.

4. For the treatment of mucormycosis** in patients who have failed, have a contraindication to, or experienced intolerance to amphotericin B; OR

   For the step-down treatment of mucormycosis** in patients who have been initially treated with amphotericin B but cannot tolerate long-term therapy with this agent.

   **Mucormycosis infection must be confirmed by fungal culture.

Note: Requests without a positive fungal culture but where the diagnosis of mucormycosis is documented by an infectious diseases consult and other tools (e.g, radiology reports, histopathology, etc.) will be considered on a case-by-case basis.

Renewals will be considered for patients who are responding to therapy but who have not experienced clinical resolution of their condition. Note that requests for renewal must be accompanied by supporting clinical information (Infectious disease consultation/ radiology report).

Chronic Renal Failure Drugs

Calcium Carbonate
Brand(s): Tums
DOSAGE FORM/ STRENGTH: 500 mg, 750 mg, 1000 mg

For patients with hypoparathyroid disease or chronic renal failure.

NOTE: Calcium supplements for patients who do not have hypoparathyroid disease or chronic renal failure are not eligible for funding consideration by the ODB program, which includes EAP.

Renewals will be considered where patient is stable.

Standard Approval Duration: 5 years for initials and renewals

Lanthanum
Brand(s): Fosrenol and Generics
DOSAGE FORM/ STRENGTH: 250 mg, 500 mg, 750 mg, 1000 mg Chewable tablet

Sevelamer Hydrochloride
Brand(s): Renagel
DOSAGE FORM/ STRENGTH: 800 mg tablet

Sevelamer Carbonate
Brand(s): Accel-Sevelamer
DOSAGE FORM/ STRENGTH: 800 mg tablet

Sevelamer Carbonate
Brand(s): Renvela
DOSAGE FORM/ STRENGTH: 800 mg tablet, 0.8 g powder sachet, 2.4 g powder sachet
Updated: June 7, 2021

i) For the treatment of hyperphosphatemia associated with end-stage renal disease (ESRD) where patients are on dialysis and have a sustained serum phosphate > 1.8 mmol/L AND adjusted serum calcium > 2.65 mmol/L; OR

ii) For dialysis patients experiencing hyperphosphatemia (sustained serum phosphate levels >1.8 mmol/L) who have calciphylaxis and/or evidence of coronary artery calcification.

Notes:

1. Calcium and phosphate levels provided to demonstrate sustained elevations should be at least 4 weeks apart.

2. Patients who demonstrate reduction of phosphate levels while on a calcium binder but who experience adjusted serum calcium > 2.65 mmol/L must provide supporting laboratory levels before treatment and while on treatment and should include the dose(s) of calcium-based binder used.

Exclusion Criteria:
Sevelamer will not be reimbursed in the following cases:
Use in combination therapy with another funded non-calcium-based phosphate binder (e.g. lanthanum carbonate hydrate, sucroferric oxyhydroxide, other sevelamer formulations)

Duration of approval: lifetime

On a case-by-case basis, requests may be considered for sevelamer under the EAP for a patient with serum phosphate less than 1.8mmol/L and calcium values less than 2.65 mmol/L.

Sucroferric Oxyhydroxide
Brand(s): Velphoro
DOSAGE FORM/ STRENGTH: 500 mg iron per chewable tab

For the treatment of hyperphosphatemia associated with end-stage renal disease (ESRD) where patients are on dialysis and have a sustained[1] serum phosphate > 1.8 mmol/L AND serum calcium > 2.65 mmol/L; OR

For dialysis patients experiencing hyperphosphatemia (sustained serum phosphate levels >1.8 mmol/L) who have calciphylaxis and/or evidence of coronary artery calcification.

Note: Dialysis patients with hyperphosphatemia meeting the above criteria who are experiencing other types of calcification (e.g. aortic) in the absence of coronary artery calcification may be considered case-by-case by faxing your request to the EAP.

Calcium and phosphate levels provided to demonstrate sustained elevations should be at least 4 weeks apart.

Exclusion criteria:

Patients with haemochromatosis or any other iron accumulation disorders.

Duration of Approval: Lifetime

Vitamin B Complex with Vitamin C

Brand(s): Replavite plus Generics

DOSAGE FORM/ STRENGTH:

For patients receiving hemodialysis or peritoneal dialysis.

Standard Approval Duration: 5 years

Anticoagulants

NOTE:

Enoxaparin biosimilars are general benefits on the Ontario drug benefit formulary and do not require EAP approval.

Other Low Molecular Weight Heparins (LMWHs) (e.g. dalteparin, tinzaparin, fraxiparine) are currently listed on the ODB Formulary as Limited Use (LU) benefits for the treatment of deep venous thrombosis (DVT) and pulmonary embolism (PE) in certain patient groups. Please consult the Formulary for further details.

Dalteparin

Brand(s): Fragmin
DOSAGE FORM/ STRENGTH: Check e-formulary for funded strengths

1. For **peri-operative bridging** for patients who require long-term warfarin therapy and must temporarily discontinue it before and after surgery, and who are at moderate- to high-risk for an embolic event while off warfarin.

   Standard Approval Duration: As requested up to a maximum of **10 days** before the date of surgery **plus up to 7 days** after the date of hospital discharge

2. For **post-operative prophylaxis of DVT** for patients who had hip or knee surgery and cannot use warfarin.

   Standard Approval Duration: As requested up to a maximum of **30 days** starting on the day of surgery

3. For the **post-operative prophylaxis of venous thromboembolism following abdominal or pelvic surgery for cancer** in patients who do not have a history of or risk factors for heparin-induced thrombocytopenia.

   Standard Approval Duration: Maximum of 30 days.

4. **For extended treatment of symptomatic acute venous thromboembolism (VTE)** in patients with cancer, who cannot use warfarin.

   Standard Approval Duration: As requested up to 6 months

Tinzaparin

Brand(s): Innohep

DOSAGE FORM/ STRENGTH: 2,500 IU, 3,500 IU, 4,500 IU, 8,000 IU, 10,000 IU, 12,000 IU, 14,000 IU, 16,000 IU, 18,000 IU, 20,000 IU Injection

1. For **peri-operative bridging** for patients who require long-term warfarin therapy and must temporarily discontinue it before and after surgery, and who are at moderate- to high-risk for an embolic event while off warfarin.

   Standard Approval Duration: As requested up to a maximum of **10 days** before the date of surgery **plus up to 7 days** after the date of hospital discharge

2. For **post-operative prophylaxis of DVT** for patients who had hip or knee surgery and cannot use warfarin.

   Standard Approval Duration: As requested up to a maximum of **30 days** starting on the day of surgery

3. For the **post-operative prophylaxis of venous thromboembolism following abdominal or pelvic surgery for cancer** in patients who do not have a history of or risk factors for heparin-induced thrombocytopenia.

   Standard Approval Duration: Maximum of 30 days.

Oral Hypoglycemic Agents

Note: Prescribers do not need to make an EAP request for patients currently receiving pioglitazone or rosiglitazone through ODB. Physicians will be required to make an application for coverage for any patient new to ODB that is being started on either of these drugs or any ODB recipient who is new to using these drugs.

Requests for ongoing treatment with pioglitazone or rosiglitazone for patients who were previously covered by other means may be considered according to renewal criteria.

Funding under the EAP for pioglitazone or rosiglitazone will not be provided in the following clinical settings:

- Patients with type 1 diabetes
- Monotherapy, even if patient is intolerant or has contraindications to both metformin and sulfonlyureas
- Combination use with either nitrates or insulin
- Patients with any stage of heart failure (NYHA Class I, II, III, IV)
- Patients at high risk for bone fracture (post-menopausal women with previously confirmed osteoporosis or osteopenia)
- Patients with recent history (in the past 3 months) of ischemic cardiovascular event (myocardial infarction, unstable angina)
- Patients with active bladder cancer, a history of bladder cancer or uninvestigated macroscopic haematuria

Pioglitazone

Brand(s): Generics
DOSAGE FORM/ STRENGTH: 15 mg, 30 mg, 45 mg tablet

For dual combination therapy of type 2 diabetes, in patients with:

a) Inadequate glycemic control (HbA1c of >7%) on maximal doses of metformin (2000 mg/day); OR

b) Inadequate glycemic control, on maximal doses of sulfonylurea (glyburide 10mg/day, gliclazide 160mg/day or gliclazide modified release (MR) 60 mg/day) or glimepiride 4 mg/day and demonstrated intolerance / contraindication to metformin

For triple combination therapy of type 2 diabetes, in patients with:

a) Inadequate glycemic control on maximal doses of metformin and a sulfonylurea AND only if:

- physician has offered insulin as alternative option first, and patient has refused or is not able to take insulin, AND both physician and patient are aware that thiazolidinediones are not indicated for use in triple therapy.

Standard Approval Duration: 5 years

Pioglitazone
Brand(s): Generics
DOSAGE FORM/ STRENGTH: 15mg, 30 mg, 45 mg tablet

Renewals: EAP will renew pioglitazone only for patients who have achieved adequate glycemic control (HbA1c of ≤ 7% while on therapy and who have no known contraindications to pioglitazone.

Standard Approval Duration: 5 years

Rosiglitazone
Brand(s): Avandia
DOSAGE FORM/ STRENGTH: 2 mg, 4 mg, 8 mg tablet

For the treatment of type 2 diabetes mellitus in patients with:

- Inadequate glycemic control (HbA1c >7%) from ALL other oral antidiabetic agents* funded through one of the Ontario Drug Benefit (ODB) Programs, in monotherapy or in combination OR
- Where ALL other oral antidiabetic agents are inappropriate due to contraindications or intolerance AND
- The patient has refused or is not able to take insulin AND
- There is no known contraindication to rosiglitazone.

* Oral antidiabetics that need to be tried prior to consideration of rosiglitazone include the following agents currently reimbursed through the Ontario Public Drug Programs;

- glyburide
- metformin
- gliclazide (Diamicron, Diamicron MR)
- sitagliptin (Januvia)
- repaglinide (GlucoNorm)
- pioglitazone (Actos)
- saxagliptin (Onglyza)

Note: A trial with acarbose is not a mandatory requirement.

Note: It is not necessary for patients to have tried the following oral antidiabetic agents that are currently not funded by the Ontario Public Drug Programs for the purposes of obtaining rosiglitazone:

Standard Approval Duration: 5 years

Rosiglitazone
Brand(s): Avandia
DOSAGE FORM/ STRENGTH: 1 mg, 4 mg, 8 mg tablet

Renewals will be considered where patients have benefited and continue to benefit from rosiglitazone treatment as demonstrated by achieving adequate glycemic control. This is shown by a recent HbA1c levels ≤7% while on treatment with rosiglitazone AND in who continue to have no known contraindication(s) to rosiglitazone.

Standard Approval Duration: 5 years

Palliative Care Medications

NOTE: Specific products used to treat ODB-eligible patients undergoing palliative care are reimbursed under the Ontario Public Drug Programs, as Limited use benefits on the ODB formulary or through the Facilitated Access process. Under this process, a select group of participating physicians and nurse practitioners are exempt from obtaining approval under EAP on a case-by-case basis. This assumes that the prescriber has met the qualifications set by their professional associations who administer the enrollment of their members. The prescriber's license number with their regulatory body must appear on the prescription, for purposes of verification.

Palliative Care medication claims to be reimbursed by the ODB program must be prescribed in accordance with the following patient eligibility criteria: "This patient has a progressive, life-limiting illness and has chosen outpatient palliative treatment. Life expectancy of one year is applied to request durations.

In order to participate in the Facilitated Access to Palliative Care Drugs process, these prescribers must be registered with their professional association as meeting the qualifications for pCFA enrollement.. For physicians this is by the Ontario Medical Association ("OMA") and must meet pre-defined criteria the OMA sets. For nurse practitioners, this may be the NPAO or the Nurse practitioners Association of Ontario (NPAO) or the RNAO, th Registered Nurse Association of Ontario. To facilitate the reimbursement process at the pharmacy, these prescribers are asked to indicate either, "Palliative" or "P.C.F.A." on the prescription.

Prescribers who are not registered through this process must obtain approval through the Exceptional Access Program. A prescriber must provide the details of the patient's diagnosis, current clinical status, and life expectancy.

For further information regarding the list of physicians and/or the criteria physicians require to be included on the list, please contact the Ontario Medical Association: (416) 340-2234, or via email. The following products can be reimbursed for the management of patients receiving palliative care through the Telephone Request Service. Note that many Palliative Care drugs have tranoptsitioned to the ODB formulary for funding under Limited Use and do not require EAP authorization.

Methadone
Brand(s): Metadol
DOSAGE FORM/ STRENGTH: 1 mg/mL oral liquid, 10 mg/mL oral liquid, 1 mg, 5 mg, 10 mg 25 mg

If traditional narcotic analgesics fail to control pain or lead to side effects.

Standard Approval Duration: 12 months

Morphine
Brand(s): Doloral 1, Doloral 5 (TEMPORARY BENEFIT)
DOSAGE FORM/ STRENGTH: 1 mg/mL oral liquid, 5 mg/mL oral liquid

For use in a palliative patient requiring oral liquid morphine. Doloral oral liquid products are interim/temporary listing authorized by the Executive Officer as oral liquid morphine products on the formulary were withdrawn from the market by the manufacturer.

Oxycodone
Brand(s): Supeudol
DOSAGE FORM/ STRENGTH:5 mg, 10 mg, 20 mg

For use when palliative patient cannot use combination oxycodone and acetaminophen.

Standard Approval Duration: 12 months

Oxycodone HCl Controlled Release
Brand(s): OxyNEO
DOSAGE FORM/ STRENGTH:10 mg, 15 mg, 20 mg, 30 mg, 40 mg tablets

For the treatment of cancer-related pain or pain in patients receiving end-of-life palliative care AND the patient has experienced intolerance or has failed an adequate trial (for example, three months) of at least one other listed long-acting opioid product.

Standard Approval Duration: 12 months

Pamidronate
Brand(s): Many Generics
DOSAGE FORM/ STRENGTH: 3 mg/mL, 6 mg/mL, 9 mg/mL

For the treatment of tumor-induced/malignancy-related hypercalcemia in a palliative care patient.

Standard Approval Duration: 12 months

High Dose Opioids

Effective January 31, 2017, meperidine 50mg tabs and the higher strengths of long-acting opioids including: morphine SR 200mg tabs; hydromorphone CR 24mg and 30 mg caps and fentanyl 75mcg/hr and 100mcg/hr patches were delisted from the ODB Formulary.

Access to the higher strengths of long-acting opioids is currently maintained for patients requiring palliative care through the ODB program's:

1. Palliative Care Facilitated Access (PCFA) mechanism, for prescribers (physicians or nurse practitioners) who are registered PCFA prescribers with their professional associations; AND

2. Exceptional Access Program (EAP) Telephone Request Service (TRS) for physicians who are not PCFA prescribers, according to specific criteria**.**

    i) Use of the high-strength opioid must be for a patient considered to have a progressive life-limiting illness requiring palliative care.
    ii) The use of the high-strength opioid can be for pain or for symptom management.
    iii) Prescriber must have a consult from a PCFA-registered prescriber with OMA; CPSO of the PCFA-registered prescriber or NPAO or RNAO; license numbers must be provided.

Standard Approval Duration: 12 months

Renewals are considered with same criteria as above. A new consult from a PCFA-registered prescriber must be provided for each renewal.

Post-transplant Drugs

Sirolimus

Brand(s): Rapamune
DOSAGE FORM/ STRENGTH: 1 mg tablet, 1 mg/mL oral liquid

For liver transplant recipients who require regimens that mandate calcineurin inhibitor avoidance. The physician must be able to explain clearly why the patient cannot use a calcineurin inhibitor.

NOTE: Rapamune is currently listed on the ODB Formulary as a Limited Use (LU) benefit for the prophylaxis of organ rejection in patients receiving allogeneic renal transplants.

Valganciclovir
Brand(s): Valcyte
DOSAGE FORM/ STRENGTH: 450 mg tablet, 50 mg/mL oral solution

For the treatment of cytomegalovirus (CMV) disease following solid organ and/or bone marrow transplant in patients who meet the following criteria:

1. Objective evidence of active CMV infection determined by any one of the following methods:
    - CMV antigenemia assay;OR
    - CMV polymerase chain reaction (PCR); OR
    - bDNA assay; OR
    - Tissue biopsy with pathological changes showing intra-nuclear inclusion bodies compatible with CMV infection (i.e. Owl's eye)
    - Primary Infection - positive CMV IgM antibodies; OR
    - Reactivation - Positive CMV IgM antibodies with four-fold or greater increase in CMV IgG antibodies
2. Consolidation phase of treatment (maintenance phase post-induction with IV ganciclovir)

Standard Approval Duration: 3 to 6 months

Renewals will be considered for patients who continue to have active CMV infection. Renewal requests not meeting the criteria will be considered on a case-by-case basis but the physician must submit a rationale of why ongoing treatment is necessary.

Standard Approval Duration: 3 months

For prophylaxis (prevention) of Epstein-Barr Virus (EBV) infection in EBV D+/R- transplant recipients.

Standard Approval Duration: 6 months

Valganciclovir
Brand(s): Valcyte
DOSAGE FORM/ STRENGTH: 450 mg tablet, 50 mg/mL oral solution

For treatment of Epstein-Barr Virus (EBV) infection in transplant patients according to the following criteria:

1. Confirmed via biopsy (rare EBV positive cells present); OR

2. Objective evidence of active EBV infection (Patient must have one of the three below):

    - Newly positive or rising EBV PCR; OR
    - Reactivation: Positive anti-VCA IgM antibodies with a four-fold or greater increase in anti-VCA IgG antibodies; OR
    - Presence of EBV DNA or protein in pathologic tissue

Standard Approval Duration: 3 months

Notes:

Valganciclovir oral solution is considered for patients who meet the above requirements but who cannot swallow tablets or cannot use the tablets to achieve the planned dosing regimen.

Renewals for patients showing continued active infection with EBV PCR may be considered on a case-by-case basis by submitting the request to the EAP.

Requests for valganciclovir not meeting the above criteria or the Limited Use criteria on the formulary will be considered on a case-by-case basis but the prescriber must submit the request to the EAP.

Valganciclovir

Brand(s): Valcyte

DOSAGE FORM/ STRENGTH: 450 mg tablet, 50 mg/mL oral solution

Approvals will be provided for the treatment of moderate to severe symptomatic congenital CMV (cCMV) in newborns who meet the following criteria:

- Prescribed by or in consultation with a pediatric ID specialist (from one of the 5 treatment centres in Ontario: London, Hamilton, Toronto, Kingston, Ottawa; or Winnipeg for the NorthWestern region of Ontario)
- Confirmed diagnosis of cCMV within the first 3 weeks[1] of birth by:
  - PCR (urine, saliva or quantitative serum CMV); OR
  - Positive culture results (urine or saliva)
- Treatment to start within one month of birth[2]
- Evidence of one or more of the following symptoms:
  - CNS disease (e.g., seizures, microcephaly, imaging abnormalities associated with CMV)
  - Eye disease (e.g., chorioretinitis)
  - Severe life-threatening organ dysfunction (must be described)[3]
- Regular monitoring of labs for toxicity while on therapy

Approval Duration: maximum 6 months at 16mg/kg/dose BID (with dose adjustments in renal dysfunction, < 32 weeks gestational age, etc.)

Renewals: No extensions will be provided unless extenuating circumstances for severely affected infants. Case-by-case review with rationale for continued treatment (must include pediatric ID specialist consult note)

Valganciclovir oral liquid will be approved for newborns.

All other requests not meeting the above criteria will be reviewed on a case-by-case basis including:

- Initiation of treatment after one month of age[2]
- Evidence of sensorineural hearing loss (SNHL) only (i.e., no other symptom described above)
- Isolated/multiple findings of mild symptoms such as: intrauterine growth retardation (IUGR), thrombocytopenia, elevated liver enzymes, jaundice, hepatitis

Sufficient rationale including consult from pediatric ID specialist must be provided before sending for external review.

Renewals of HIV Drugs

Enfuvirtide
Brand(s): Fuzeon
DOSAGE FORM/ STRENGTH: 108 mg/vial Injection

Initial approvals require case-by-case review through the EAP upon receiving sufficient clinical information for an external review by a medical expert.

EAP will renew for patients who have responded to therapy and have undetectable viral load or increasing / stable CD4 count.

Standard Approval Duration: 6 months

Tipranavir
Brand(s): Aptivus
DOSAGE FORM/ STRENGTH: 250 mg capsules

Initial approvals require case-by-case review through the EAP upon receiving sufficient clinical information.

EAP will renew for patients who have responded to therapy and have undetectable viral load or increasing / stable CD4 count.

Standard Approval Duration: 12 months

Renewals of Multiple Sclerosis Drugs

Dimethyl Fumarate
Brand(s): Tecfidera
DOSAGE FORM/ STRENGTH: 120mg and 240 mg capsule

EAP will renew coverage of dimethyl fumarate for patients who are stable and experienced no more than one disabling attack/relapse in the past year and have an EDSS score less than or equal to 5.

Prescriber must provide the following information:

- Description of the patient's clinical course in the last year, including details of all attacks;
- Date and details of the most recent neurological examination (within the last 90 days); and
- EDSS score

Dosage: 120 mg twice daily
Maintenance: 240 mg twice daily

Standard Approval Duration: 2 years for first renewal, 5 years for 2nd and subsequent renewals

Fingolimod
Brand(s): Gilenya and generics
DOSAGE FORM/ STRENGTH: 0.5 mg Capsule

EAP will renew coverage of Fingolimod for patients with RRMS who are stable and experienced no more than one disabling attack/relapse in the past year and have an EDSS score less than or equal to 5.5.

Prescriber must provide the following information:

- Description of the patient's clinical course in the last year, including details of all attacks;
- Date and details of the most recent neurological examination (within the last 90 days); and
- EDSS score

Standard Approval Duration: 2 years for first renewal, 5 years for 2nd and subsequent renewals

Renewal requests where patients have experienced more than 1 attack in the past year will be externally reviewed.

Interferon beta-1a

Brand(s): Avonex, Rebif
DOSAGE FORM/ STRENGTH: (Avonex) 30 mcg/0.5 mL prefilled syringe, 30 mcgs prefilled autoinjector; (Rebif) 22 mcg and 44 mcg syringe injection, 66 mcg and 132 mcg prefilled cartridge

In RRMS/CDMS and CIS:

EAP will renew coverage of Interferon beta-1a only for patients who have benefited from therapy and have an EDSS score ≤ 6.

The physician must provide the following information:

- Description of the patient's clinical course in the last year, including details of all attacks;
- Date and details of the most recent neurological examination (within the last 90 days); and
- EDSS score

Standard Approval Duration: 2 years for first renewal, 5 years for 2nd and subsequent renewals

Renewal requests where patients have experienced more than 1 attack in the past year will be externally reviewed.

Interferon beta-1b

Brand(s): Betaseron, Extavia
DOSAGE FORM/ STRENGTH: Betaseron 9.6 MIU = 0.3mg inj
Extavia 0.3 mg vial injection

IN RRMS/CDMS and CIS:

EAP will renew coverage of Interferon beta-1b only for patients who have benefited from therapy and have an EDSS score ≤ 6.

The prescriber must provide the following information:

- Description of the patient's clinical course in the last year, including details of all attacks;
- Date and details of the most recent neurological examination (within the last 90 days); and
- EDSS score

Standard Approval Duration: 2 years for first renewal, 5 years for 2nd and subsequent renewals

Renewal requests where patients have experienced more than 1 attack in the past year will be externally reviewed.

Natalizumab
Brand(s): Tysabri
DOSAGE FORM/ STRENGTH: 300 mg/15 mL

EAP will renew coverage of Natalizumab for patients with RRMS who have benefited from therapy and have an EDSS score less than or equal to 5.

The physician must provide the following information:

- Description of the patient's clinical course in the last year, including details of all attacks;
- Date and details of the most recent neurological examination (within the last 90 days); and
- EDSS score

Standard Approval Duration: 2 years

Standard Approval Duration: 2 years for first renewal, 5 years for 2nd and subsequent renewals

Renewal requests where patients have experienced more than 1 attack in the past year will be externally reviewed.

Ocrelizumab
Brand(s): Ocrevus
DOSAGE FORM/ STRENGTH: 14mg tablet

EAP will renew coverage of ocrelizumab for patients with Relapsed Refractory Multiple Sclerosis (RRMS) who are stable and experienced no more than one disabling attack/relapse in the past year and have an EDSS score less than or equal to 6.5.

Prescriber must provide the following information:

- Description of the patient's clinical course in the last year, including details of all attacks;
- Date and details of the most recent neurological examination (within the last 90 days); and
- EDSS score

Exclusion criteria:

1. Combination therapy with another disease modifying therapy for RRMS will not be reimbursed.

2. Patients with an EDSS score equal to or greater than 7.0

Standard Approval Duration: 18 months

Renewal requests where patients have experienced more than 1 attack in the past year will be externally reviewed.

EAP will renew coverage of ocrelizumab for patients with Primary Progressive Multiple Sclerosis (PPMS) who continue to benefit from treatment and who have an Expanded Disability Status Scale (EDSS) score less than 7.0

Prescriber must provide the following information:

- Description of the patient's clinical status in the past year
- Date and details of the most recent neurological examination; and
- EDSS score

Exclusion Criteria:

Patients with an EDSS score equal to or greater than 7.0

Dosage: Initial dose of 300 mg intravenous infusion, followed 2 weeks later by a second 300 mg intravenous infusion. Subsequent doses of single 600 mg intravenous infusion every 6 months after the first initial dose.

Standard Approval Duration: 18 months

Ofatumumab
Brand(s): Kesimpta
DOSAGE FORM/ STRENGTH: 20 mg/0.4 mL prefilled pen

EAP will renew coverage of ofatumumab for patients with Relapsed Refractory Multiple Sclerosis (RRMS) who are stable and experienced no more than one disabling attack/relapse in the past year and have an EDSS score less than or equal to 7.0.

Prescriber must provide the following information:

- Description of the patient's clinical course in the last year, including details of all attacks;
- Date and details of the most recent neurological examination (within the last 90 days); and
- EDSS score
- Confirmation that patient is stable/not demonstrating a sub-optimal response

Exclusion criteria:

1. Combination therapy with another disease modifying therapy for RRMS will not be reimbursed.

2. Patients with an EDSS score equal to or greater than 7.0

Standard Approval Duration: 12 months

Renewal requests where patients have experienced more than 1 attack in the past year will be externally reviewed.

Peginterferon beta-1a
Brand(s): Plegridy
DOSAGE FORM/ STRENGTH: 125mcg/0.5mL, 94mcg/0.5mL Injection, Starter Pack: 63mcg/0.5mL, 94mcg/0.5mL

EAP will renew coverage of peginterferon beta-1a only for patients who have benefited from therapy and have an EDSS score ≤ 6.

The prescriber must provide the following information:

- Description of the patient's clinical course in the last year, including details of all attacks;
- Date and details of the most recent neurological examination (within the last 90 days); and
- EDSS score

Standard Approval Duration: 2 years, 5 years for 2nd and subsequent renewals

Renewals

Renewal requests where patients have experienced more than 1 attack in the past year will be externally reviewed.