Frequently Asked Questions: Ustekinumab

1. **What is the difference between Jamteki™ (ustekinumab injection), Wezlana™/Wezlana™ I.V. (ustekinumab injection/ustekinumab for injection) and Stelara®/Stelara® I.V. (ustekinumab injection/ustekinumab for injection)?**
   Jamteki™ (ustekinumab injection), Wezlana™/Wezlana™ I.V. (ustekinumab injection/ustekinumab for injection) and Stelara®/Stelara® I.V. (ustekinumab injection/ustekinumab for injection) are all ustekinumab products. Ustekinumab is an anti-inflammatory medicine that belongs to the class of drugs called biological response modifiers. Jamteki™ and Wezlana™ have been approved by Health Canada as biosimilar versions of Stelara®, and Wezlana™ I.V. has been approved by Health Canada as a biosimilar version of Stelara® I.V. Jamteki™, Wezlana™/Wezlana™ IV, and Stelara®/Stelara® I.V. are manufactured and marketed by different companies.

2. **What is the funding status of Jamteki™ (ustekinumab injection) and Wezlana™/Wezlana™ I.V. (ustekinumab injection/ustekinumab for injection)?**

   Effective as of the April 2024 update to the Ontario Drug Benefit Formulary/Comparative Drug Index (Formulary), Jamteki™ and Wezlana™/Wezlana™ I.V. will be listed on the Formulary as Limited Use (LU) benefits for certain indications, as follows:
   - Jamteki™: plaque psoriasis and psoriatic arthritis
   - Wezlana™: plaque psoriasis, psoriatic arthritis, ulcerative colitis, and Crohn's disease
   - Wezlana™ I.V.: ulcerative colitis and Crohn's disease

3. **What are the Limited Use criteria for Jamteki™ (ustekinumab injection) and Wezlana™/Wezlana™ I.V. (ustekinumab injection/ustekinumab for injection)?**

   As of the effective date of the April 2024 update to the Formulary, the LU Codes applicable for each ustekinumab product and the corresponding Clinical Criteria will be as set out below.

   Please refer to the e-Formulary for the most up-to-date information, at:

Formulary / Comparative Drug Index (CDI) Edition 43 | Ontario Drug Benefit (ODB)
Formulary / Comparative Drug Index (CDI) and Monthly Formulary Updates | ontario.ca

Applicable LU Codes by Product:

Jamteki™ - 668, 669

Wezlana™ - 669, 670, 671, 672

Wezlana™ I.V. – 671, 672

A. Plaque Psoriasis (LU Code 668)

For the treatment of severe* plaque psoriasis in patients who have experienced failure, intolerance, or have a contraindication to adequate trials of several standard therapies**.

Claims for the first 6 months must be written by a dermatologist.

Monitoring of patients is required to determine if continuation of therapy beyond 12 weeks is required.

Patients not responding adequately at 12 weeks should have treatment discontinued.

* Definition of severe plaque psoriasis:

Body Surface Area (BSA) involvement of at least 10%, or involvement of the face, hands, feet or genital regions, AND

Psoriasis Area and Severity Index (PASI) score of at least 10 (not required if there is involvement of the face, hands, feet or genital regions), AND

Dermatology Life Quality Index (DLQI) score of at least 10.

** Definition of failure, intolerance or contraindication to adequate trials of standard therapies:

- 6 month trial of at least 3 topical agents including vitamin D analogues and steroids; AND

- 12 week trial of phototherapy (unless not accessible); AND
- 6 month trial of at least 2 systemic, oral agents used alone or in combination

    -Methotrexate 15-30mg per week

    -Acitretin (could have been used with phototherapy)

    -Cyclosporine

Maintenance/Renewal:

After 3 months of therapy, patients who respond to therapy should have:

    - At least a 50% reduction in PASI, AND

- at least a 50% reduction in BSA involvement, AND

- at least a 5 point reduction in DLQI score

Recommended dose:

The recommended dose of ustekinumab is 45 mg administered subcutaneously at weeks 0 and 4, then every 12 weeks thereafter.

Alternatively, 90 mg may be used in patients with a body weight of over 100 kg. In patients weighing over 100 kg, both the 45 mg and 90 mg doses were shown to be efficacious. However, 90 mg was efficacious in a higher percentage of these patients.

For patients who inadequately respond to dosing every 12 weeks, consideration may be given to treating as often as every 8 weeks.

If the patient has not responded after 12 weeks of treatment, the prescriber should consider switching to an alternative biologic agent.

LU authorization period: 1 year

B. Psoriatic Arthritis (LU Code 669)

For the treatment of psoriatic arthritis in patients who have severe active disease (greater than or equal to 5 swollen joints and radiographic evidence of psoriatic arthritis) despite:

i) treatment with methotrexate (20mg/week) for at least 3 months; AND
ii) 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 (20mg/day) or sulfasalazine (1g twice daily) for at least 3 months is required.

Maintenance/Renewal:

After 12 months of treatment, maintenance therapy is funded for patients with objective evidence of at least a 20 percent reduction in swollen joint count and a minimum of improvement in 2 swollen joints over the previous year. For funding beyond the second year, the patient must have objective evidence of preservation of treatment effect.

Therapy must be prescribed by a rheumatologist or a physician with expertise in rheumatology.

The recommended dosing regimen is 45 mg administered subcutaneously at weeks 0 and 4, then every 12 weeks thereafter. Alternatively, 90 mg may be used in patients with a body weight greater than 100 kg.

Ustekinumab may be used alone or in combination with methotrexate (MTX).

LU authorization period: 1 year

C. Plaque Psoriasis (LU Code 670)

For the treatment of severe* plaque psoriasis in patients who have experienced failure, intolerance, or have a contraindication to adequate trials of several standard therapies**.

Claims for the first 6 months must be written by a dermatologist.

Monitoring of patients is required to determine if continuation of therapy beyond 12 weeks is required.

Patients not responding adequately at 12 weeks should have treatment discontinued.

* Definition of severe plaque psoriasis:

Body Surface Area (BSA) involvement of at least 10%, or involvement of the face, hands, feet or genital regions, AND

Psoriasis Area and Severity Index (PASI) score of at least 10 (not required if there is involvement of the face, hands, feet or genital regions), AND

Dermatology Life Quality Index (DLQI) score of at least 10.

** Definition of failure, intolerance or contraindication to adequate trials of standard therapies:

• 6 month trial of at least 3 topical agents including vitamin D analogues and steroids; AND

• 12 week trial of phototherapy (unless not accessible); AND

• 6 month trial of at least 2 systemic, oral agents used alone or in combination

-Methotrexate 15-30mg per week

-Acitretin (could have been used with phototherapy)

-Cyclosporine

Maintenance/Renewal:

After 3 months of therapy, patients who respond to therapy should have:

- At least a 50% reduction in PASI, AND

- at least a 50% reduction in BSA involvement, AND

- at least a 5 point reduction in DLQI score

Recommended dose:

The recommended dose of ustekinumab for adult patients is 45 mg administered subcutaneously at weeks 0 and 4, then every 12 weeks thereafter.

Alternatively, 90 mg may be used in patients with a body weight of over 100 kg. In patients weighing over 100 kg, both the 45 mg and 90 mg doses were shown to be efficacious. However, 90 mg was efficacious in a higher percentage of these patients.

Refer to the appropriate product monograph for dosing in pediatric patients weighing less than 60 kg.

For patients who inadequately respond to dosing every 12 weeks, consideration may be given to treating as often as every 8 weeks.

If the patient has not responded after 12 weeks of treatment, the prescriber should consider switching to an alternative biologic agent.

LU Authorization Period: 1 year

D. Ulcerative Colitis (LU Code 671)

For the treatment of moderate to severe ulcerative colitis in patients who meet the following criteria:

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

B. Failed conventional treatment with a corticosteroid (prednisone 40-60mg/day [or equivalent]) for a minimum of 14 days (or intravenous corticosteroid for 1 week); OR

Responded to/stabilized on conventional treatment with a corticosteroid, with or without an immunosuppressant (e.g., azathioprine, 6-mercaptopurine); OR

Conventional treatment with a corticosteroid is contraindicated; AND

C. Ustekinumab 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.

The recommended induction dosing is a single intravenous (IV) dose based on body weight (for patients less than or equal to 55kg a dose of ustekinumab IV 260mg, for patients greater than 55kg to less than or equal to 85kg a dose of ustekinumab IV 390mg, and for patients greater than 85kg a dose of ustekinumab IV 520mg).

The recommended maintenance dosing regimen is 90mg administered subcutaneously at week 8 following the IV induction dose, followed by subsequent doses every 8 weeks thereafter.

Consideration should be given to discontinuing treatment in patients who show no evidence of therapeutic benefit 16 weeks after the IV induction dose.

Maintenance/Renewal:

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 or discontinuation of corticosteroids.

Prescribers may wish to consider other funded alternatives for patients unable to discontinue corticosteroid therapy.

Exclusion criteria (initial and renewal coverage):

- Combination therapy with another biologic used to treat inflammatory disease will not be funded.

Patients with mild ulcerative colitis (e.g., Mayo score less than 6) may be considered on a case-by-case basis through the Exceptional Access Program.

LU Authorization Period: 1 year

E. Crohn’s Disease (LU Code 672)

For the treatment of moderate to severe (luminal) Crohn's disease in patients who meet the following criteria:

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

B. Failed conventional treatment with a corticosteroid (prednisone 40-60mg/day [or equivalent]) for a minimum of 14 days (or intravenous corticosteroid for 1 week); OR

Responded to/stabilized on conventional treatment with a corticosteroid, with or without an immunosuppressant (e.g., azathioprine, 6-mercaptopurine, methotrexate); OR

Conventional treatment with a corticosteroid is contraindicated; AND

C. Ustekinumab is being used to induce remission or as a steroid-sparing maintenance therapy.

The recommended induction dosing is a single intravenous (IV) dose based on body weight (for patients less than or equal to 55kg a dose of ustekinumab IV 260mg, for patients greater than 55kg to less than or equal to 85kg a dose of ustekinumab IV 390mg, and for patients greater than 85kg a dose of ustekinunab IV 520mg).

The recommended maintenance dosing regimen is 90mg administered subcutaneously at week 8 following the IV induction dose, followed by subsequent doses every 8 weeks thereafter.

Consideration should be given to discontinuing treatment in patients who show no evidence of therapeutic benefit 16 weeks after the IV induction dose.

Maintenance/Renewal:

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.

Exclusion criteria (initial and renewal coverage):

- Combination therapy with another biologic used to treat inflammatory bowel disease will not be funded.

Patients with mild Crohn's disease (e.g., HBI less than 7) may be considered on a case-by-case basis through the Exceptional Access Program.

Patients with fistulising Crohn's disease may be considered on a case-by-case basis through the Exceptional Access Program.

LU Authorization Period: 1 year

4. **What is the rationale for funding biosimilar ustekinumab products?**

Jamteki™ and Wezlana™/Wezlana™ I.V. were approved by Health Canada as biosimilar versions of the originator biologic Stelara®/Stelara® I.V. Biosimilars are not identical to originator biologics. However, Health Canada conducts rigorous testing to ensure that biosimilars have a highly similar structure, are equally as safe, and have the same therapeutic effect as an originator biologic. Biosimilars also present an opportunity to achieve better value for money for biologic drugs that will help to support the long-term sustainability of the Ontario Public Drug Programs.

5. **Will patients whose treatment with Stelara® (ustekinumab) is already funded by the ministry be required to switch to a biosimilar ustekinumab product?**

Stelara® is currently funded as a LU benefit on the Formulary for the treatment of plaque psoriasis only. At this time, patients whose ustekinumab treatment with Stelara® is already funded by the ministry can continue to receive funding for Stelara®.

Ustekinumab is subject to the ministry's biosimilar policy and the transition period for Stelara® for plaque psoriasis will be announced and communicated at a later time.

During the transition period, recipients who are on Stelara® for plaque psoriasis that is being funded under the ODB program will be required to transition to one of the ODB funded biosimilar versions of ustekinumab, in order to maintain publicly funded coverage for ustekinumab.

6. **Will the ministry consider requests for Stelara® (ustekinumab) reimbursement under the Exceptional Access Program (EAP)?**

   Subject to the exception below, the ministry will not accept EAP requests for Stelara®. The ministry did not fund Stelara® for the indications of psoriatic arthritis, Crohn's disease, or ulcerative colitis under the EAP. Patients who require ustekinumab for these indications will be required to use a biosimilar version, even if they are transitioning from another source of funding or access.

   As an exception to the above general rule, the EAP will consider funding Stelara® if the patient has a medically necessary exemption that requires them to use Stelara® instead of a biosimilar version, but only for the indication of plaque psoriasis.

7. **Will the ministry consider EAP requests for Stelara® (ustekinumab) for patients who do not respond to Jamteki™ or Wezlana™/Wezlana™ IV?**

   Patients who do not respond to ustekinumab biosimilars Jamteki™ or Wezlana™/Wezlana™ IV will not be considered for Stelara® for indications that were not routinely funded under the ODB program prior to April 30, 2024. This applies even if a patient has been established on treatment with Stelara® for that indication/condition through another source of funding or access and are transitioning to public funding under the ODB program. Patients who are using ustekinumab for an indication other than plaque psoriasis and who are not able to use a biosimilar version may wish to consider other ODB funded biologic alternatives.

   The EAP will ONLY consider funding of ustekinumab as its originator Stelara® for patients who were established on originator Stelara® for the indication of plaque psoriasis and who meet the ODB LU criteria for ustekinumab for plaque psoriasis and who meet a medical exemption. The medical exemption generally requires the patient to have tried at least two biosimilar versions of ustekinumab and experienced adverse effects to both of them, intolerances, and/or lack of efficacy documented by their prescriber on the Health Canada side effect form for each biosimilar used. The request for a medical exemption with the completed Health Canada side effect forms may be submitted to the EAP for case-by-case review.

8. **Will the ministry consider EAP requests for the ustekinumab biosimilars Jamteki™ or Wezlana™/Wezlana™ IV in patients who do not meet the limited use criteria on the ODB formulary?**

   The EAP may consider requests for funding of biosimilar ustekinumab listed on the ODB formulary in patients who do not meet the LU criteria on the ODB formulary on a case-by-case basis.

9. **How should pharmacies submit claims for Jamteki™ or Wezlana™/Wezlana™ I.V.?**
   Pharmacies should submit claims using the appropriate drug identification number (DIN) of the respective ustekinumab product and the appropriate LU / Reason for Use (RFU) code.

   Jamteki™ and Wezlana™/Wezlana™ I.V. are ustekinumab products approved by Health Canada as biosimilar versions of Stelara®/Stelara® I.V. However, these products are not “interchangeable” – i.e., pharmacists will require a prescription from the prescriber specific to the brand of ustekinumab that they are dispensing with the relevant LU/RFU code provided by the prescriber.

10. **What are biosimilars?**

    Biosimilars, also referred to as subsequent entry biologics or follow-on biologics, are biologics that are highly similar to an originator biologic. Biosimilars may enter the market after the patents and data protection for the originator biologic have expired. Health Canada conducts rigorous testing to ensure that biosimilars have a highly similar structure, are equally as safe, and have the same therapeutic effect as an originator biologic. Ontario is confident in the safety and efficacy of biosimilars based on our experience over the past 7 years, as well as the experiences of many places around the world. The use of biosimilar medicines has been well-established in Europe over the past 20 years of positive experience with more than 50 approved biosimilar medicines. Please refer to Health Canada’s fact sheet on biosimilars for more information:

    Biosimilar biologic drugs in Canada: Fact Sheet - Canada.ca

    Additional information:

For pharmacies: Please call ODB Pharmacy Help Desk at: 1-800-668-6641

For all other health care providers and the public:

Please call ServiceOntario, Infoline at 1-866-532-3161 TTY 1-800-387-5559. In Toronto, TTY 416-327-428