Adalimumab Frequently Asked Questions

1. **What is the difference between Amgevita® (adalimumab), Hadlima® (adalimumab), Hulio® (adalimumab), Hyrimoz® (adalimumab), and Idacio® (adalimumab)?**

Amgevita®, Hadlima®, Hulio®, Hyrimoz®, and Idacio® are all adalimumab products. Adalimumab is an anti-inflammatory medicine that belongs to the class of drugs called biological response modifiers. Amgevita®, Hadlima®, Hulio®, Hyrimoz®, and Idacio® are approved by Health Canada as biosimilar versions of adalimumab. Each product is manufactured and marketed by different companies.

2. **What is the funding status of Amgevita® (adalimumab), Hadlima® (adalimumab), Hulio® (adalimumab), Hyrimoz® (adalimumab), and Idacio® (adalimumab)?**

Effective March 29, 2021, Amgevita®, Hadlima®, Hulio®, Hyrimoz®, and Idacio® will be listed on the Ontario Drug Benefit Formulary/Comparative Drug Index (Formulary) as Limited Use (LU) benefits for the treatment of rheumatoid arthritis, polyarticular juvenile idiopathic arthritis, psoriatic arthritis, ankylosing spondylitis, Crohn's disease, ulcerative colitis, hidradenitis suppurativa, plaque psoriasis and uveitis.

3. **What are the Limited Use criteria for Amgevita® (adalimumab), Hadlima® (adalimumab), Hulio® (adalimumab), Hyrimoz® (adalimumab), and Idacio® (adalimumab)?**

As of the March 2021 Formulary effective date, the Reason for Use (RFU) Codes applicable for each adalimumab 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.

Applicable RFU Codes by product:

Amgevita®, Hadlima®, Hulio®, and Idacio® - 600, 601, 602, 603, 604, 605, 606, 607, 609, and 611

Hyrimoz® - 600, 601, 602, 603, 604, 605, 606, 608, 609, and 612

A. Rheumatoid Arthritis (Code 600)

For the treatment of rheumatoid arthritis (RA) in patients who have severe active disease (greater than or equal to 5 swollen joints and rheumatoid factor positive and/or, anti-CCP positive, and/or radiographic evidence of rheumatoid arthritis) and have experienced failure, intolerance, or have a contraindication to adequate trials of disease-modifying anti-

rheumatic drugs (DMARDs) treatment regimens, such as one of the following combinations of treatments:

A. i) Methotrexate (20mg/week) for at least 3 months, AND
ii) leflunomide (20mg/day) for at least 3 months, in addition to
iii) an adequate trial of at least one combination of DMARDs for 3 months; OR

B. i) Methotrexate (20mg/week) for at least 3 months, AND
ii) leflunomide in combination with methotrexate for at least 3 months; OR

C. i) Methotrexate (20mg/week), sulfasalazine (2g/day) and hydroxychloroquine(400mg/day) for at least 3 months. (Hydroxychloroquine is based by weight up to 400mg per day.)

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 renewals beyond the second year, the patient must demonstrate objective evidence of preservation of treatment effect.

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

Approvals will only allow for standard dosing for adalimumab.

The recommended dosing regimen is 40mg every two weeks.

LU Authorization Period: 1 Year

B. Polyarticular Juvenile Idiopathic Arthritis (Code 601)

For the treatment of polyarticular juvenile idiopathic arthritis (pJIA) in patients who have active disease (greater than or equal to 3 swollen joints and greater than or equal to 5 active joints) despite a trial of optimal doses of subcutaneously administered methotrexate (i.e. 15mg/m2 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 should be documented.

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 demonstrate objective evidence of preservation of treatment effect.

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

The recommended dosing regimen is for pediatric patients 2 years of age and older:

- 10kg to less than 30kg: 20mg every other week*

- 30kg and greater: 40mg every other week

* a dose of 10mg every other week can be considered for patients weighing 10kg to less than 15kg

It should be noted that some adalimumab products may not be available as 20mg injectables.

Prescribers should be informed and stay current with a drug's official Health Canada approved product monograph including available dosage formats.

LU Authorization Period: 1 Year

C. Psoriatic Arthritis (Code 602)

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 40mg every 2 weeks.

Higher doses may be considered case-by-case through the Exceptional Access Program.

LU Authorization Period: 1 Year

D. Ankylosing Spondylitis (Code 603)

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

- Age of disease onset equal to or younger than 50; 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

- Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) score of greater than or equal to 4 for at least 4 weeks while on standard therapy.

NOTE: Radiographic evidence demonstrating the presence of "SI joint fusion" or "SI joint erosion" on x-ray or CT scan, or MRI demonstrating the presence of "inflammation" or "edema" of the SI joint.

Maintenance/Renewal:

After 12 months of treatment, maintenance therapy is funded for patients with objective evidence of at least a 50 percent reduction in BASDAI score or greater than or equal to 2 absolute point reduction in BASDAI score. For funding beyond the second year, the patient must demonstrate 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 40mg every 2 weeks.

Higher doses may be considered case-by-case through the Exceptional Access Program.

LU Authorization Period: 1 Year

E. Moderate-to-Severe Crohn's Disease (Code 604)

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; AND

B. Failed to respond to conventional treatment with a corticosteroid equivalent to a daily dose of prednisone 40mg daily for at least 2 weeks OR the patient is stabilized on corticosteroid but cannot be tapered to a corticosteroid dose below prednisone 20mg daily or equivalent; AND

C. Failed to respond to an immunosuppressive agent (azathioprine, 6-mercaptopurine, methotrexate, or cyclosporine) tried for at least 3 months (or where the use of immunosuppressants is contraindicated).

Approvals will only allow for standard dosing for adalimumab.

The recommended dosing regimen is 160mg at week 0; 80mg at week 2; followed by 40mg every two weeks.

Maintenance/Renewal:

Maintenance therapy is funded for patients who meet the Ministry initiation criteria and whose disease is maintained with a 50% reduction in the HBI from pre-treatment measurement, AND improvement of symptoms (e.g. absence of bloody diarrhea, weight is stable or increased), AND no longer using corticosteroids.

For continued funding beyond the first year, the patient must continue to demonstrate benefit and if unable to be discontinued on corticosteroids, the physician may wish to consider other funded alternatives.

Approvals will only allow for standard dosing for adalimumab.

The recommended dosing regimen is 40mg every 2 weeks.

LU Authorization Period: 1 Year

F. Fistulising Crohn's Disease (Code 605)

For the treatment of fistulising Crohn's disease with concomitant luminal disease in patients who meet the following criteria:

A. 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); AND

B. Harvey Bradshaw Index (HBI) score greater than or equal to 7

Approvals will only allow for standard dosing for adalimumab.

The recommended dosing regimen for induction is 160mg at week 0, followed by 80mg at week 2, then 40mg every other week.

Maintenance/Renewal:

Maintenance therapy is funded for patients who meet the Ministry initiation criteria and achieve and maintains response to therapy.

Approvals will only allow for standard dosing for adalimumab.

The recommended dosing regimen is 40mg every other week.

LU Authorization Period: 1 Year

G. Moderate-to-Severe Ulcerative Colitis (Code 606)

For the treatment of ulcerative colitis disease in patients who meet the following criteria:

1. 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 greater than or equal to 40mg (or a 1 week course of IV equivalent) and 3 months of azathioprine (AZA)/6-mercatopurine (6-MP) (or where the use of immunosuppressants is contraindicated);

OR

Stabilized with 2 weeks of oral prednisone at daily doses greater than or equal to 40mg (or 1 week of IV equivalent) but the corticosteroid dose cannot be tapered despite 3 months of AZA/6MP (or where the use of immunosuppressants is contraindicated).

2. Severe disease

A. Mayo score greater than 10; AND

B. Endoscopy* subscore of greater than or equal to 2; AND

C. Failed 2 weeks of oral prednisone at daily doses greater than or equal to 40mg (or 1 week of IV equivalent)

OR

Stabilized with 2 weeks oral prednisone at daily doses greater than or equal to 40mg (or 1 week of IV equivalent) but demonstrated that the corticosteroid 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 12 months prior to initiation of treatment.

Approvals will only allow for standard dosing for adalimumab.

The recommended dosing regimen for induction is 160 mg at week 0, followed by 80 mg at week 2, then 40 mg every other week.

Maintenance/Renewal:

Maintenance therapy is funded for patients who meet the Ministry initiation criteria and whose disease is maintained at Mayo score less than 6 AND who demonstrate at least 50% reduction in the dose of prednisone compared with the starting dose following the first 6 months of treatment with adalimumab or be off corticosteroids after the first year of treatment.

Approvals will only allow for standard dosing for adalimumab.

The recommended dosing regimen is 40 mg every other week.

LU Authorization Period: 1 Year

H. Hidradenitis Suppurativa (Adult and Adolescent) (Code 607)

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

A. A total abscess and nodule count of 3 or greater; AND

B. Lesions in at least two distinct anatomic areas, one of which must be Hurley Stage II or III; AND

C. Experienced an inadequate response to a 90-day trial of oral antibiotics.

Therapy must be prescribed by a practitioner with expertise in the management of patients with HS.

The recommended adult dosing regimen is 160 mg at week 0, followed by 80 mg at week 2,

then 40 mg at week 4, and 40 mg weekly thereafter.

The recommended adolescent dosing regimen is 80 mg at week 0, followed by 40 mg every other week starting at week 1 up to 40 mg weekly in those with inadequate response.

If there is no improvement after 12 weeks of treatment with adalimumab at the Health Canada approved dose, higher doses are not recommended and the prescriber should discontinue treatment.

Prescribers should be informed and stay current with a drug's official Health Canada approved product monograph including available dosage formats.

Maintenance/Renewal:

Maintenance therapy is funded for patients beyond the first 12 weeks in those who meet the Ministry initiation criteria and who have responded to treatment 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.

Maintenance therapy beyond the second year is funded for patients using adalimumab for HS, where there is objective evidence of the preservation of treatment effect (i.e. the current abscess and inflammatory nodule count should be compared to the count prior to initiating treatment with adalimumab).

The recommended maintenance dose is 40 mg weekly.

Prescribers should be informed and stay current with a drug's official Health Canada approved product monograph including available dosage formats.

LU Authorization Period: 1 Year

I. Hidradenitis Suppurativa (Adult Only) (Code 608)

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

A. A total abscess and nodule count of 3 or greater; AND
B. Lesions in at least two distinct anatomic areas, one of which must be Hurley Stage II or III; AND
C. Experienced an inadequate response to a 90-day trial of oral antibiotics.

Therapy must be prescribed by a practitioner with expertise in the management of patients with HS.

The recommended adult dosing regimen is 160 mg at week 0, followed by 80 mg at week 2, then 40 mg at week 4, and 40 mg weekly thereafter.

If there is no improvement after 12 weeks of treatment with adalimumab at the Health Canada approved dose, higher doses are not recommended, and the prescriber should discontinue treatment.

Prescribers should be informed and stay current with a drug's official Health Canada approved product monograph including available dosage formats.

Maintenance/Renewal:

Maintenance therapy is funded for patients beyond the first 12 weeks in those who meet the Ministry initiation criteria and who have responded to treatment 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.

Maintenance therapy beyond the second year is funded for patients using adalimumab for HS, where there is objective evidence of the preservation of treatment effect (i.e. the current abscess and inflammatory nodule count should be compared to the count prior to initiating treatment with adalimumab).

The recommended maintenance dose is 40 mg weekly.

Prescribers should be informed and stay current with a drug's official Health Canada approved product monograph including available dosage formats.

LU Authorization Period: 1 Year

J. Plaque Psoriasis (Code 609)

For the treatment of severe* plaque psoriasis in patients 18 years of age or older 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
12 week trial of phototherapy (unless not accessible)
6 month trial of at least 2 systemic, oral agents used alone or in combination
-Methotrexate 15-30 mg 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

Approvals will only allow for standard dosing for adalimumab.

The recommended dose is an initial 80 mg administered subcutaneously at week 0, followed by 40 mg subcutaneously given every other week starting at week 1, as approved by Health Canada.

If the patient has not responded adequately after 12 weeks of treatment at the Health Canada approved dose, higher doses are not recommended, and the physician should consider switching to an alternative biologic agent.

LU Authorization Period: 1 Year

K. Uveitis (Adult and Pediatric) (Code 611)

For the treatment of severe uveitis in patients meeting the following criteria:

A. Has experienced failure or intolerance to an oral corticosteroid (or topical corticosteroid for anterior uveitis) or where the use of corticosteroids is contraindicated, and has experienced failure or intolerance to at least one immunosuppressive therapy; AND

B. Treatment must be prescribed by an ophthalmologist specialized in uveitis or retinal disease, a uveitis specialist, or a retina specialist familiar with ocular inflammatory diseases.

Requests not meeting the above criteria may be considered on a case-by-case basis through the Exceptional Access Program.

The recommended adult dose is an initial 80 mg administered subcutaneously at week 0, followed by 40 mg subcutaneously given every other week starting at week 1, as approved by Health Canada. Note: Higher doses up to 40 mg weekly may be considered in patients who have failed to respond to lower doses.

The recommended dose for pediatric patients (2 years of age and older) with anterior uveitis is:

Less than 30 kg: 20 mg every other week in combination with methotrexate.

30 kg or greater: 40 mg every other week in combination with methotrexate.

For patients 6 years of age or older and less than 30 kg, an optional loading dose of 40 mg at week 0 may be administered before starting maintenance therapy.

For patients 6 years of age or older and weighing 30 kg or greater, an optional loading dose of 80 mg at week 0 may be administered before starting maintenance therapy.

It should be noted that some adalimumab products may not be available as 20 mg injectables.

Prescribers should be informed and stay current with a drug's official Health Canada approved product monograph including available dosage formats.

Maintenance/Renewals:

Maintenance therapy is funded for patients who meet the Ministry initiation criteria and who have experienced improvement and/or stability of vision and other treatment goals (e.g. reduction or control of ocular inflammation).

LU Authorization Period: 1 Year

L. Uveitis (Adult Only) (Code 612)

For the treatment of severe uveitis in patients meeting the following criteria:

A. Has experienced failure or intolerance to an oral corticosteroid (or topical corticosteroid for anterior uveitis) or where the use of corticosteroids is contraindicated, and has experienced failure or intolerance to at least one immunosuppressive therapy; AND

B. Treatment must be prescribed by an ophthalmologist specialized in uveitis or retinal disease, a uveitis specialist, or a retina specialist familiar with ocular inflammatory diseases.

Requests not meeting the above criteria may be considered on a case-by-case basis through the Exceptional Access Program.

The recommended adult dose is an initial 80 mg administered subcutaneously at week 0, followed by 40 mg subcutaneously given every other week starting at week 1, as approved by Health Canada. Note: Higher doses up to 40 mg weekly may be considered in patients who have failed to respond to lower doses.

Prescribers should be informed and stay current with a drug's official Health Canada approved product monograph including available dosage formats.

Maintenance/Renewals:

Maintenance therapy is funded for patients who meet the Ministry initiation criteria and who have experienced improvement and/or stability of vision and other treatment goals (e.g. reduction or control of ocular inflammation).

LU Authorization Period: 1 Year

4. What is the rationale for funding biosimilar adalimumab products?

Amgevita®, Hadlima®, Hulio®, Hyrimoz®, and Idacio® were approved by Health Canada as biosimilar versions of the biologic drug adalimumab. The originator version of adalimumab is Humira®. 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 Humira® (adalimumab) is already funded by the ministry be required to switch to a biosimilar adalimumab product?

No. Patients whose adalimumab treatment with Humira® is already funded by the ministry can continue to receive funding for Humira® for the duration of the approval period. The ministry will consider funding renewals for Humira® for these patients.

The LU criteria for Amgevita®, Hadlima®, Hulio®, Hyrimoz®, and Idacio® will apply to both new and existing patients for the funded indications.

6. Will the ministry consider new requests for Humira® (adalimumab) reimbursement under the Exceptional Access Program (EAP)?

The ministry will no longer accept new EAP requests for Humira® for patients who are treatment-naïve to Humira®.

7. Will the ministry consider EAP requests for Humira® (adalimumab) for patients who do not respond to Amgevita® (adalimumab), Hadlima® (adalimumab), Hulio® (adalimumab), Hyrimoz® (adalimumab), or Idacio® (adalimumab)?

The ministry will not consider funding requests for Humira® for patients who do not respond to or are intolerant to a biosimilar adalimumab product. The physician may wish to consider other therapeutic options.

8. Will the ministry consider EAP requests for Amgevita® (adalimumab), Hadlima®, Hulio® (adalimumab), Hyrimoz® (adalimumab) or Idacio® (adalimumab) for patients who do not meet Limited Use criteria?

Amgevita®, Hadlima®, Hulio®, Hyrimoz®, or Idacio® may be considered for patients who do not meet the LU criteria for specific indications or dosing regimens through the Exceptional Access Program (EAP) on a case-by-case basis.

9. How should pharmacies submit claims for Amgevita® (adalimumab), Hadlima® (adalimumab), Hulio® (adalimumab), Hyrimoz® (adalimumab) or Idacio® (adalimumab)?

Pharmacies should submit claims using the drug identification number (DIN) of the product and the appropriate Reason for Use code.

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:

https://www.canada.ca/en/health-canada/services/drugs-health-products/biologics-radiopharmaceuticals-genetic-therapies/applications-submissions/guidance-documents/fact-sheet-biosimilars.html

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 416-327-4282