Renflexis (infliximab) Frequently Asked Questions

1. What is the funding status of Renflexis (infliximab)?

Effective **September 27, 2018**, Renflexis (infliximab) will be added to the Ontario Drug Benefit (ODB) Formulary as a Limited Use (LU) benefit for the treatment of rheumatoid arthritis (RA), ankylosing spondylitis (AS), psoriatic arthritis (PsA), plaque psoriasis (PsO), ulcerative colitis (UC), and Crohn's Disease (CD).

2. What are the Limited Use Criteria for Renflexis (infliximab)?

Reason For Use (RFU) Code and Clinical Criteria

A. Rheumatoid Arthritis (Code 541)
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.

The recommended dosing regimen is 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.

LU Authorization Period: 1 year

B. Ankylosing Spondylitis (Code 542)
For the treatment of ankylosing spondylitis (AS) in patients who have severe active disease (confirmed by radiographic evidence (see notes below) with:

I. Age of disease onset less than or equal to 50; AND
II. Low back pain and stiffness for greater than 3 months that improves with exercise and not relieved by rest; AND
III. 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
IV. 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 3 to 5mg/kg/dose at 0, 2 and 6 weeks followed by maintenance therapy of up to 5mg/kg/dose every 6 to 8 weeks.

LU Authorization Period: 1 year

C. Psoriatic Arthritis (Code 543)

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% 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 5mg/kg/dose at 0, 2 and 6 weeks followed by maintenance therapy of 5mg/kg/dose every 8 weeks.

LU Authorization Period: 1 year

D. Plaque Psoriasis (Code 544)

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.

*Severe plaque psoriasis:

- Body Surface Area (BSA) involvement of at least 10 percent, 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.

**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 to 30mg/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

The recommended dosing regimen is 5mg/kg/dose at 0, 2 and 6 weeks followed by maintenance therapy of 5mg/kg/dose every 8 weeks.

LU Authorization Period: 1 year

E. Ulcerative Colitis (Code 545)

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 ≥ 40mg (or a 1 week course of IV equivalent)
    OR
    d. Stabilized with 2 weeks oral prednisone at daily doses ≥ 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)

2. Severe disease
    a. Mayo score > 10 AND
    b. Endoscopy* subscore of greater than or equal to 2 AND
    c. Failed 2 weeks of oral prednisone at daily doses ≥ 40mg (or 1 week IV equivalent)
    OR
    d. Stabilized with 2 weeks oral prednisone at daily doses ≥ 40mg (or 1 week of IV equivalent) but the 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.

The recommended dosing regimen for induction is 5mg/kg/dose at 0, 2 and 6 weeks followed by 5mg/kg/dose every 8 weeks.

Maintenance/Renewal:
Maintenance therapy is funded for patients who meet the Ministry initiation criteria and whose disease is maintained at Mayo score < 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 Renflexis or be off corticosteroids after the first year of treatment.

The recommended dosing regimen is 5mg/kg/dose every 8 weeks.

LU Authorization Period: 1 year

F. Moderate to Severe (luminal) Crohn's Disease (Code 546)

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

- HBI (Harvey Bradshaw Index) score greater than or equal to 7; AND
- 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
- 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).

The recommended dosing regimen is 5mg/kg/dose at 0, 2 and 6 weeks followed by 5mg/kg/dose every 8 weeks. (Note: Higher doses up to 10mg/kg/dose may be considered in patients who have failed to respond to lower doses).

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 Harvey Bradshaw Index (HBI) from pre-treatment measurement, AND improvement of symptoms (For example: absence of bloody diarrhea, weight is stable or increased), AND the use of corticosteroids and/or other immunosuppressive therapy is reduced, being tapered, or discontinued.

For funding beyond the second 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.

LU Authorization Period: 1 year

G. Fistulizing Crohn's Disease (Code 547)

For the treatment of fistulizing Crohn's Disease in patients with actively draining perianal or enterocutaneous fistula(e) who meet the following criteria;

Fistula has persisted despite a course of antibiotic therapy (ciprofloxacin and/or metronidazole) and immunosuppressive therapy (azathioprine or 6-mercaptopurine).

The recommended dosing regimen is 5mg/kg/dose at 0, 2 and 6 weeks followed by 5mg/kg/dose every 8 weeks. (Note: Higher doses up to 10mg/kg/dose may be considered in patients who have failed to respond to lower doses).

Maintenance/Renewal:
Maintenance therapy is funded for patients who meet the Ministry initiation criteria for fistulizing Crohn's disease and who have demonstrated benefit from treatment (e.g. partial resolution of fistulae and symptom improvement.). The recommended dosing regimen is 5mg/kg/dose every 8 weeks.

LU Authorization Period: 1 year

3. What is difference between Renflexis (infliximab) and Inflectra (infliximab)?

Infliximab is an anti-inflammatory medicine that belongs to the class of drugs called biological response modifiers. Renflexis and Inflectra are both infliximab products that have been approved by Health Canada as biosimilars to Remicade, the innovator product. Renflexis, Inflectra, and Remicade are manufactured and marketed by different companies. Like Remicade, Reflexis has Health Canada approval for use in pediatric patients with inflammatory bowel diseases such as Crohn's disease and Ulcerative Colitis. Please refer to the product monograph for information on the appropriate use of Renflexis in pediatric patients.

Please refer to Health Canada's website for further details on biosimilars.

4. Are patients with existing Exceptional Access Program (EAP) approval for Remicade (infliximab) required to switch to Renflexis (infliximab)?

No. Patients who have an existing Exceptional Access Program (EAP) approval for Remicade (infliximab) can continue to receive Remicade (infliximab) for the duration of the EAP approval period. The ministry will also consider EAP renewal requests for Remicade (infliximab) for patients with existing EAP approvals.

The LU criteria for Renflexis (infliximab) will apply to patients new to infliximab and to those already using infliximab for RA, AS, PsA, PsO, UC, and CD.

Claims for Renflexis (infliximab) will be reimbursed under the ODB program when prescribed in accordance with the LU criteria and accompanied by a valid, fully completed prescription with the appropriate LU documentation (RFU code).

5. Will the ministry consider new requests for Remicade (infliximab) reimbursement under the Exceptional Access Program, for the treatment of rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, plaque psoriasis, ulcerative colitis, and Crohn's disease?

The ministry does not accept new requests for Remicade for the treatment of rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, plaque psoriasis, ulcerative colitis, and Crohn's disease in patients who are treatment-naïve to Remicade. This policy was implemented since the formulary listing of Inflectra as a limited use benefit in 2016. This will remain the policy when Renflexis becomes publicly funded.

The funding of only biosimilar infliximab products for new requests for patients starting on infliximab is intended to be applied to all six conditions noted above.

The EAP will continue to consider requests for Remicade for other indications.

6. Will the ministry consider new requests for Remicade (infliximab) reimbursement under the Exceptional Access Program, for the treatment of pediatric patients with ulcerative colitis or Crohn's disease?

Renflexis has Health Canada approval for use in pediatric patients with inflammatory bowel diseases such as Crohn's disease and Ulcerative colitis. As such, new requests for Remicade for pediatric patients who are treatment-naïve to Remicade will no longer be considered by the Exceptional Access Program once Renflexis is listed on the formulary. For pediatric patients requiring Renflexis for the treatment of Crohn's disease or Ulcerative Colitis, the prescriber should fax a request to the Ministry's Exceptional Access Program that includes complete and appropriate clinical information for a case-by-case review if the child's circumstances do not meet the LU criteria for access as a formulary listed benefit. The LU criteria were based on studies in the adult population and may not be completely applicable to pediatric patients.

7. Will the ministry consider requests for Remicade reimbursement under the Exceptional Access Program for patients who do not respond to Renflexis (infliximab), or are intolerant to Renflexis (infliximab)?

The ministry will not consider requests for Remicade (infliximab) reimbursement for patients who do not respond to Renflexis (infliximab), or are intolerant to Renflexis (infliximab) under any program. The physician may wish to consider other therapeutic options.

8. Is Renflexis (infliximab) currently funded for indications other than rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, plaque psoriasis, ulcerative colitis, and Crohn's disease?

Effective September 27, 2018 Renflexis (infliximab) will be listed on the ODB Formulary as a Limited Use (LU) benefit for the following indications: rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, plaque psoriasis, ulcerative colitis, and Crohn's disease. At this time, there is no reimbursement for Renflexis (infliximab) for any other indications either as an LU benefit or through the Exceptional Access Program.

9. How should pharmacies submit claims for Renflexis (infliximab)? Are Renflexis and Inflectra "interchangeable"?

Pharmacies should be submitting claims using the drug identification number (DIN) of the product and the appropriate reason for use code (RFU) for each drug.
Renflexis and Inflectra are both infliximab products that are approved by Health Canada as biosimilars to Remicade. However, the two products are not "interchangeable" – i.e., pharmacists do not have the ability to change a patient from one drug to the other drug without authorization from the prescriber.

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