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.

Adalimumab
Brand(s): Humira
DOSAGE FORM/ STRENGTH: 40 mg/0.8mL prefilled syringe and 40 mg/0.8mL prefilled pen 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

Etanercept – see formulary for funded biosimilars
Brand(s): Enbrel
DOSAGE FORM/ STRENGTH: 25 mg/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 biosimilar funded options
Brand(s): Remicade
DOSAGE FORM/ STRENGTH: 100 mg/10 mL intravenous infusion

Reference biologics (e.g. Remicade, Enbrel) with a provincially funded biosimilar are only considered for provincial funding in patients who are treatment experienced and stable on the reference biologic or those with existing EAP approvals. Prescribers should refer to the ODB formulary for biosimilars and their funded conditions.

It should be noted that after the date when a biosimilar becomes publicly funded for an approved indication, patients initiated on a reference biologic for this same provincially funded indication through support from a manufacturer's patient support program, may be expected to be provided ongoing access of the reference biologic through the patient support program or to use a biosimilar upon meeting specified criteria. The Ministry will only consider funding of Reference biologics in those who are treatment experienced and stabilized on the product prior to transitioning to the ODB program or in patients with an existing EAP approval.

Refer to the Executive Officer Communications on the Ministry website for Frequently asked questions and notifications of funded biosimilars at
http://www.health.gov.on.ca/en/pro/programs/drugs/opdp_eo/eo_communiq.aspx

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

(Note that effective December 22, 2016, Tofacitinib (Xeljanz) 5 mg is available on the ODB Formulary in patients meeting the Limited Use criteria)

Duration of Approval: First Renewal – 1 Year, Subsequent Renewals – 5 Years

Rituximab
Brand(s): Rituxan
DOSAGE FORM/ STRENGTH: 10 mg/mL intravenous injection

First course of Rituxan 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.

More information describing one of the Committee to Evaluate Drugs' review of rituximab can be found on the Ministry website.

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, 162 mg/0.9 mL solution for injection

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

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