

October 10, 2003

Pharmacare Reimbursement Coverage Update:

An overview of biologic response modifying medications and their province-by-province formulary coverage for Canadians living with rheumatoid arthritis—in consumer-friendly language

As a service to Canadians living with rheumatoid arthritis, the following information was gathered from provincial Pharmacare programs in provinces where “biologic response modifier” (the name of the class of medications) coverage is provided. The information has been translated into consumer-friendly language to make it more accessible to people with arthritis and the general public.

Information about Pharmacare reimbursement coverage changes frequently. Please check with the Pharmacare program in your province for the latest updates on formulary coverage for medications used in the treatment of rheumatoid arthritis.

Also, while you may meet your province’s biologic response modifier reimbursement criteria outlined in this document, remember that each province has different rules to determine who gets access to reimbursement. Eligibility for reimbursement depends on a number of factors, like age or household income.

At this writing, biologic response modifiers are not listed on the provincial drug formularies for reimbursement in Prince Edward Island or Newfoundland and Labrador. If this is affecting you and your health, get your immediate health care needs heard at government by writing, visiting or calling your local government representative. For help in doing that, please refer to the section of the ACE web site entitled “**Arthritis and the Health Care System**”.

In some provinces, biologic response modifiers are approved for certain other forms of arthritis (i.e. psoriatic arthritis in Ontario). Biologic response modifiers have been approved in the United States and Europe for the treatment of ankylosing spondylitis, but as of this writing, they are still under review at Health Canada.

To help you with terms and abbreviations used in this document that may be unfamiliar to you, a glossary is provided on the last pages.

Please note the information contained in this document is not medical advice. Please talk to your doctor about your specific treatment needs to help you successfully manage your rheumatoid arthritis.

BRITISH COLUMBIA

Pharmacare reimbursement coverage for the biologic response modifying medications etanercept (Enbrel®) and infliximab (Remicade®) is provided in British Columbia.

Individuals with rheumatoid arthritis meeting a set of criteria are eligible for coverage:

Initial coverage (first eight to 12 week period):

For initial coverage, a person with rheumatoid arthritis must meet all of the following criteria:

- ❑ Adult patients must have the signs and symptoms of severely active rheumatoid arthritis, and the biologic response modifier being prescribed to them must be used in combination with methotrexate;
- ❑ The biologic response modifier must be prescribed by a rheumatologist
- ❑ Patient is refractory (a medication doesn't work, causes side effects, or there are warnings against its use in a particular individual) to the following other medications:
 1. Methotrexate: weekly parenteral (by injection, subcutaneous or intramuscular) therapy at 25mg or greater (15mg or greater if patient is 65 years of age or over) for more than 8 weeks.

PLUS

2. Gold: weekly injections for 20 weeks or sulfasalazine: at least 2gm daily for 3 months or azathioprine: 3mg/kg/day for 3 months.

PLUS

3. Leflunomide: 20mg daily for 10 weeks (not a requirement for patients who began infliximab / etanercept therapy prior to June 2001)

PLUS

4. One of the following combinations:
 - i. methotrexate with cyclosporin (minimum 4 months trial on both or intolerance)
 - ii. methotrexate with hydroxychloroquine and sulfasalazine (minimum 4 month trial on triple therapy or intolerance)
 - iii. methotrexate with gold

Or, for etanercept special authorities only:

In patients who cannot tolerate (usually because of side effects) or who have contraindications (other health risks) to methotrexate therapy, refractory¹ to a combination of at least two of the following drugs: gold, cyclosporine, leflunomide, and sulfasalazine.

Notes:

1. Refractory defined as one or more of the following:

- Lack of effect at doses and for duration specified above
- Intolerable side-effects (specify side-effect at dose and duration of treatment)
- Contraindications to therapy as defined in product monographs (please specify)

Contraindications (if any of the below listed contraindications exist, patient is ineligible for coverage):

Infliximab	Y	N	Severe infection (such as sepsis, abscesses, tuberculosis and opportunistic infections)
	Y	N	Hypersensitivity to infliximab
	Y	N	Pregnancy/lactation
Etanercept	Y	N	Patient with, or at risk of, sepsis syndrome
	Y	N	Active infection(s)
	Y	N	Hypersensitivity to etanercept

For coverage beyond the first eight to 12 weeks of treatment:

For continuing coverage, the rheumatologist must reassess (by conducting a physical examination) the patient at the 8th to 12th week of treatment to ensure that the patient meets specific improvement criteria. Coverage is continued up to one year if the patient meets the following criteria:

- Prescribed by a rheumatologist
- Patient has been assessed after the eighth to twelfth of anti-TNF therapy to determine response to treatment and meets the following response criteria:

1. Greater than 20% reduction in the number of tender and the number of swollen joints

PLUS

2. Greater than 20% improvement in the physician global assessment scale

PLUS, EITHER

3. Greater than 20% improvement in the patient global assessment scale,

OR

4. Greater than 20% reduction in the acute phase as measured by ESR or CRP (measurements of inflammation and disease activity).

For coverage to continue beyond the first year of treatment, the patient must meet the following criteria:

- Patient has been reassessed after one year of treatment by the prescribing rheumatologist and a copy of the assessment report is attached for review by the Rheumatoid Arthritis Drug Benefit Adjudication Advisory Committee.

Remember to make a note in your calendar to remind your rheumatologist to apply for continuing coverage at least a month or several months before your current coverage expires.

ALBERTA

Pharmacare coverage for biologic therapy—either etanercept (Enbrel®) or infliximab (Remicade®)—is provided to individuals over 18 year of age with rheumatoid arthritis meeting the following criteria:

Initial coverage:

For etanercept or infliximab use in combination with methotrexate for patients over 18 years of age. To be eligible, individuals must meet the following criteria:

- Refractory¹ to the following:
 1. Methotrexate ≥ 20 mg (PO, SC, IM)/week for >12 weeks (>65 years old, max 15mg/wk). Patients not tolerating/unresponsive to PO methotrexate must have a trial of parenteral methotrexate before it can be deemed refractory

AND

2. Methotrexate in combination with other DMARDs for ≥ 4 months

AND

3. Leflunomide ≥ 20 mg/day for > 10 weeks

Notes:

1. Refractory is defined as either lack of effect at doses and duration specified above, serious adverse effects (for example, leukopenia or hepatitis) or contraindications to treatments as defined in product monographs.

AND

4. Must consent to participate in the Alberta Post-Marketing Study

Initial coverage is for 8 weeks.

Reimbursement approval for etanercept (Enbrel®) is at the dosage of 25mg twice-weekly sub-cutaneous injections.

For continuing coverage (beyond the first eight to 12 weeks), the individual must meet the following criteria:

- ❑ Reassessment by a rheumatologist after eight to 12 weeks treatment
- ❑ Individuals must achieve the following responses (as measured by established improvement guidelines) after being on the therapy for eight to 12 weeks:
 1. ACR20 or Improvement by 1.2 in DAS 28 score

AND

2. Improvement of 0.22 in HAQ

If the individual meets these criteria, coverage will be provided for a maximum of 6 months.

Rheumatologists must reassess (by conducting a physical examination) the individual every 6 months and the individual must continue to meet the two criteria above for the coverage to continue.

Remember to make a note in your calendar to remind your rheumatologist to apply for continuing coverage at least a month or several months before your current coverage expires.

SASKATCHEWAN

Pharmacare reimbursement coverage is provided for etanercept (Enbrel®) and infliximab (Remicade®) for the treatment of individuals with active rheumatoid arthritis who have failed or are intolerant to methotrexate and leflunomide. Exceptions to these coverage criteria can be considered in individuals where methotrexate or leflunomide are contraindicated. The product should be used in consultation with a specialist in this area.

MANITOBA

There are no set guidelines for the use of biologic response modifying medications— anakinra (Kineret®), etanercept (Enbrel®) or infliximab (Remicade®)—in Manitoba. The prescribing rheumatologist must apply in writing to the Special Consideration Committee including details of the patient's case, their previous disease modifying anti-rheumatoid drug history, etc.

If the rheumatologist makes a valid clinical case for early biologic response modifier treatment (for example, before an individual fails on older disease modifying anti-rheumatic drugs), then the Special Consideration Committee has the authority to approve it.

The Special Consideration Committee meets every 15 days.

ONTARIO

RHEUMATOID ARTHRITIS:

Pharmacare reimbursement coverage for anakinra (Kineret®), etanercept (Enbrel®) and infliximab (Remicade®) is provided for a one-year duration for individuals who meet the following criteria:

- Active rheumatoid arthritis¹ who are intolerant² of, or have had an inadequate response to, at least 3 separate courses of disease modifying anti-rheumatic (DMARDs³), including each of the following:
 1. Methotrexate at 20mg/week for at least 3 months;
 2. Leflunomide at 20mg/day for at least 3 months (or another DMARD³ if there is a contraindication/intolerance to leflunomide);
 3. One combination of DMARDs for at least 3 months.

Notes:

¹Active disease is defined as:

- Patients must have at least 5 swollen joints
- Patients must be rheumatoid factor positive and have radiographic evidence of joint erosion

² Intolerance and/or contraindications should be described. Contraindications to leflunomide include: female patients with plans to become pregnant, previous hypersensitivity, severe immunodeficiency states (e.g. AIDS, bone marrow suppression, serious infections), moderate to severe renal insufficiency, current impaired liver function.

³ DMARDs include leflunomide, hydroxychloroquine, methotrexate, sulfasalazine, cyclosporine, azathioprine, penicillamine, chloroquine and gold compounds.

Continuing coverage beyond the first year:

For reimbursement renewal requests at one year, objective evidence of improvement must be provided (at least 20% reduction in swollen joint count). For renewals beyond the second year, objective evidence of the continuing beneficial effect of the treatment should be provided (for example, the current joint count should be compared to the count prior to initiating treatment with the biologic agent).

Requests that do not meet these criteria will undergo "Individual Clinical Review".

Remember to make a note in your calendar to remind your rheumatologist to apply for continuing coverage at least a month or several months before your current coverage expires.

For etanercept (Enbrel®) only:

PSORIATIC ARTHRITIS

- Approvals will be provided to patients who have had an inadequate response to the following:
 1. Methotrexate 20mg/week for 3 months

AND

2. Sulfasalazine 1gm BID for 3 months

- Patients must have a minimum of 5 swollen joints and have radiographic evidence of joint erosion.

Individuals who meet these criteria will receive approval for medication costs reimbursement for one year.

Requests for other biologic agents and those that do not meet these criteria will undergo external review.

Continuing coverage:

All continuing coverage requests will be reviewed externally.

Remember to make a note in your calendar to remind your rheumatologist to apply for continuing coverage at least a month or several months before your current coverage expires.

JUVENILE IDIOPATHIC ARTHRITIS

- ❑ Approvals will be provided to patients who have had an inadequate response to a three-month course of treatment with injectable methotrexate in a dosage equal to or greater than 15mg/m².
- ❑ Patients must have a minimum of 3 swollen joints and a total of 5 active joints.

Approval for coverage is for one year.

Continuing coverage beyond the first year:

For reimbursement renewal requests at one year, objective evidence of improvement must be provided (at least 20% reduction in swollen joint count). For renewals beyond the second year, objective evidence of the continuing beneficial effect of the treatment should be provided (for example, the current joint count should be compared to the count prior to initiating treatment with the biologic agent).

Requests that do not meet these criteria will undergo "Individual Clinical Review".

Any requests for infliximab and anakinra will be reviewed externally.

Remember to make a note in your calendar to remind your rheumatologist to apply for continuing coverage at least a month or several months before your current coverage expires.

QUEBEC

Etanercept/Infliximab

MODERATE TO SEVERE RA:

At the time of treatment initiation or for patients already on treatment for less than 5 months:

- ❑ A patient must have 8 or more joints with active synovitis and one of the 5 following elements:
 1. Positive rheumatoid factor
 2. Erosions on radiographs
 3. A HAQ score higher than 1
 4. Increase in C-reactive protein level
 5. Increase in sedimentation rate

AND

- The patient still has active disease even though treatment with 2 DMARDS used singly or in combination for a period of at least 3 months each. Unless the patient is intolerant or has significant contra-indications, one of those 2 agents must be:

1. Methotrexate at a dose of 20 mg or more per week

OR

2. Leflunomide at a dose of 20 mg/day

The initial request is approved for a period of 5 months maximum.

Approvals are given for the following dosages:

Infliximab:

The approvals are for 3 mg/kg for 3 doses with the possibility to increase the dose up to 5 mg/kg after 3 doses or at week 14.

Etanercept:

The approvals are for 25 mg 2 times a week.

Continuing coverage beyond the first five months of treatment:

When requesting authorization to continue treatment, the physician must include the following information in order to demonstrate the treatment benefits:

- At least a 20% decrease in the number of joints presenting active synovitis (joint swelling) PLUS one of the 4 following elements:
 1. At least a 20% reduction in the C-reactive protein
 2. At least a 20% reduction in the sedimentation rate
 3. A 0.20 improvement on the HAQ score
 4. The patient is back to work

The first continuing coverage request is authorized for a 6-month period and subsequent continuing coverage requests will be for 12 months.

Remember to make a note in your calendar to remind your rheumatologist to apply for continuing coverage at least a month or several months before your current coverage expires.

**MODERATE TO SEVERE POLYARTICULAR OR SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS
(JUVENILE RHEUMATOID ARTHRITIS AND JUVENILE CHRONIC ARTHRITIS):**

At the time of treatment initiation or for patients already on treatment for less than 5 months:

- ❑ Before initiating treatment the patient must have 5 or more joints with active synovitis and one of these 2 following elements:
 1. Increase in CRP level
 2. Increase in sedimentation rate (ESR)

AND

- ❑ The disease is still active despite a treatment with methotrexate at a dose of 15mg/m² or more (maximum of 20mg/m²) for a period of at least 3 months, unless the patient is intolerant or has contra-indications to methotrexate.

The initial request is approved for a period of 5 months maximum.

Approvals are given for the following dosages:

Infliximab:

The approvals are for 3 mg/kg for 3 doses with the possibility to increase the dose up to 5 mg/kg after 3 doses or at week 14.

Etanercept:

The approvals are for 25 mg 2 times a week.

Continuing coverage beyond the first five months of treatment:

When requesting authorization to continue treatment, the physician must include the following information in order to demonstrate the treatment benefits:

- ❑ At least a 20% decrease in the number of joints presenting active synovitis PLUS one of the 4 following elements:
 - at least a 20% reduction in the C-reactive protein
 - at least a 20% reduction in the sedimentation rate
 - a 0.13 improvement on the CHAQ score or a return to school
 - at least a 20% improvement in the global physician assessment (visual analogue scale)
 - at least a 20% improvement in the global patient or parent assessment (visual analogue scale)

Remember to make a note in your calendar to remind your rheumatologist to apply for continuing coverage at least a month or several months before your current coverage expires.

NOVA SCOTIA

Etanercept/Infliximab

Etanercept (Enbrel®) and infliximab (Remicade®) are insured under the Nova Scotia Pharmacare Programs upon a written request of a rheumatologist, according to the following criteria:

- For patients with a diagnosis of active RA who:
 - have not responded or who have had intolerable toxicity to an adequate trial¹ of combination therapy of at least 2 traditional DMARDS²

OR

- if combination therapy is not an option, an adequate trial of at least 3 traditional DMARDS in sequence as monotherapy

AND

- patients must have had an adequate trial¹ of leflunomide. Exceptions can be considered in cases where leflunomide is contraindicated or not tolerated
- Therapy must include methotrexate³ alone or in combination unless contraindicated or not tolerated.

Notes:

1. An adequate trial for hydroxychloroquine is four months. An adequate trial for injectable gold is five months. An adequate trial for D-penicillamine is six months. For all other traditional DMARDS and for leflunomide, etanercept and infliximab, and adequate trial is three months.
2. Traditional DMARDS include methotrexate, injectable gold, sulfasalazine, hydroxychloroquine, azathioprine, chloroquine, D-penicillamine and cyclosporine.
3. Unless a person cannot tolerate it due to side effects, the methotrexate dosage should be increased up to 25 mg / wk unless response is achieved at a lower dose.

First time coverage will be approved for six months.

Continuing coverage beyond the first six months of treatment:

Reassessment for continuing yearly coverage is provided when the patient has at least a 20% improvement in symptoms.

Etanercept is administered subcutaneously at a recommended dose of 25 mg twice weekly, 72-96 hours apart. Higher doses have not been studied. The presence of renal (kidney) and/or hepatic (liver) impairment should not require a change in dosage.

Infliximab is administered as an IV infusion at a recommended dose of 3 mg / kg at week 0,2 and 6; then every 8 weeks thereafter. This medication should be administered in combination with methotrexate.

Remember to make a note in your calendar to remind your rheumatologist to apply for continuing coverage at least a month or several months before your current coverage expires.

NEW BRUNSWICK

Etanercept / Infliximab

Must be prescribed by a rheumatologist. For the treatment of patients with active rheumatoid arthritis who:

- Have not responded to, or have had intolerable side effects with, an adequate trial of combination traditional DMARD (disease modifying anti-rheumatic drug) therapy. Combination DMARD therapy must include methotrexate unless contraindicated or not tolerated.

OR

- Patients who are not candidates for combination DMARD therapy must have had adequate trial of at least three traditional DMARDs in sequence, one of which must have been methotrexate unless contraindicated.

AND

- Have had an adequate trial of leflunomide unless it is contraindicated or not tolerated.
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PRINCE EDWARD ISLAND & NEWFOUNDLAND AND LABRADOR

There is no provincial health care coverage for biologic DMARDs in these provinces and territory at this writing.

GLOSSARY OF TERMS USED IN THIS DOCUMENT

ACR 20:

This acronym stands for “American College of Rheumatology” 20; a set of criteria used to measure an individual’s improvement while they are taking a specific medication and to monitor the medication’s effectiveness over time. The ACR 20 is a research tool that specifically measures the number of swollen or tender joints, and three out of five of the following: Patient global assessment; physician global assessment; Pain; Disability; ESR or CRP etc.

BID:

A medication to be taken two times each day.

Contraindication:

Reasons or warnings that a person should not take or undergo a particular medication or treatment.

CRP

This acronym stands for “C-reactive protein”. CRP is a plasma protein in the blood. The CRP count rises in the blood with inflammatory conditions like rheumatoid arthritis.

DAS 28:

This acronym stands for “Disease Activity Scale”. Like the ACR 20 the DAS is a composite score that measures an individual’s tender and swollen joint count as well as other variables.

ESR:

This stands for “erythrocyte sedimentation rate” (also commonly referred to as the “sed rate”). The ESR is a blood test that detects and monitors inflammation in the body. Specifically, the test measures the rate that red blood cells dropped into a test tube separate from blood serum over time and become sediment in the bottom of the tube. The higher the test result number, the more inflammation is present in the body.

HAQ:

This acronym stands for “Health Assessment Questionnaire”. The HAQ is a set of questions answered by a “patient”. The questions focus on how well the patient can do typical daily activities (like bathing, preparing meals, walking, etc.). The answers provided by the patient helps physicians to better understand how well (or not) a person is doing with their disease.

IM injection:

This acronym stands for “intra-muscular” injection. Typically, this is how gold salts and a few other medications used in rheumatoid arthritis are given. It is an injection or “shot” given into a large muscle, such as the buttock muscle.

Inadequate response:

When a person fails to get as well as hoped or expected on a particular medication or therapy.

Leukopenia:

Shortage of white blood cells.

Parenteral:

A medication that enters the body through a subcutaneous, intramuscular or intravenous route.

Patient global assessment scale:

This is a visual scale that represents how active the disease is based on the patient’s viewpoint. The scale is a 10 centimetre line that ranges from “doing very well” to “doing poorly”. The patient will make a mark on the scale to indicate how he/she is doing.

Physician global assessment scale:

This is a visual scale that represents how active the disease is based on the physician’s viewpoint. The scale is a 10 centimetre line that ranges from “doing very well” to “doing poorly”. The physician will make a mark on the scale to indicate how the patient is doing.

Refractory:

A person (typically) who is not responsive to treatment.

SC injection:

This stands for “sub-cutaneous” injection. With a subcutaneous injection, a short needle (like those used to administer insulin) is inserted under the skin to deliver a medication (for example, etanercept) into the subcutaneous (“below the skin) tissues. The small blood vessels soak up the medication and it then enters the bloodstream.

Synovitis:

Where two bones come together a “joint” is formed. On the ends of each bone is a smooth material called “cartilage”. Surrounding the area where the two bones come together is an envelope of moveable soft tissue called the “joint capsule”. Lining the inside of the joint capsule are “cells”. These cells make up the “synovium”. “Synovitis” is the inflammation of the synovium.

TNF alpha:

This acronym stands for “tumour necrosis factor” alpha. TNF alpha is produced by cells in the body and plays an important role in promoting inflammation. Therapies that specifically target TNF alpha are called “biological response modifiers”.