

B.C. Ministry of Health Services Drug Coverage Decisions

About PharmaCare

B.C. PharmaCare helps British Columbians with the cost of eligible prescription drugs and specific medical supplies.

PharmaCare Coverage

The Ministry of Health Services (Ministry) makes PharmaCare coverage decisions by considering existing PharmaCare policies, programs and resources and the evidence-based recommendations of an independent advisory body called the Drug Benefit Council (DBC). The DBC's advice to the Ministry is based upon a review of many considerations, including available clinical and pharmacoeconomic evidence, clinical practice and ethical considerations, and the recommendations of the national Common Drug Review, when applicable.

Inside

Page 1 includes the Ministry decision and reasons in wording that is easier for readers without a medical background to understand. **Pages 2 and 3** summarize the DBC recommendation, the Ministry's decision and the reasons for the Ministry's decision.

Adalimumab (Humira®) for difficult to treat Crohn's disease

Understanding the DBC Recommendation and PharmaCare Coverage Decision

Background

- **Crohn's disease** is a chronic illness. Cells on the inside of the digestive tract become inflamed causing swelling and ulcers. Mostly it affects the end of the small intestine (ileum).
 - Patients with active disease have symptoms of diarrhea, abdominal pain, loss of appetite, weight loss, and fever. Patients without active disease are said to be in **remission**.
 - Some patients develop connections in the intestine called fistulas.
 - Drugs are used to control the disease or to produce remission.
- The cause of Crohn's disease is not known. However, patients have higher levels of a protein called tumor necrosis factor (TNF) which can attack healthy tissue in the body.
- **Adalimumab** has the trade name **Humira®**. This drug is given by needle into the outer layer of the skin (**subcutaneous injection**).
 - In Crohn's disease, it works by binding and blocking TNF in the body. This drug is an immunosuppressant because it suppresses the immune system.
 - It is part of the class of drugs called biological response modifiers.
 - It is also used to treat other diseases where cells cause inflammation (e.g. rheumatoid arthritis and psoriasis).

Why was this drug reviewed?

- Drug company request.

What did the review find?

- Studies in patients with Crohn's disease show treatment with adalimumab results in improved symptoms, better quality of life, and increased number of patients in remission.
- There is a concern for side effects with long-term use, i.e. infections and cancer, seen with similar drugs in this class.
- This drug is more costly than standard therapy for Crohn's disease; however, it is at least as cost-effective as drugs in the same class (i.e. infliximab). PharmaCare currently provides **limited coverage** for infliximab.

What decision was made?

- Adalimumab will have **limited coverage** at specific doses for:
 - Prescription by a gastrointestinal specialist; and
 1. Patients with medium to severe Crohn's disease not responding to, or allergic to, or unable to take: 5-aminosalicylic acid, and corticosteroids, and at least one immunosuppressive drug; or
 2. Patients with fistulas from Crohn's disease not responding to, or allergic to, or unable to take: ciprofloxacin or metronidazole, and at least one immunosuppressive drug.

Key Term(s)

- **Limited Coverage** drugs are not normally considered the first choice in treatment, or other drugs may offer better value. To receive coverage, the patient's physician must submit a Special Authority request to PharmaCare. If the request is approved, the drug is covered up to the usual PharmaCare coverage limits. Actual reimbursement depends on the rules of a patient's PharmaCare plan including any annual deductible requirement.

This document is intended for information only. It does not take the place of advice from a physician or other qualified health care provider.

Please visit us online to find out more about the Pharmaceutical Services Division and the PharmaCare program at www.health.gov.bc.ca/pharmacare. To find out more about how drugs are considered for PharmaCare coverage, visit www.health.gov.bc.ca/pharmacare/formulary.



Adalimumab (Humira®) for unresponsive Crohn's disease

Drug Class

- Biological Response Modifier

Available Dosage Forms

- 40 mg in 0.8 mL solution for subcutaneous injection

Sponsor/Requestor

- Abbott Laboratories Ltd.

Submission (Request) to PharmaCare

- Drug review of adalimumab for the following indications:
 - For adult patients with moderate to severe active Crohn's disease who have had an inadequate response to appropriate therapy such as corticosteroids, immunosuppressants, etc.
 - For adult patients with fistulizing Crohn's disease (actively draining perianal or enterocutaneous fistula) who have had an inadequate response to appropriate therapy.

Drug Benefit Council (DBC) Recommendations

- Adalimumab be listed as a limited coverage drug with the following Special Authority criteria:
 - Prescribed by gastroenterologists, and
 - For moderate to severely active Crohn's disease in patients refractory, or with contraindication, to an adequate course of 5-aminosalicylic acid and corticosteroids and other immunosuppressive therapy.
- Eligible patients should receive an induction dose of 160 mg followed by 80 mg two weeks later. Clinical response to adalimumab should be assessed four weeks after the first induction dose, using criteria such as 100 point reduction in the Crohn's Disease Activity Index (CDAI).
- Ongoing coverage for adalimumab maintenance therapy should only be provided for responders, as noted above, and for a dose not exceeding 40 mg every two weeks.
- Initial approval period: limited to 12 months in patients that respond after 4 weeks of therapy.

Reasons for the Ministry of Health Services Decision

- A literature search identified four randomized controlled trials (RCTs) comparing adalimumab to placebo in patients with moderate to severe active Crohn's disease. Two RCTs were induction trials of four weeks duration and two trials were one-year maintenance trials.
 - There is sufficient evidence from the induction therapy trials that adalimumab provides a statistically significant and clinically important improvement in clinical response (CR-70, CR-100: defined by ≥ 70 or 100 point reduction in CDAI) and rate of remission (CDAI <150 : defined as a CDAI score of less than 150) with a number needed to treat (NNT) of 4 to 7. There were also quality of life improvements (based on the Inflammatory Bowel Disease Questionnaire score) with induction therapy.
 - There are statistically significant and clinically important improvements in clinical response and rate of remission (NNT = 4), and quality of life at one year in patients that responded to induction therapy with adalimumab as defined by ≥ 70 point reduction in CDAI.
- There is a concern regarding potential for serious adverse events with long term use of adalimumab, such as infections and malignancies, as is the case with all anti-TNF agents.
- The economic model submitted by the manufacturer reported an incremental cost per quality adjusted life-year (QALY) gained of \$113,000 compared to standard therapy over a 56-week time horizon. Although incremental cost per QALY gained is in excess of traditional standards, adalimumab represents an alternative to infliximab that is at least as cost effective. Infliximab is currently provided as a **limited coverage** drug for Crohn's disease.

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Adalimumab (Humira®) for unresponsive Crohn's disease

Decision and Status

- **Limited coverage**, as per the Special Authority (page 2) criteria set-forth in the DBC recommendation and in addition for the following criteria:
 - For fistulizing Crohn's disease where the patient has lack of effect, intolerance, or contraindication to:
 - ciprofloxacin or metronidazole, and
 - one or more immunosuppressants.
- Effective September 9, 2008

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