

Drug Coverage Decision for B.C. PharmaCare

About PharmaCare

B.C. PharmaCare is a government-funded drug plan. It helps British Columbians with the cost of eligible prescription drugs and specific medical supplies.

Details of Drug Reviewed

Drug	tocilizumab
Brand Name	Actemra®
Dosage Form	162 mg/ 0.9 mL solution for subcutaneous injection in pre-filled syringe
Manufacturer	Hoffmann-La Roche Limited
Submission Type	New Indication
Use Reviewed	Giant Cell Arteritis
Common Drug Review (CDR)	Yes, CDR recommended: to Reimburse with clinical criteria and/or conditions . Visit the CDR website for more details: www.cadth.ca/sites/default/files/cdr/complete/SR0534_Actemra_GCA_complete_Mar-27-18.pdf
Drug Benefit Council (DBC)	DBC met on April 9, 2018. DBC considered: the final review completed by the CDR, which included clinical and pharmacoeconomic evidence review material and the recommendation from Canadian Drug Expert Committee (CDEC). DBC also considered Clinical Practice Reviews from one specialist, Patient Input Questionnaire responses from one patient and one Patient Group, CDR Patient Input submissions, Clinical Practice Reviews from one specialist, Other Drug Agencies Review Recommendations document prepared by the Canadian Agency for Drugs and Technologies in Health (CADTH), as well as a Budget Impact Assessment (BIA).
Drug Coverage Decision	Coverage decision: Limited Coverage Benefit. Access the tocilizumab criteria from: www.gov.bc.ca/pharmacarespecialauthority
Date	March 12, 2019
Reasons	Drug coverage decision is consistent with the DBC and CDR recommendations. <ul style="list-style-type: none"> Based on the available evidence, tocilizumab with prednisone taper was more effective than placebo with prednisone taper in achieving sustained remission in patients. There was also no signal of increased harm with tocilizumab. The Ministry of Health and the pan-Canadian Pharmaceutical Alliance (pCPA) were able to address the concerns identified by the DBC and CDR regarding the cost-effectiveness and value for money of this drug.
Other Information	None

The Drug Review Process in B.C.

A manufacturer submits a request to the Ministry of Health (Ministry).

An independent group called the [Drug Benefit Council \(DBC\)](#) gives advice to the Ministry. The DBC looks at:

- whether the drug is safe and effective
- advice from a national group called the [Common Drug Review \(CDR\)](#)
- what the drug costs and whether it is a good value for the people of B.C.
- ethical considerations involved with covering or not covering the drug
- input from physicians, patients, caregivers, patient groups and drug submission sponsors

The Ministry makes PharmaCare coverage decisions by taking into account:

- the existing PharmaCare policies, programs and resources
- the evidence-informed advice of the DBC
- the drugs already covered by PharmaCare that are used to treat similar medical conditions
- the overall cost of covering the drug

Visit the [The Drug Review Process in B.C. - Overview](#) and [Ministry of Health - PharmaCare](#) for more information.

This document is intended for information only.

It does not take the place of advice from a physician or other qualified health care provider.

Drug Benefit Council (DBC) Recommendation and Reasons for Recommendation

FINAL

**tocilizumab (Actemra®)
Hoffmann-La Roche Limited**

Description:

Drug review of **tocilizumab (Actemra®)** for the following Health Canada approved indications:

For the treatment of giant cell arteritis (GCA) in adult patients when used in combination with a tapering course of glucocorticoids.

In their review, the DBC considered the following: the final reviews completed by the Common Drug Review (CDR) on March 27, 2018, which included clinical and pharmacoeconomic evidence review material and the recommendations from the Canadian Drug Expert Committee (CDEC). The DBC also considered Patient Input Questionnaire responses from one patient and one Patient Group, CDR Patient Input submissions, Clinical Practice Reviews from one specialist, an Other Drug Agencies Review Recommendations document from the Canadian Agency for Drugs and Technologies in Health (CADTH), and a Budget Impact Assessment.

Dosage Forms:

Actemra® is available as tocilizumab 162 mg/0.9 mL solution for SC injection (pre-filled syringe).

Recommendations:

1. The Drug Benefit Council (DBC) recommends that tocilizumab (Actemra®) not be listed at the submitted price.

Of Note:

- The DBC agrees the criteria recommended by CDEC would be appropriate if the price is reduced.

Reasons for the Recommendation:

1. Summary

- One 52-week double-blind randomized placebo-controlled trial showed clear evidence of benefit in the increased proportion of patients in sustained remission and in reducing the median cumulative prednisone dose.
- Other treatments for GCA (i.e. corticosteroids) are associated with significant serious adverse events.
- At the manufacturer submitted price, the annual cost per patient for tocilizumab is significant.

2. Clinical Efficacy

- The DBC considered the CDR systematic review, which included one 52-week double-blind randomized placebo-controlled trial of patients 50 years of age or older with GCA (the GiACTA study). Patients enrolled were either newly diagnosed, or had relapsing disease, and were receiving treatment with 20 mg to 60 mg of prednisone daily.
- Patients were randomized either to tocilizumab 162 mg SC weekly with a 26-week prednisone taper, tocilizumab every other week with a 26-week prednisone taper, placebo with 26-week prednisone taper, or placebo with 52-week prednisone taper.
- The primary outcome in GiACTA was the proportion of patients in sustained remission at week 52 following induction and adherence to the protocol-defined prednisone taper regimen.
- The proportion of patients with sustained remission at week 52 was statistically significantly higher for both tocilizumab regimens compared with placebo plus 26-week taper in the intention-to-treat (ITT) population.
- The key secondary end point demonstrated the non-inferiority and superiority of both tocilizumab regimens compared with placebo plus 52-week taper in the ITT population.
- The median cumulative prednisone dose over the 52-week blinded treatment period (which included scheduled taper doses and all escape or commercial prednisone doses) was 1,862 mg in both tocilizumab groups, 3,296 mg in the placebo plus 26-week taper group, and 3,818 mg in the placebo plus 52-week taper group.
- Few clinically important differences between tocilizumab and placebo groups were detected on health-related quality of life based on the Short Form Health Survey 36 (SF-36) and Patient's Global Assessment of disease activity visual analogue scale (VAS). However, the trial was not powered for patient-reported outcomes and the instruments used may not be responsive to change in GCA patients.
- The GiACTA study was not adequately powered or of sufficient duration to evaluate longer-term GCA- and prednisone-related morbidities such as fractures and cardiovascular events, which are important to patients.
- For detailed information on the systematic review of Actemra® please see the CDEC Final Recommendation at: <https://www.cadth.ca/tocilizumab-29>.

3. Safety

- Most patients in the 52-week GiACTA study experienced one or more adverse events, including serious adverse events, which were reported in 14% to 15% of tocilizumab-treated patients and 22% to 26% of placebo-treated patients.
- Infections or infestations were the most commonly reported system organ class group of adverse events.
- The safety profile of tocilizumab is generally known, as the drug is approved in Canada for rheumatoid arthritis and juvenile idiopathic arthritis.
- For detailed information on the safety and tolerability of Actemra® please see the CDEC Final Recommendations at the links above.

4. Economic Considerations

- At the recommended dose of 162 mg administered via subcutaneous injection weekly, and at the manufacturer submitted price, the annual drug cost is \$18,663 per patient.
- The CDR reanalysis of the manufacturer's economic submission found the incremental cost utility ratio (ICUR) for tocilizumab plus prednisone was \$187,389 per quality adjusted life year (QALY) when compared with prednisone alone.
- The CDR reported that a price reduction of at least 65% for tocilizumab would be required to reduce the ICUR to \$50,000 per QALY.

5. Of Note

- Patient input from patients and patient groups, which included patients who had received tocilizumab, reported that remission rates were higher with the drug than with prednisone alone.
- Patients also reported many fewer serious adverse events with tocilizumab than with prednisone alone. Patients expressed the importance of reducing their reliance on high doses of prednisone, a corticosteroid which has several related serious adverse events such as fractures and diabetes mellitus.