

# 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

<b>Drug</b>	<b>Rituximab</b>
Brand Name	Rituxan <sup>®</sup>
Dosage Form(s)	10 mg/ml Intravenous Infusion
Manufacturer	Hoffman La Roche Ltd.
<b>Submission Type</b>	<b>Ministry Initiated</b>
Use Reviewed	Relapsing Remitting Multiple Sclerosis (RRMS)
Common Drug Review (CDR)	No, CDR did not review
Drug Benefit Council (DBC)	DBC met on May 14, 2018. DBC considered the <i>clinical evidence review of Effectiveness and Safety of Rituximab in Multiple Sclerosis</i> completed in 2017. The DBC also considered Patient Input Questionnaire responses from two patients, Clinical Practice Reviews from three specialists, and a Budget Impact Assessment
<b>Drug Coverage Decision</b>	<b>Limited Coverage Benefit for the treatment of RRMS</b> <b>Access the rituximab (Rituxan<sup>®</sup>) criteria from <a href="http://www.gov.bc.ca/pharmacarespecialauthority">www.gov.bc.ca/pharmacarespecialauthority</a></b>
Date	November 27, 2018
Reason(s)	<b>Drug coverage decision is consistent with the DBC recommendation</b> <ul style="list-style-type: none"> <li>• The drug demonstrated advantage over placebo with respect to efficacy and safety.</li> <li>• Based on economic considerations and the submitted product price, the drug was cost effective and offered value for money.</li> </ul>
Other Information	The Ministry Initiated review of rituximab for the treatment of multiple sclerosis was initiated based on the requests from physicians.

### 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

**Rituximab (Rituxan®)**  
**Hoffmann-La Roche Ltd.**

#### Description:

Ministry initiated drug review of **rituximab (Rituxan®)** for:

The treatment of all the subtypes of Multiple Sclerosis (MS), including relapsing-remitting MS (RRMS), secondary-progressive MS (SPMS), primary-progressive MS (PPMS), and progressive-relapsing MS (PRMS).

In their review, the DBC considered the *clinical evidence review of Effectiveness and Safety of Rituximab in Multiple Sclerosis* completed in 2017. The DBC also considered Patient Input Questionnaire responses from two patients, Clinical Practice Reviews from three specialists, and a Budget Impact Assessment.

#### Dosage Forms:

Rituxan® is available as rituximab 10 mg/mL intravenous injection.

#### Recommendations:

1. The Drug Benefit Council (DBC) recommends that rituximab (Rituxan®) be listed for treatment of RRMS with the following condition:
  - Patient under the care of a neurologist experienced in treating MS.

#### Of Note:

- The DBC discussed the evidence for SPMS, PPMS, and PRMS and recommended rituximab not be listed for these subtypes.

#### Reasons for the Recommendation:

##### 1. Summary

- In one clinical trial comparing rituximab and placebo, rituximab reduced gadolinium-enhancing lesions and annualized relapse rates in RRMS patients.
- One clinical trial comparing rituximab and placebo in PPMS patients found no difference in time to disease progression, a small increase in volume in lesions in both rituximab and placebo groups, and no difference in other exploratory variables, including quality of life.
- No randomized controlled trials were identified that compared rituximab with placebo or any other MS treatments in SPMS and PRMS.
- At the manufacturer list price, the annual cost of rituximab is less than other drugs that are approved for treatment of MS.

## 2. Clinical Efficacy

- The DBC considered the clinical evidence review of *Effectiveness and Safety of Rituximab in Multiple Sclerosis*, completed November 29, 2017. The review included two randomized controlled trials (RCTs) examining the effect of rituximab in MS: the Hauser study and the Hawker study.
- The Hauser study was a randomized, double-blind, placebo-controlled trial in patients with RRMS comparing rituximab, administered as a fixed 1,000 mg dose on days one and 15, with placebo. The primary outcome was the sum of gadolinium-enhancing lesions of serial T<sub>1</sub>-weighted magnetic resonance imaging (MRI) brain scans at weeks 12, 16, 20, and 24.
- The Hauser study found rituximab-treated RRMS patients had reduced numbers of brain lesions as detected by T<sub>1</sub>-weighted MRI brain scan, lower 24-week relapse rates, and lower projected annualized relapse rates (based on 24-week data).
- The Hawker study was a randomized, double-blind, placebo-controlled trial in patients with a PPMS diagnosis comparing rituximab to placebo, administered as a fixed 1,000 mg dose at weeks 0, 2, 24, 26, 48, 50, 72, and 74 weeks. The primary outcome was the time to confirmed disease progression, defined as a sustained increase in Kurtzke Expanded Disability Status Scale (EDSS) scoring of at least 1 point for patients with EDSS scores of 5.5 or less, and 0.5 points for patients with scores above 5.5. For the purposes of the outcome, the “sustained” period was defined as at least 12 weeks. Additional outcomes included the volume of T<sub>2</sub> lesions and change in brain volume at 96 weeks.
- The Hawker study’s primary end point, time to disease progression, was not different between groups at 48 weeks or 96 weeks. T<sub>2</sub> volumes increased in both groups, but to a lesser extent in the rituximab-treated patients. Brain volume was not different. The Hawker study reported several exploratory variables, including EDSS change, which was not different between groups.
- The review was unable to find RCT evidence for the use of rituximab in treating the SPMS and PRMS. The relative effectiveness of rituximab compared to other MS therapies has also not been studied in RCTs.

## 3. Safety

- The Hauser study found rituximab had a similar rate of serious adverse events as placebo.
- The Hawker study found the overall rate of adverse events in the rituximab group was similar between groups, although serious adverse events were more common in the rituximab group than in the placebo group. First-dose infusion reactions were more common in rituximab-treated patients than in placebo-treated patients.

## 4. Economic Considerations

- At manufacturer list prices, the annual cost of therapy with rituximab is significantly less than that of drugs approved for the treatment of MS, including interferons beta-1a and beta-1b, biologics (alemtuzumab, daclizumab, natalizumab, and ocrelizumab), other injectable immunomodulatory drugs (glatiramer), and oral medications (dimethyl fumarate, fingolimod, and teriflunomide).

## 5. Of Note

- Patients indicated that an IV infusion of rituximab, delivered every six months, would be preferable to the daily or weekly injections other MS treatments may require. One patient, who had tried rituximab as part of a clinical trial, indicated their quality of life had been significantly improved, especially in comparison to other MS treatments they had received.