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	**Ocrelizumab**
Brand Name	**Ocrevus™**
Dosage Form(s)	Concentrate for intravenous infusion
Manufacturer	Hoffmann-La Roche Limited
Submission Type	**New Indication**
Use Reviewed	Relapsing Remitting Multiple Sclerosis (RRMS) Primary Progressive Multiple Sclerosis (PPMS)
Common Drug Review (CDR)	**RRMS:** 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/SR0519_Ocrevus_RMS_complete_Nov-23-17.pdf **PPMS:** 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/SR0542_cdr_complete_Ocrevus_PPMS_Apr_30_18_e.pdf
Drug Benefit Council (DBC)	**RRMS:** DBC met on February 19, 2018. DBC considered various inputs including: final review completed by the Common Drug Review (CDR) on November 21, 2017, which included clinical and pharmacoeconomic evidence review material and the recommendation from the Canadian Drug Expert Committee (CDEC). The DBC also considered Patient Input Questionnaire responses from 10 patients, one caregiver and one Patient Group, Patient Group input provided to the CDR, Clinical Practice Reviews from one specialist, an Other Drug Agencies Review Recommendations document from the CDR, as well as a Budget Impact Assessment.

	PPMS: DBC met on August 4, 2018. DBC considered various imputs including: the final reviews completed by the Common Drug Review (CDR) on April 26, 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 four patients, patient input provided to the CDR, Clinical Practice Reviews from two specialists, a Budget Impact Assessment, and an Other Drug Agencies Review Recommendations document from the Canadian Agency for Drugs and Technologies in Health (CADTH).
Drug Coverage Decision	**RRMS: Non-Benefit** **PPMS: Limited Coverge Benefit** **Access the ocrelizumab criteria from www.gov.bc.ca/pharmacarespecialauthority**
Date	August 20, 2020
Reason(s)	**RRMS:** Drug coverage decision is consistent with the DBC recommendation**.** • Based on economic considerations and the submitted product price, the drug was not cost effective and did not offer optimal value for money. **PPMS:** Drug coverage decision is inconsistent with the DBC recommendation that recommended that ocrelizumab not be listed at the submitted price**.** The Ministry did not address the cost conerns identified by the DBC. However, based on the available clinical evidence, ocrelizumab meets an unmet clinical need for patients with PPMS.
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 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

Ocrelizumab (Ocrevus™)
Hoffmann-La Roche Limited

Description:

Drug review of **ocrelizumab (Ocrevus™)** for the following Health Canada approved indication:

For the treatment of relapsing-remitting multiple sclerosis (RRMS).

In their review, the DBC considered the following: final review completed by the Common Drug Review (CDR) on November 21, 2017, which included clinical and pharmacoeconomic evidence review material and the recommendation from the Canadian Drug Expert Committee (CDEC). The DBC also considered Patient Input Questionnaire responses from 10 patients, one caregiver and one Patient Group, Patient Group input provided to the CDR, Clinical Practice Reviews from one specialist, an Other Drug Agencies Review Recommendations document from the CDR, as well as a Budget Impact Assessment.

Dosage Forms:

Ocrevus™ is available as ocrelizumab 300 mg/10 mL vial (concentrate for intravenous infusion).

Recommendations:

1. The Drug Benefit Council (DBC) recommends that **ocrelizumab (Ocrevus™)** not be listed.

Reasons for the Recommendation:

1. Summary

- Two randomized controlled trials (RCTs) found that ocrelizumab was superior to interferon beta-1a in reducing the annualized relapse rate (ARR), increasing the proportion of patients with disability improvement, and increasing the proportion of patients with no evidence of disease activity at 96 weeks.
- However, there was no evidence from clinical trials comparing ocrelizumab to any of the numerous other therapeutic options for the treatment of RRMS.
- At the manufacturer submitted price, ocrelizumab is not cost-effective as it is significantly more expensive than most other drugs for treatment of RRMS.

2. Clinical Efficacy

- The DBC considered the CDR systematic review, which included two identically designed, multi-centre, parallel-group, double-blind, double-dummy, active comparator, phase III RCTs (OPERA-I and OPERA-II), which randomized patients (1:1) to receive ocrelizumab 600 mg IV once every six months or interferon beta-1a 44 mcg subcutaneously three times per week.
- In both OPERA-I and OPERA-II, ocrelizumab was superior to interferon beta-1a for reducing the ARR.

- Treatment with ocrelizumab was also associated with an increase in the proportion of patients with disability improvement and an increase in the proportion of patients with no evidence of disease activity at 96 weeks compared with interferon beta-1a. Evaluations using MRI suggest that lower proportions of ocrelizumab-treated patients developed new or newly enlarging T2 hyperintense lesions, new T1 hypointense lesions, and new T1 GdE lesions.
- No clinical trials compared ocrelizumab to the other monoclonal antibodies used to treat RRMS. The CDR reviewed two network meta-analyses, which reported that treatment with ocrelizumab as compared with natalizumab and alemtuzumab were not statistically significantly different for reducing the risk of relapse.

3. Safety

- The proportion of patients with at least one serious adverse event ranged from 6.9% to 7.0% with ocrelizumab and 7.8% to 9.6% with interferon beta-1a. Serious infections were more commonly reported for patients who received treatment with interferon beta-1a compared with the ocrelizumab group; however, opportunistic infections were more commonly reported in the ocrelizumab group. Withdrawals due to adverse events were more frequently reported in the interferon beta-1a groups compared with the ocrelizumab groups.
- Infusion-related reactions were the most commonly reported adverse events in both of the pivotal trials and occurred at a greater frequency in the ocrelizumab groups. Nearly all of the infusion-related adverse events were mild or moderate in severity and the proportion of ocrelizumab-treated patients who experienced infusion-related reactions tended to decrease over the course of the trial.

4. Economic Considerations

- At the manufacturer submitted price, the annual cost of ocrelizumab is significantly higher than the interferons, dimethyl fumarate, fingolimod, glatiramer acetate, daclizumab beta, and teriflunomide, but is less than alemtuzumab and natalizumab.
- The CDR reanalysis of the manufacturer submission found that, at the submitted price, ocrelizumab was not a cost-effective treatment for adult patients with RRMS, and that a price reduction of at least 50% of the submitted price would be required to increase the probability that ocrelizumab is cost-effective.

5. Of Note

- Patient input submitted to the DBC and to the CDR indicated that patients preferred the once every six months dosing schedule of ocrelizumab compared with treatment regimens that require more frequent dosing.

DBC Meeting – February 19, 2018
DBC Recommendation and Reasons for Recommendations

Drug Benefit Council (DBC) Recommendation and Reasons for Recommendation

FINAL

ocrelizumab (Ocrevus™)
Hoffmann-La Roche Limited

Description:

Drug review of **ocrelizumab (Ocrevus™)** for the following Health Canada approved indications:

For the treatment of primary progressive multiple sclerosis (PPMS).

In their review, the DBC considered the following: the final reviews completed by the Common Drug Review (CDR) on April 26, 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 four patients, patient input provided to the CDR, Clinical Practice Reviews from two specialists, a Budget Impact Assessment, and an Other Drug Agencies Review Recommendations document from the Canadian Agency for Drugs and Technologies in Health (CADTH).

Dosage Forms:

Ocrevus™ is available as 300 mg/10 mL single-use vial concentrate for intravenous infusion.

Recommendations:

2. The DBC recommends that ocrelizumab (Ocrevus™) not be listed at the submitted price.

Reasons for the Recommendation:

6. Summary

- In one randomized controlled trial (RCT) ocrelizumab was superior to placebo in reducing the risk of confirmed disability progression (CDP) lasting at least 12 weeks and CDP lasting at least 24 weeks, and was associated with reductions in magnetic resonance imaging (MRI) endpoints compared to placebo.
- Ocrelizumab is the only drug approved in Canada for the treatment of PPMS.
- At the manufacturer submitted price, ocrelizumab is not considered cost-effective compared with best supportive care.

7. Clinical Efficacy

- The DBC considered the CDR systematic review, which included one phase 3, multinational, multicenter, parallel-group, double-blind, placebo-controlled, RCT (ORATORIO) that randomized patients to receive IV infusions of ocrelizumab or placebo every six months.
- ORATORIO evaluated clinical endpoints (e.g., CDP), MRI endpoints (e.g., changes in T1 and T2 lesions), walking ability (timed 25 foot walk [T25FW]), and patient-reported endpoints (e.g., Short Form-36 Physical Component Summary [SF-PCS] and Short Form-36 Mental Component Summary [SF-36 MCS]).

- Ocrelizumab was superior to placebo for reducing the risk of CDP lasting at least 12 weeks and CDP lasting at least 24 weeks.
- Ocrelizumab treatment was associated with reductions in the following MRI endpoints compared with placebo: T2 lesion volume; rate of new and enlarging T2 hyperintense lesions; rate of T1 Gd-enhancing lesions; and brain volume loss.
- T25FW times increased in both ocrelizumab and placebo groups throughout the trial.
- There was no statistically significant difference between the ocrelizumab and placebo groups in change from baseline to week 120 in the SF36-PCS. Ocrelizumab-treated patients demonstrated an improvement in mean SF-36 MCS, whereas those treated with placebo experienced a reduction in mean SF-36 MCS.
- For detailed information on the systematic review of ocrelizumab please see the CDEC Final Recommendation at: https://www.cadth.ca/ocrelizumab-0.

8. Safety

- Ocrelizumab is associated with serious infusion-related reactions and increased risk of infections (overall and opportunistic infections).
- Nearly all patients experienced at least one adverse event (AE) during the double-blind phase of the ORATORIO study. Infections and infestations were the most frequently reported category of AE, with a similar frequency in the ocrelizumab and placebo groups.
- The proportion of patients who experienced a serious adverse event (SAE) categorized as an infection or infestation was similar in both the ocrelizumab and placebo groups. The proportion of patients with an SAE that was categorized as a neoplasm was greater in the placebo group compared with the ocrelizumab group.
- Malignancies were reported in a greater proportion of ocrelizumab-treated patients compared with placebo-treated patients.
- The lack of long-term safety evidence for ocrelizumab creates uncertainty with regard to its assessment of benefits versus harms.
- For detailed information on the safety and tolerability of ocrelizumab, please see the CDEC Final Recommendations at the links above.

9. Economic Considerations

- The CDR reanalysis of the cost-utility analysis submitted by the manufacturers resulted in in an incremental cost-utility ratio (ICUR) for ocrelizumab of $588,143 when compared with best supportive care (outpatient visits, rehabilitation care, hospitalizations, and medication to manage symptoms, as there are no licensed pharmacological treatments for PPMS in Canada).
- The CDR reanalysis suggested an 82% reduction in the submitted price would be required to achieve an incremental cost per quality adjust life year (QALY) of $50,000.

10. Of Note

- The DBC considered Patient Input Questionnaire responses from four patients and patient input provided to the CDR. Patients emphasized that PPMS is a debilitating, progressive disease that severely impairs their mobility, their ability to perform routine tasks, and severely impacts their quality of life.
- Patients also emphasized that ocrelizumab is the only drug approved in Canada for the treatment of PPMS.
- None of the patients responding to questionnaires had tried ocrelizumab, although most had received some other medications for symptomatic relief, and some had tried medications approved for other forms of MS. Patients noted these medications were either ineffective or were accompanied by severe side effects.

Drug Benefit Council (DBC) Recommendation and Reasons for Recommendation

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Hoffmann-La Roche Limited

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Dosage Forms:

Ocrevus™ is available as 300 mg/10 mL single-use vial concentrate for intravenous infusion.

Recommendations:

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Reasons for the Recommendation:

11. Summary

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