BRITISH COLUMBIA | Ministry of Health

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	**obeticholic acid**
Brand Name	Ocaliva
Dosage Forms	5 mg and 10 mg tablets
Manufacturer	Intercept Pharmaceuticals Canada, Inc.
Submission Type	**New Submission**
Use Reviewed	Primary biliary cholangitis (PBC)
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/SR0509_complete_Ocaliva_Jul_27_17_e.pdf
Drug Benefit Council (DBC)	DBC met on September 11, 2017. DBC considered various inputs including: clinical and pharmacoeconomic evidence review material and the recommendation from the Canadian Drug Expert Committee (CDEC). DBC also considered Clinical Practice Reviews from three specialists, and patient input from one Patient Group.
Drug Coverage Decision	**Limited Coverage Benefit.** Access the obeticholic acid criteria at: **www.gov.bc.ca/pharmacarespecialauthority**
Date	October 30, 2018
Reason(s)	**Drug coverage decision is consistent with the DBC recommendation.** • One double-blind, randomized controlled trial demonstrated that treatment with obeticholic acid produced improved liver function compared with placebo as measured by blood tests. • The DBC and CDEC recommended that price of obeticholic acid should be reduced. BC participated in the pan-Canadian Pharmaceutical Alliance (pCPA) negotiations with manufacturer and an agreement was reached.
Other Information	None

Drug Benefit Council (DBC) Recommendation and Reasons for Recommendation

FINAL

Obeticholic acid (Ocaliva™)

Intercept Pharma Canada, Inc.

Description:

Drug review of **obeticholic acid (OCA) (Ocaliva™)** for the following Health Canada approved indications:

> For the treatment of primary biliary cholangitis (PBC) in combination with ursodeoxycholic acid (UDCA) in adults with an inadequate response to UDCA, or as a monotherapy in adults unable to tolerate UDCA.

In their review, the DBC considered the following: the final reviews completed by the Common Drug Review (CDR) on July 25, 2017, 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 Groups, input from Patient Groups submitted to the CDR, Clinical Practice Reviews from three specialists, and a Budget Impact Assessment.

Dosage Forms:

Ocaliva™ is available as OCA 5 mg and 10 mg oral tablets.

Recommendations:

1. The Drug Benefit Council (DBC) recommends that Ocaliva™ be listed for treatment of PBC in combination with UDCA in:
   a. Adults with inadequate response to UDCA; or
   b. As monotherapy in patients unable to tolerate UDCA.
2. Patients should be under the care of a specialist with experience in the diagnosis and management of PBC.
3. A substantial price reduction should be negotiated with the manufacturer.

Of Note:

- OCA was granted a Notice of Compliance with conditions (NOCc) from Health Canada pending the results of ongoing trials to verify its clinical benefit.
- The cost-effectiveness of OCA is highly uncertain and the CDEC specified that a price reduction of at least 60% would increase the probability of OCA being cost-effective in the targeted populations.

Reasons for the Recommendation:

1. Summary

- One double-blind randomized controlled trial found a greater proportion of patients treated with the Health Canada approved recommended dosage of OCA achieved improved biochemical outcomes at 12 months compared with placebo.
- At the manufacturer-submitted price, the cost-effectiveness of OCA was uncertain due to limitations in the trial, but with a substantial price reduction, OCA might become cost-effective.
- PBC is a serious disease with possible life-threatening complications. The only other available PBC treatment is UDCA. Many patients have an inadequate response to UDCA and some are intolerant to it.

2. Clinical Efficacy

- The DBC considered the CDR systematic review, which included one manufacturer-sponsored multi-centre double-blind randomized controlled trial (POISE) with adult patients with PBC who either had failed to achieve targets on UDCA or had not tolerated UDCA.
- Patients in POISE were randomized in a 1:1:1 manner to 12 months of therapy with OCA 10 mg daily, placebo, or OCA starting at 5 mg and increasing to 10 mg daily after six months for those with an inadequate response.
- POISE was designed to test the superiority of each of the OCA interventions to placebo; the primary end point was to assess the superiority of the OCA 10 mg intervention to placebo. The key secondary efficacy end point was to test the superiority of the OCA titration arm to placebo, but, as OCA 10 mg is not indicated as a starting dose in Canada due to the increased risk of pruritus, this arm was not considered relevant for the review.
- A greater proportion of patients treated with the Health Canada approved recommended dosage of OCA achieved the key secondary composite endpoint (measured by alkaline phosphatase [ALP] < 1.67 times the upper limit of normal [ULN] and total bilirubin ≤ ULN and ALP decrease of at least 15% from baseline) at 12 months compared with placebo.
- There was no statistically significant difference between the OCA titration arm and the placebo arm in mean change from baseline for any of the individual components of the disease-specific health-related quality-of-life instrument (PBC-40) after 12 months.
- There was no improvement in fibrosis scores versus placebo; however, this result and the lack of clinical events may be due to the short duration of the study.
- The relatively short duration of the POISE study also makes it difficult to ascertain whether the improved biochemical outcomes experienced by patients will translate into clinically meaningful improvements in quality of life or survival.
- The majority of patients included in the POISE trial were receiving UDCA at baseline. Therefore, there is limited evidence about the safety and efficacy of OCA for patients who are intolerant to UDCA.
- For detailed information on the systematic review of OCA, please see the CDEC Final Recommendation at: https://www.cadth.ca/obeticholic-acid.

3. Safety

- In POISE, there were more serious adverse events with OCA compared with placebo, although there was no pattern of specific serious adverse events that occurred more frequently than others.
- The proportion of patients experiencing adverse events were similar with OCA compared with placebo.
- Pruritus, a key symptom of the disease itself, is the major tolerability issue associated with OCA therapy. The proportion of patients experiencing pruritus was higher in the OCA titration arm than in the placebo arm. According to the data, the extent to which pruritus became a tolerability issue appears to be dose-dependent.
- For detailed information on the safety and tolerability of OCA, please see the CDEC Final Recommendation at the link above.

4. Economic Considerations

- The DBC considered the CDR re-analysis of the manufacturer's economic submission, which concluded that the cost-effectiveness of OCA remains highly uncertain given the limited clinical evidence that is available, the limitations of the manufacturer's model, and uncertainty in the long-term clinical course of PBC.
- The CDR recommended that a price reduction would increase the probability that OCA is cost-effective for all patients who meet the Health Canada–approved indication. In combination with UDCA, a price reduction of at least 60% would be required to achieve an incremental cost-utility ratio (ICUR) of $50,000 per quality-adjusted life-year (QALY).

5. Of Note

- PBC is a serious disease that can lead to life-threatening complications and can significantly affect patients' quality of life.
- Only one other treatment for PBC, UDCA, is currently available. Approximately 40% to 50% of patients have an inadequate response to UDCA and approximately 10% of patients are intolerant.
- The Patient Group that responded indicated the few patients who had tried both UDCA and OCA noticed improvements in their quality of life on OCA. Patients emphasized the importance of having another treatment for PBC available for those who are intolerant to or who have an inadequate response to UDCA.
- More data are expected in 2023 from two trials studying the clinical effects of obeticholic acid, including death and transplant, in patients with early to advanced PBC and moderate to severe hepatic impairment.

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.