Drug Coverage Decision for BC PharmaCare

About PharmaCare BC PharmaCare is a publicly funded drug plan that helps B.C. residents pay for most prescription drugs and pharmacy services, and some medical devices and supplies.

Details of Drug Reviewed

Drug	odevixibat
Brand name	Bylvay™
Dosage form(s)	200 mcg, 400 mcg, 600 mcg and 1200 mcg oral capsules
Manufacturer	Medison Pharma Canada Inc.
Submission type	**New Submission**
Indication reviewed	For the treatment of: • pruritus in patients aged six months or older with progressive familial cholestasis (PFIC) • cholestatic pruritus in patients aged 12 months or older with Alagille syndrome (ALGS)
Canada's Drug Agency (CDA-AMC) Reimbursement Review	CDA-AMC recommended: **to Reimburse with clinical criteria and/or conditions**. Visit the CDA-AMC website for more details: • PFIC • ALGS
Drug Benefit Council (DBC) and Ministry of Health (the Ministry) Review	**PFIC**: The DBC met on May 4, 2024, to review odevixibat for the treatment of pruritus in patients aged six months or older with PFIC. In its deliberations, the DBC considered clinical and pharmacoeconomic evidence, the recommendations of the Canadian Drug Expert Committee (CDEC), patient input submitted to CDEC, and a budget impact assessment. The Ministry also received input from one clinical specialist in response to clinical questions. No Your Voice patient input questionnaire responses were received from patients, caregivers, or patient groups.

	The DBC recommended that odevixibat not be reimbursed for the treatment of pruritus in patients aged six months or older with PFIC (Appendix A). **ALGS**: The Ministry reviewed reports prepared through the CDA-AMC Reimbursement Review process, including the clinical and pharmacoeconomic evidence reviews and the recommendations of the CDEC. The Ministry also considered patient input submitted to CDEC and a budget impact assessment. In addition, the Ministry received Your Voice patient input questionnaire responses from two patient groups. No specialist input was provided in response to clinical questions.
Drug Coverage Decision	**Non-benefit**
Date	October 21, 2026
Reason(s)	**Drug coverage decision is consistent with the DBC recommendation for PFIC and with CDEC's pricing condition for ALGS.** • There is insufficient evidence to demonstrate that odevixibat provides a clinical advantage over maralixibat (Livmarli®), which is reimbursed through the Ministry's Expensive Drugs for Rare Diseases (EDRD) process for the treatment of cholestatic pruritus associated with ALGS and PFIC. • Based on the submitted price and the available economic evidence, odevixibat was not considered cost-effective and did not represent optimal value for money. • In its recommendation for ALGS, CDEC noted the absence of direct comparative evidence and limitations in the sponsor's indirect comparison of odevixibat and maralixibat. As a result, there was insufficient evidence to support a price premium for odevixibat relative to maralixibat.

The drug review process in B.C.

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

An independent group called the Drug Benefit Council (DBC) gives advice to the Ministry by considering:

- whether the drug is safe and effective
- advice from a national group called Canada's Drug Agency – L'Agence des medicaments du Canada (CDA-AMC)
- what the drug costs and whether funding it provides good value to the province
- ethical considerations of covering and not covering the drug
- input from physicians, patients, caregivers, patient groups and drug submission sponsors

The Ministry makes a BC PharmaCare coverage decision by taking into account:

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

Visit BC PharmaCare and Drug reviews 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.

Appendix A

Drug Benefit Council (DBC) Recommendation and Reasons for Recommendation

FINAL

Odevixibat (Bylvay™)
Medison Pharma Canada Inc.

Description:

Drug review of **odevixibat (Bylvay)** for the following Health Canada-approved indication:

> For the treatment of pruritus in patients aged 6 months or older with progressive familial intrahepatic cholestasis (PFIC).

In its review, the DBC considered the following: the final review completed by Canada's Drug Agency (CDA) on February 13, 2024, which included clinical and pharmacoeconomic evidence reviews and recommendations from the Canadian Drug Expert Committee (CDEC). The DBC did not receive Your Voice Patient Input Questionnaire responses from patients, caregivers, or Patient Groups, and considered patient input provided to the CDEC and a Budget Impact Assessment.

Dosage Form:

Odevixibat is available as capsules in 200 mcg, 400 mcg, 600 mcg, and 1200 mcg strengths.

Recommendation:

The Drug Benefit Council (DBC) recommends not to list odevixibat (Bylvay).

Reasons for the Recommendation:

1. **Summary**

- Results from one phase III, double-blind, randomized, placebo-controlled trial (PEDFIC 1, N=62) demonstrated that, compared to placebo, treatment with odevixibat improved pruritus based on the PRUCISION observer-reporter (ObsRO) instrument for patients with PFIC1 and PFIC2.
- The PRUCISION pruritus scale used to assess pruritus and its impact on other outcomes, such as sleep, was developed by the sponsor. The DBC noted that it is not ideal that the instrument used by the sponsor has only been validated within its own trial, rather than being externally validated in another separate trial that they were not sponsoring.
- The evidence is very uncertain about the effects of odevixibat on the need for surgery (liver transplant or biliary diversion) and the effects on health-related quality of life (HRQoL) after 24 weeks follow-up. The trial was not of sufficient

size or duration to adequately assess key clinical outcomes such as mortality or need for surgical intervention.
- Additionally, the dosing used in PEDFIC 1 and 2 did not align with the proposed product monograph for all patients, as some started on 120 mcg/kg/day, and others escalated to this dosage despite responding to the lower dose.
- A price reduction of 98.6% would be required for odevixibat plus standard of care to achieve an incremental cost-effectiveness ratio of $50,000 per quality-adjusted life year gained compared to standard of care alone.

2. Clinical Efficacy

- PEDFIC 1 (N=62) was a phase III, multicentre, double-blind, randomized, placebo-controlled study to demonstrate the efficacy and safety of odevixibat in children with PFIC1 and PFIC2.
- The primary outcome of PEDFIC 1 was the proportion of patients who experienced at least a 70% reduction in fasting serum bile acid (sBA) concentration from baseline to the end of treatment or reached a level of 70 umol/L or lower after 24 weeks of treatment.
- The secondary outcomes included the proportion of positive pruritus assessments at the patient level over the 24 week treatment period based on the PRUCISION ObsRO instrument, the change from baseline to week 24 in growth, change from baseline in sleep parameters measured with the PRUCISION PRO and ObsRO instruments by each 4-week interval over the 24-week treatment period, proportion of individual assessments meeting the definition of a positive pruritus assessment at the patient level from Weeks 0-4 and Weeks 0-12, and number of patients undergoing biliary diversion surgery or liver transplantation.
- HRQOL was assessed as an exploratory outcome using the Pediatrics Quality of Life (PEDSQL) instrument. Other safety endpoints included: adverse events, serious adverse events, and withdrawals due to adverse events.
- Although there were no deaths and no surgeries for liver transplant or biliary diversion in the study, the trial was not of sufficient size or duration to adequately assess key clinical outcomes such as mortality or need for surgical intervention.
- The proportion of patients who experienced at least a 70% reduction in fasting sBA after 24 weeks of treatment between odevixibat 40 mcg/kg/day or 120 mcg/kg/day and placebo was 44.1% and 21.6% respectively. The CDEC noted that pruritis and disease progression are more important outcomes to patients and clinicians. Additionally, the CDEC discussed that the relationship between sBA levels, disease progression, and pruritus has not been established.

- The CDA and DBC identified that the effects of odevixibat on outcomes such as sleep, eating, and growth, and the impact on patients' and caregivers' quality of life were uncertain due to the imprecision in results of the PEDFIC 1 trial.
- Additional information can be found in the CDA Final Recommendation.

3. Safety

- Treatment-emergent adverse events (TEAEs) were reported in 83% of the treatment group and 85% of the placebo group in PEDFIC 1. The most commonly reported TEAE were GI disorders and infections, with diarrhea (31%), pyrexia (29%), upper respiratory tract infection (19%), vomiting (17%), ALT increased (14%) and blood bilirubin increased (12%).
- Serious adverse events (SAEs) were reported in 7% of patients who received odevixibat and 25% who received placebo, with the most common being infection (5% and 20%, respectively). One patient discontinued the study drug due to a TEAE of diarrhea.

4. Economic Considerations

- Using the sponsor-submitted price for odevixibat and publicly listed prices for all other drug costs, the incremental cost-effectiveness ratio (ICER) for odevixibat plus standard of care was $3,462,139 per quality-adjusted life-year (QALY) gained, compared with standard of care alone. At this ICER, odevixibat is not cost-effective at a $50,000 per QALY willingness to pay (WTP) threshold for the treatment of pruritus in patients aged 6 months or older with PFIC.
- Based on public list prices, odevixibat is estimated to cost the public drug plans approximately $60 million over the next 3 years. The annual per patient cost of treatment with odevixibat is expected to be between $64,256 and $2,313,233 based on weight and dosage received.
- CADTH recommends a price reduction of 98.6% for odevixibat to be cost-effective at a $50,000 per QALY threshold.

5. Of Note

- PFIC is a spectrum of rare, inherited, liver diseases where the normal flow of bile acids is disrupted. Patients experience severe itching, which can disrupt patients' activities and negatively affect their health-related quality of life, as well as bile acids build up in the body, thus damaging the liver.
- Until odevixibat, there have been no drugs approved to treat itching specifically in PFIC. Patients often have been treated with surgeries, such as biliary diversion and liver transplant, which may be associated with risks.
- Patients identified a need for effective treatments for PFIC that reduce pruritis, delay the course of the disease, avoid, or delay the need for surgery or liver transplant, and improve HRQoL.