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	Dalbavancin hydrochloride
Brand name	Xydalba®
Dosage form(s)	500 mg dalbavancin per vial for intravenous (IV) injection
Manufacturer	Paladin Labs Inc.
Submission type	**New Submission**
Indication reviewed	for the treatment of adult patients with acute bacterial skin and skin structure infections (ABSSSI)
Canada's Drug Agency (CDA-AMC) Clinical Reimbursement Reviews (CRR)	CADTH recommended: **to Reimburse with clinical criteria and/or conditions**.Visit the CRR website for more details: dalbavancin | CDA-AMC
Drug Benefit Council (DBC)	The DBC met on January 9, 2023. The DBC considered various input, including the final reviews completed by the CRR on November 16, 2022, which included clinical and pharmacoeconomic evidence review material and the recommendations from the Canadian Drug Expert Committee (CDEC). The DBC received no Patient Input Questionnaire responses from patients, caregivers, or patient groups, and so considered patient input provided to the CRR, as well as Clinical Practice Reviews from two specialists and a Budget Impact Assessment.
Drug Coverage Decision	**Dalbavancin (Xydalba) is funded in hospitals by the Provincial Health Services Authority (PHSA). Dalbavancin (Xydalba) will be a non-benefit for PharmaCare.**
Date	September 17, 2024

Reason(s)	Drug coverage decision is consistent with the CDEC recommendation that Xydalba should be reimbursed for the treatment of adult patients with ABSSSI known or suspected to be caused by methicillin-resistant Staphylococcus aureus (MRSA) and are unlikely to adhere to outpatient antibiotic treatment or prolonged hospitalization. • Evidence from 3 randomized controlled trials (RCT) demonstrated that patients with known or suspected Gram-positive ABSSSI had similar likelihood of treatment response (based on signs and symptoms and need for new antibiotic treatment) and generally similar side effects with Xydalba as with vancomycin and IV linezolid each. • Based on CADTH's assessment of the health economic evidence, Xydalba does not represent good value to the health care system at the submitted public list price. • The Ministry participated in the pan-Canadian Pharmaceutical Alliance (pCPA) negotiations on behalf of the PHSA with the manufacturer for dalbavancin which were able to address the concerns identified by the CDEC with respect to the unknown cost-effectiveness and value for money.
Other Information	None

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 and Health Technology Agency (CADTH)
- 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

Drug Benefit Council (DBC) Recommendation and Reasons for Recommendation

FINAL

Dalbavancin (Xydalba®)
Endo Ventures Ltd.

Description:

Drug review of **dalbavancin (Xydalba®)** for the following Health Canada approved indications:

> For the treatment of adult patients with acute bacterial skin and skin structure infections (ABSSSI), caused by susceptible isolates of the following gram-positive microorganisms: *Staphylococcus aureus [including methicillin-susceptible and methicillin-resistant strains (MRSA)], Streptococcus pyogenes, Streptococcus agalactiae, Streptococcus dysgalactiae, Streptococcus anginosus group (including Streptococcus anginosus, Streptococcus intermedius, Streptococcus constellatus)* and *Enterococcus faecalis (*vancomycin susceptible strains).

In their review, the DBC considered the following: the final reviews completed by the Common Drug Review (CDR) of the Canadian Agency for Drugs and Technologies in Health (CADTH) on November 16, 2022, which included clinical and pharmacoeconomic evidence review material and the recommendations from the Canadian Drug Expert Committee (CDEC). The DBC received no Patient Input Questionnaire responses from patients, caregivers, or patient groups, and so considered patient input provided to the CDR, as well as Clinical Practice Reviews from two specialists and a Budget Impact Assessment.

Dosage Forms:

Xydalba® is available as dalbavancin hydrochloride 500 mg lyophilized powder for solution.

Recommendations:

1. The Drug Benefit Council (DBC) recommends not to list dalbavancin (Xydalba®) at the submitted price.

Of Note:

- If the Ministry is able to negotiate a significant price reduction, the reimbursement criteria and conditions recommended by CADTH are an appropriate basis for coverage.
- Dalbavancin should not be priced more than the least costly IV antibiotic treatment for adult patients with known or suspected MRSA ABSSSI.
- Dalbavancin should only be covered for patients who have known or suspected MRSA ABSSSI and are unlikely to adhere to outpatient antibiotic treatment or prolonged hospitalization.

Reasons for the Recommendation:

1. Summary

- Evidence from randomized controlled trials (RCTs) demonstrated that patients with known or suspected Gram-positive ABSSSI had similar likelihood of treatment response (based on signs and symptoms and need for new antibiotic treatment) and generally similar side effects with dalbavancin as with vancomycin and IV linezolid.
- At the manufacturer-submitted price, dalbavancin was more costly compared to other included IV antibiotic treatments. Limitations in the data concerning infection-related hospital days meant the magnitude of comparative effectiveness between treatments was unknown.

2. Clinical Efficacy

- The DBC considered the CADTH review of dalbavancin, which included four RCTs: DISCOVER 1, DISCOVER 2, DUR001-303, and VER001-9. The first 3 RCTs were considered pivotal trials by Health Canada.
- DISCOVER 1 (N = 573) and DISCOVER 2 (N = 739) were phase III, multicentre, 1:1 randomized, double-blind (DB), non-inferiority studies comparing the efficacy and safety of dalbavancin to vancomycin (with a possible switch to oral linezolid) in patients with known or suspected Gram-positive ABSSSI.
- The primary objective in both trials was to compare clinical efficacy 48 to 72 hours after study drug initiation between dalbavancin and a vancomycin and linezolid regimen.
- In both trials the key secondary objectives included: clinical response at 48 to 72 hours post study drug initiation based on measurements of ABSSSI lesion size (≥ 20% reduction in lesion area); clinical efficacy at Day 14 to 15 post study drug initiation (end of treatment [EOT] visit) based on lesion size, local signs, temperature and receipt of non-study antibiotics; and clinical efficacy at the Day 28 short-term follow-up (SFU) visit based on lesion size, local signs, temperature and receipt of non-study antibiotics.

DUR001-303 (N = 698) was a phase III, multicentre, 1:1 randomized, DB, non-inferiority study designed to compare single-dose versus 2-dose IV dalbavancin regimens in patients with known or suspected Gram-positive ABSSSI. The primary

- objective was to compare the efficacy of treatment with a single dose of dalbavancin 1500 mg to treatment with a 2-dose regimen of dalbavancin (1000 mg on Day 1 followed by 500 mg on Day 8) at 48 to 72 hours after initiation of treatment.
- Secondary objectives were clinical status at day 14 to 15 (EOT visit) and day 28 (± 2 days) post study drug initiation and safety. Other were health care resource utilization, including hospital length of stay (LOS). Patients in the single-dose group received a single dose of dalbavancin IV on Day 1, and a dalbavancin-matching placebo on day 8.
- VER001-9 (N = 854) was a phase III, multicentre, 2:1 randomized DB non-inferiority study that aimed to determine whether dalbavancin was non-inferior to IV linezolid (with a possible switch to oral linezolid) in adult patients with complicated skin and skin structure infections (SSSIs) due to Gram-positive pathogens based on clinical response, defined as survival status, temperature and no rescue therapy. The primary objective of VER001-9 was to compare the clinical efficacy and safety of dalbavancin (2-dose regimen) with that of a linezolid regimen in the treatment of adult patients with complicated SSSIs due to Gram-positive pathogens. Additional objectives included hospital utilization and LOS.
- Overall, the 2-dose regimen of dalbavancin was considered non-inferior to the comparator regimens regarding clinical response at 48 to 72 hours across the pivotal trials and at day 28 in VER001-9.
- In addition, single-dose dalbavancin was non-inferior to 2-dose dalbavancin.
- For detailed information on the systematic review of dalbavancin please see the CDEC Final Recommendation at: https://www.cadth.ca/dalbavancin.

1. Safety

- Across the pivotal trials, the number and type of treatment emergent adverse events (TEAEs) were similar between groups, with the most commonly reported TEAEs being headache, nausea, hypertension, and rash.
- In DISCOVER 1, treatment-emergent serious adverse events (SAEs) were less commonly reported in the dalbavancin treatment group than in the comparator group (1.8% versus 4.2%, respectively). In DISCOVER 2, similar numbers of treatment-emergent SAEs were reported between treatment groups. In DUR001-303, the percentages of patients with SAEs were similar across treatment groups. In VER001-9, similar rates of SAEs were reported in the dalbavancin and linezolid groups.
- The proportion of patients who discontinued treatment due to AEs was similar in the 2 treatment groups across the RCTs.
- The number of deaths were similar between groups in all trials, except for DISCOVER 1 where there were deaths in 1.8% of the vancomycin/linezolid group and none in the dalbavancin group.
- For detailed information on the safety and tolerability of dalbavancin, please see the CDEC Final Recommendations at the links above.

1. Economic Considerations

- The CADTH reanalysis of the manufacturer submission found that, given the key limitations with the available clinical evidence (including the assumption of equivalent efficacy between dalbavancin IV and active comparators, insufficient evidence to support early discharge rates associated with dalbavancin IV, and omission of oral therapies that clinical experts consulted by CADTH deemed relevant in clinical practice in Canada) the comparative clinical effects of dalbavancin IV compared to active comparators for ABSSSI were highly uncertain.
- CADTH found a lack of evidence to justify a greater cost for Xydalba® compared with other currently reimbursed IV antibiotics appropriate for the treatment of known or suspected MRSA ABSSSI (i.e. daptomycin, linezolid, and vancomycin).

2. Of Note

- CDEC noted that dalbavancin would require fewer IV administrations than comparators in patients requiring IV antibiotic treatment.