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	**ospemifene**
Brand Name	Osphena®
Dosage Form(s)	60 mg tablets
Manufacturer	Duchesnay Inc.
Submission Type	**New Submission**
Use Reviewed	Dyspareunia (pain with intercourse) and/or vaginal dryness, associated with of postmenopausal vulvovaginal atrophy
Canadian Agency for Drugs and Technologies in Health (CADTH) Reimbursement Reviews (CRR)	Yes, the CRR recommended: **to Reimburse with clinical criteria and/or conditions**. Visit the CRR website for more details: cadth.ca/sites/default/files/DRR/2022/SR0709%20Osphena%20-%20Final%20CADTH%20Rec%20Final.pdf
Drug Benefit Council (DBC)	The DBC met on June 6, 2022. In their review, the DBC considered the following: the final reviews completed by the CRR of the Canadian Agency for Drugs and Technologies in Health (CADTH), 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 two patients, as well as patient input provided to the CRR and a Budget Impact Assessment.
Drug Coverage Decision	**Non-Benefit**
Date	May 30, 2023.
Reasons	**Drug coverage decision is consistent with the DBC and CDEC recommendations.** • Ospemifene demonstrated some advantage over placebo in reducing severity of dyspareunia. • At the submitted price ospemifene was not considered cost-effective for this indication. The Ministry participated in the pan-Canadian Pharmaceutical Alliance negotiations with the

	manufacturer which were not able to address the concerns identified by the CDEC and DBC with respect to the 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 (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 Canadian Agency for Drugs and Technologies in Health (CADTH) Reimbursement Reviews(CRR)
- 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.

Appendix

Drug Benefit Council (DBC) Recommendation and Reasons for Recommendation

FINAL

Ospemifene (Osphena®)

Duchesnay Inc.

Description:

Drug review of **ospemifene (Osphena®)** for the following Health Canada approved indications:

> For the treatment of moderate to severe dyspareunia and/or vaginal dryness, associated with postmenopausal vulvovaginal atrophy (VVA).

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 May 13, 2022, 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 two patients, as well as patient input provided to the CDR and a Budget Impact Assessment.

Dosage Forms:

Osphena® is available as ospemifene 60 mg oral tablets.

Recommendations:

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

Of Note:

- Treatment with ospemifene should not cost more than treatment with the least costly vaginal estrogen product currently reimbursed for postmenopausal VVA.
- If a price reduction is achieved, ospemifene should only be reimbursed if it is not used with other estrogen therapies.

Reasons for the Recommendation:

1. Summary

- Results from 5 phase III, double-blind, placebo-controlled randomized controlled trials (RCTs) in postmenopausal women with VVA demonstrated that, in 3 trials, 12 weeks of treatment with ospemifene was associated with statistically significant improvements compared with placebo in severity of dyspareunia, percentage of vaginal superficial cells, percentage of vaginal parabasal cells, and vaginal pH.
- Results from two trials demonstrated statistically significant improvements in change in severity of vaginal dryness with ospemifene compared with placebo.
- Treatment with ospemifene is associated, in rare case, with notable harms, and there are multiple treatment alternatives available.
- CADTH estimated a price reduction of 93% in the price of ospemifene would be required for it to be considered cost-neutral compared to the lowest cost local estrogen therapy.

2. Clinical Efficacy

- The DBC considered the CADTH systematic review, which included 5 phase III, double-blind, placebo controlled RCTs in postmenopausal women with VVA: Study 310 (N = 544, excluding the ospemifene 30 mg treatment group), Study 821 (N = 919), Study 231 (N = 631), Study 718 (N = 426) and Study 310X (N = 118, continued from Study 310).
- Studies 310, 821, and 231 were designed to assess the efficacy and safety of ospemifene 60 mg over 12 weeks, Study 718 was designed to assess the efficacy and long-term safety of ospemifene 60 mg over 52 weeks, and Study 310X was a 52-week long-term safety extension (LTSE) of Study 310 that only assessed safety outcomes.
- Studies 310, 821, 231, and 718 included the following as co-primary endpoints assessed at week 12: percentage of vaginal superficial and vaginal parabasal cells on a vaginal smear, and vaginal pH. Studies 310, 821, and 231 also included severity of the most bothersome symptom (MBS) of VVA as a co-primary endpoint. Secondary endpoints assessed in 12-week studies include urinary symptoms using the Urinary Distress Inventory-Short Form (UDI-6), and sexual function (Study 821 and 231 only) using the Female Sexual Function Index (FSFI).

- Studies 310, 821, and 231 demonstrated that 12 weeks of treatment with ospemifene was associated with statistically significant improvements compared with placebo in changes of the following: severity of dyspareunia, percentage of vaginal superficial cells, percentage of vaginal parabasal cells, and vaginal pH.
- Studies 310 and 231 also demonstrated statistically significant improvements in change in severity of vaginal dryness with ospemifene compared with placebo.
- Studies 718 and 310X provided evidence of safety for up to 52 weeks of treatment with ospemifene.
- Health-related quality of life, mental health-related outcomes, bone mineral density, and adherence were identified as outcomes of interest to but were not assessed in any of the included studies.
- As the trials were placebo-controlled, none compared ospemifene with an active comparator such as estrogen therapies.
- For detailed information on the systematic review of ospemifene, please see the CDEC Final Recommendation at: https://www.cadth.ca/ospemifene.

3. Safety

- During the 12-week treatment period of Studies 310, 821, and 231, patients who received ospemifene reported adverse events (AEs) at a similar or slightly higher frequency than patients who received placebo (60%, 63%, and 35% of patients that received ospemifene vs. 52%, 51%, and 33% of patients who received placebo in Studies 310, 821, and 231, respectively). Similar results were observed during the 52-week treatment period of Study 718, although the frequency of AEs was higher overall than in the 12-week studies.
- The most commonly reported AE in each of the 4 studies was hot flashes. Vaginal infections, vaginal discharge, and muscle spasms were also commonly reported AEs more frequent with ospemifene than placebo.
- The proportion of patients reporting at least 1 serious adverse event (SAE) in Study 821 and 231 were similar between treatment groups (1.3% vs. 1.5% in Study 821 and 1.6% vs. 1.0% in Study 231 for ospemifene vs. placebo). In Study 718, 4.9% of patients in the ospemifene group and 6.5% of patients in the placebo treatment group reported at least 1 SAE.
- Patients with comorbidities such as a history of cancer or cardiovascular disorders were excluded from the trials, leading to uncertainty regarding the generalizability of the safety results.
- Safety evidence in patients who received treatment for up to 52 weeks was available, but subject to high and imbalanced discontinuation rates. Evidence of safety beyond 52 weeks is unknown.
- The Osphena Product Monograph includes serious warnings for endometrial cancer, stroke, and deep vein thrombosis and has contraindications that include estrogen-dependent neoplasia and arterial thromboembolic disease.
- For detailed information on the safety and tolerability of ospemifene, please see the CDEC Final Recommendations at the links above.

4. Economic Considerations

- At the manufacturer submitted price, ospemifene was more costly and less effective compared with local estrogen therapies.
- Based on CADTH reanalyses, at the manufacturer submitted price, ospemifene was dominated (i.e., more costly and less effective) by local estrogen therapies. A reduction of 93% in the price of ospemifene would be required for it to be considered cost-neutral to the lowest cost local estrogen therapy.

5. Of Note

- Neither of the patients who completed the Patient Input Questionnaire reported trying ospemifene. Patients reported symptoms from VVA included mild irritation and discomfort, as well as painful intercourse which can affect mental wellbeing.
- Ospemifene may provide an option for patients who prefer oral products over localized therapies, as the latter can be difficult to self-administer, particularly for patients with mobility issues or severe pain.