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	**prasterone**
Brand Name	Intrarosa™
Dosage Form	6.5 mg vaginal ovules
Manufacturer	Lupin Pharma Canada Ltd.
Submission Type	**New Submission**
Use Reviewed	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: www.cadth.ca/sites/default/files/DRR/2022/SR0707%20Intrarosa%20-%20CADTH%20Final%20Rec-meta.pdf
Drug Benefit Council (DBC)	The DBC met on June 6, 2022, and considered various inputs including: the final reviews completed by the CRR on May 3, 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 a Budget Impact Assessment.
Drug Coverage Decision	**Non-Benefit**
Date	May 30, 2023.
Reasons	**Drug coverage decision is consistent with the CDEC and DBC recommendations.** • Prasterone has demonstrated advantage over placebo in treating symptoms of postmenopausal vulvovaginal atrophy. Prasterone was not compared to existing treatments for the same indication. • At the submitted price prasterone was not considered cost-effective for the treatment of postmenopausal vulvovaginal atrophy.

	• 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 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

Prasterone (Intrarosa™)

Lupin Pharma Canada Ltd.

Description:

Drug review of prasterone (Intrarosa™) for the following Health Canada approved indications:

For the treatment of postmenopausal vulvovaginal atrophy.

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 3, 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 a Budget Impact Assessment.

Dosage Forms:

Intrarosa™ is available as a vaginal ovule with 6.5 mg of prasterone.

Recommendations:

1. The Drug Benefit Council (DBC) recommends not to list prasterone (Intrarosa™) at the submitted price.

Of Note:

- The cost of listing prasterone (Intrarosa™) should not exceed the price of conjugated estrogens (Premarin®).

Reasons for the Recommendation:

1. Summary

- Results from clinical trials showed that treatment with prasterone 6.5 mg intravaginal ovule daily for 12 weeks was associated with statistically significant improvements compared with placebo in change from baseline to week 12 in severity of dyspareunia, severity of vaginal dryness, percentage of vaginal superficial cells, percentage of vaginal parabasal cells, and vaginal pH in patients with postmenopausal VVA with moderate to severe dyspareunia as the most bothersome symptom.
- The clinical trials compared prasterone with placebo, and no comparative data between prasterone and other active comparators was available. The trials also did not include health-related quality of life (HRQoL) measures.
- At the manufacturer's submitted price, prasterone is more costly compared with most vaginal estrogen therapies. CADTH estimated a price reduction of 89% would be required for prasterone to be considered cost-effective.

2. Clinical Efficacy

- The DBC considered the CDEC systematic review, which included three trials: ERC-238, ERC-231, and ERC-230.
- ERC-238 was a phase III, double-blind, placebo-controlled, multicentre trial to compare the efficacy of 12 weeks of treatment with a once-daily intravaginal prasterone ovule at 0.5% (N = 374) compared with a once-daily intravaginal placebo ovule (N = 180) on pain at sexual activity (dyspareunia) in postmenopausal individuals aged 40 years to 80 years with dyspareunia as their most bothersome symptom of VVA.
- ERC-231 was a phase III, double-blind, placebo-controlled, multicentre trial that assessed the efficacy of intravaginal prasterone at 6.5 mg (N = 87) or 3.25 mg compared with placebo (N = 80) in postmenopausal individuals with moderate to severe dyspareunia as their most bothersome symptom of VVA at baseline. Only the prasterone 0.5% (6.5 mg) group was considered relevant for the CADTH review because this is the dose approved by Health Canada. The trial duration was 12 weeks.
- ERC-230 was a phase III, open-label, single-group study (N = 521) that examined the long-term safety of daily treatment with intravaginal prasterone (6.5 mg). The trial duration was 52 weeks.
- The co-primary end points of ERC-238 and ERC-231 included percentage of parabasal cells, percentage of superficial cells, vaginal pH, and severity of dyspareunia score. Secondary end points included sexual function (measured using the Female Sexual Function Index [FSFI]), vaginal dryness, vaginal irritation and/or itching, and safety.
- The primary objective of ERC-230 was to evaluate the long-term safety of prasterone in postmenopausal individuals with VVA; safety was assessed through AEs, mammography, Papanicolaou (Pap) test, endometrial biopsy, and other outcomes. Secondary end points of ERC-230 trial included percentage of parabasal cells, percentage of superficial cells, vaginal pH, severity score of dyspareunia, sexual function (measured using the FSFI), vaginal dryness, and vaginal irritation and/or itching.

- Results from ERC-238 and ERC-231 showed that treatment with prasterone 6.5 mg intravaginal ovule daily for 12 weeks was associated with statistically significant improvements compared with placebo in change from baseline to week 12 in severity of dyspareunia, severity of vaginal dryness, percentage of vaginal superficial cells, percentage of vaginal parabasal cells, and vaginal pH in patients with postmenopausal VVA with moderate to severe dyspareunia as the most bothersome symptom.
- ERC-230 was supportive of maintained efficacy of prasterone for up to 52 weeks of treatment.
- Health-related quality of life (HRQoL) was not assessed in the ERC-238, ERC-231, and ERC-230 trials.
- As the trials did not include and active comparator, there was insufficient evidence to support a clinical benefit with prasterone versus relevant comparators.
- There are limited data for long-term efficacy and safety of prasterone considering that postmenopausal VVA is a chronic condition.
- There is limited evidence available to support the efficacy and safety of prasterone in individuals with postmenopausal VVA who have contraindications (e.g., active or confirmed history of thromboembolism or estrogen-dependent cancer) to vaginal estrogen therapies.
- For detailed information on the systematic review of prasterone (Intrarosa™) please see the CDEC Final Recommendation at: https://www.cadth.ca/prasterone.

3. Safety

- The proportion of patients reporting at least one adverse event (AE) in the ERC-238 trial was similar in both treatment groups: 179 patients (47.9%) in the prasterone group and 77 patients (42.8%) in the placebo group. In the ERC-231 trial, there was a higher proportion of patients with at least one AE in the prasterone group than the placebo group: 46 (52.9%) patients in the prasterone group and 35 (43.8%) patients in the placebo group. A greater proportion of AEs were reported in the ERC-230 trial, with 418 patients (80.2%) experiencing AEs.
- The most commonly reported AEs across all trials were application site discharge (ERC-238: 6.1% in the prasterone group versus 5.6% in the placebo group; ERC-231: 5.7% versus 6.3%, respectively; ERC-230: 14.0% in the prasterone group) and urinary tract infections (4.5% in the prasterone group versus 2.8% in the placebo group; ERC-231: 5.7% versus 5.0%, respectively; ERC-230: 10.2% in the prasterone group
- Serious AEs (SAEs) were rare in all trials, and few patients discontinued treatment due to an AE in any of the trials.
- There is no evidence to support a safety benefit with prasterone over vaginal estrogen therapies; however, prasterone does not have the same contraindications and serious warnings that are associated with vaginal estrogen therapies.
- Because of the short length of the trials, longer follow-up is required to better understand the long-term safety of prasterone and whether it provides any safety benefit over vaginal estrogen therapies.
- For detailed information on the safety and tolerability of prasterone, please see the CDEC Final Recommendations at the links above.

4. Economic Considerations

- At the manufacturer's submitted price, prasterone was more costly compared with most vaginal estrogen therapies.
- Based on CADTH reanalyses of the manufacturer's submission, prasterone was dominated by conjugated estrogen cream given prasterone was more costly than CE cream while being equally effective. CADTH estimated a price reduction of 89% would be required for prasterone to be considered cost-effective.

5. Of Note

- Vaginal estrogen therapies have contraindications for certain patient populations (e.g., patients with breast cancer or a history of breast cancer, venous thromboembolism, or arterial thromboembolic disease) and serious warnings (some based on evidence from systemic estrogen replacement therapies) that can cause hesitancy in individuals for whom local estrogen therapies are appropriate.
- Patient input provided to CADTH indicated that many patients experienced vaginal dryness, decline in libido, and urinary problems, which significantly impacted their quality of life.