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	roflumilast
Brand name	Zoryve™
Dosage form(s)	0.3% topical cream
Manufacturer	Arcutis Biotherapeutics, Inc.
Submission type	**New Submission**
Indication reviewed	Topical treatment of plaque psoriasis (PsO), including treatment of PsO in the intertriginous areas (skin folds), in patients 12 years of age and older.
Canada's Drug Agency (CDA-AMC) Clinical Reimbursement Reviews (CRR)	CDA-AMC recommended: **to Reimburse with clinical criteria and/or conditions**. Visit the CDA-AMC website for more details.
Drug Benefit Council (DBC)	The DBC met on November 6, 2023. The DBC considered various inputs, including clinical and pharmacoeconomic evidence review material and the Canadian Drug Expert Committee (CDEC) recommendations. The DBC also considered Patient Input Questionnaire responses from one patient and three patient groups, as well as patient input provided to the CDA-AMC, a Clinical Practice Review from one specialist, and a Budget Impact Assessment (BIA).
Drug Coverage Decision	**Non-benefit**
Date	December 12, 2024
Reasons	**Drug coverage decision is consistent with the CDEC and DBC recommendations that roflumilast be reimbursed on the condition that its**

	price does not exceed the cost of the least costly topical therapy reimbursed for the treatment of PsO: • Results from 2 phase III, double-blind, parallel-group, randomized, vehicle-controlled clinical trials demonstrated that Zoryve improves severity of psoriasis, including intertriginous areas, and reduces the severity of itch compared to treatment with vehicle (placebo). • There were no active comparators in the clinical trials. Thus, there was insufficient evidence to show that Zorvye has advantages over its comparators with respect to efficacy, safety and/or quality of life. • Based on the CDA-AMC's assessment of the health economic evidence, Zoryve does not represent good value to the health care system at the public list price. The DBC determined that there is not enough evidence to justify a greater cost for Zoryve compared with the least expensive topical therapy reimbursed for the treatment of PsO. • 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.

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

Roflumilast (Zoryve™)
Arcutis Biotherapeutics Inc.

Description:

Drug review of **roflumilast (Zoryve™)** for the following Health Canada approved indications:

> For topical treatment of plaque psoriasis, including treatment of psoriasis in the intertriginous areas, in patients 12 years of age and older.

In their review, the DBC considered the following: the final reviews completed by the Common Reimbursement Review (CRR) of the Canadian Agency for Drugs and Technologies in Health (CADTH) on August 16, 2023, which included clinical and pharmacoeconomic evidence review material and the CADTH recommendations. The DBC also considered Patient Input Questionnaire responses from one patient and three patient groups, as well as patient input provided to the CRR, a Clinical Practice Review from one specialist, and a Budget Impact Assessment.

Dosage Forms:

Zoryve™ is available as roflumilast 0.3% (3 mg of roflumilast per gram) cream.

Recommendations:

1. The Drug Benefit Council (DBC) recommends not to list roflumilast for topical treatment of plaque psoriasis, including treatment of psoriasis in the intertriginous areas, in patients 12 years of age and older.

Reasons for the Recommendation:

1. Summary

- Results from 2 clinical trials demonstrated that Zoryve improves severity of psoriasis, including intertriginous areas (skin folds) and reduced the severity of itch compared to treatment with vehicle.
- The DBC agrees with CDEC that an active comparator would have been more appropriate. In a chronic and common disease, such as plaque psoriasis, with a wide range of alternative treatment options available, a comparative clinical trial is feasible and should have been included.
- At the manufacturer's submitted price, Zoryve is not considered cost-effective and there is insufficient evidence to justify a greater cost for Zoryve compared with the least expensive topical therapy reimbursed for the treatment of plaque psoriasis.

2. Clinical Efficacy

- Two phase III, randomized, double-blind, parallel-group, vehicle-controlled trials (DERMIS-1, N = 439 and DERMIS-2, N = 442) that assessed success in Investigator Global Assessment (IGA), defined as an IGA score of clear or almost clear plus a 2-grade or more improvement from baseline at week 8, with roflumilast cream 0.3% compared to matching vehicle in patients with chronic plaque psoriasis involving 2% to 20% body surface area (BSA) (excluding the scalp, palms, and soles) were included in the sponsor's submission.
- IGA is an investigator-reported static evaluation of the overall severity of psoriasis of the whole body. The minimal important difference (MID) in IGA has not been estimated. However, achieving a score of 0 (clear) or 1 (almost clear) on the IGA has generally been accepted as clinically meaningful. The primary endpoint, IGA success at week 8, was met for both trials in the intention-to-treat (ITT) population.
- Secondary outcomes included measures of symptoms and involvement and measure of Quality of Life (QoL). Exploratory outcomes included measures of involvement (e.g., BSA), measures of health-related quality of life (HRQoL), local tolerability, and safety.
- Intertriginous psoriasis refers to psoriasis affecting the groin, axillae, inframammary region, abdominal body folds, gluteal cleft, perianal region, and retroarticular fold areas. Intertriginous-Investigator Global Assessment (I-IGA) was defined as the IGA scale but was used to evaluate only intertriginous areas in the trials. In both trials, an improvement in the severity of intertriginous psoriasis was measured based on the proportion of patients who achieved I-IGA success (defined as a score of 0 [clear] or 1 [almost clear] plus a ≥ 2-grade improvement from baseline) at week 8, which was a secondary endpoint tested in a hierarchical manner and adjusted for multiple comparisons. In both trials, the proportion of patients who achieved I-IGA success was greater in the roflumilast treatment groups compared to vehicle.
- Psoriasis Area and Severity Index (PASI) is an investigator-reported evaluation of the extent and severity of psoriasis. An MID in PASI has not been estimated. In both trials, an improvement in the extent and severity of disease was measured based on the proportion of patients who achieved PASI-75 (75% improvement in PASI) at week 8, which was a secondary endpoint tested in a hierarchical manner and adjusted for multiple comparisons. In both trials, the proportion of patients who achieved PASI-75 was greater in the roflumilast treatment groups compared to vehicle.
- Evidence from 1 indirect comparison (ITC) suggests that Zoryve may provide a benefit compared to other topical treatments used alone, including vitamin D analogues, tazarotene, and corticosteroids, but the magnitude of benefit is uncertain.
- The results of the ITC did not clearly demonstrate that treatment with Zoryve offered a benefit over combination therapies (including corticosteroids plus vitamin D analogues and corticosteroids plus tazarotene, or calcineurin inhibitors) for patients with intertriginous involvement.
- For detailed information on the systematic review of roflumilast please see the CDEC Final Recommendation at: https://www.cadth.ca/roflumilast-0.

3. Safety

- There were no safety or tolerability concerns associated with the use of topical roflumilast identified by the CADTH review.
- For detailed information on the safety and tolerability of roflumilast, please see the CDEC Final Recommendations at the links above.

4. Economic Considerations

- The CADTH reanalysis of the manufacturer submission included other topical treatments for plaque psoriasis as comparators such as high-potency corticosteroids, vitamin D analogues, tazarotene, corticosteroids plus vitamin D analogues, and corticosteroids plus tazarotene.

- Compared with corticosteroids, roflumilast was associated with incremental quality adjusted life-years (QALYs) of 0.0005 (equivalent to 4 quality adjusted life hours over a 5-year time horizon) and an incremental cost-effectiveness ratio (ICER) of $1,085,171 per QALY gained. A price reduction of at least 74% is required for roflumilast to be considered cost-effective compared to corticosteroids at a willingness to pay threshold of $50,000 per QALY.

5. Of Note

- Input received from one patient with plaque psoriasis emphasized that many current treatments were ineffective, or were effective but inconvenient to use (e.g., phototherapy, which cannot be managed at home) or difficult to tolerate (e.g., corticosteroids) or could not be used in all affected areas.
- Of the patient group input received, ten patients reported having tried roflumilast through participation in a clinical trial. Nine patients reported noticeable benefits while using roflumilast, including significant clearing of skin, reduced itch, and redness, and clearing of skin plaques. Patients noted that roflumilast was easy to use and could be used in all affected areas, including the face.
- Roflumilast may fulfill an unmet clinical need for patients with face and intertriginous involvement where other available agents may not be desirable, not appropriate, or not tolerated.