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	**deferiprone**
Brand Name	Ferriprox™
Dosage Form(s)	1,000 mg oral tablet 100 mg/mL oral solution
Manufacturer	Chiesi Canada Corp.
Submission Type	**New Submission**
Use Reviewed	For the treatment of patients with transfusional iron overload due to sickle cell disease (SCD) or other anemias.
Canadian Agency for Drugs and Technologies in Health (CADTH) Reimbursement Reviews (CRR)	Yes, CRR recommended: **to Reimburse with clinical criteria and/or conditions**. Visit the CRR website for more details: Deferiprone (Ferriprox) (cadth.ca)
Drug Benefit Council (DBC)	The DBC met on March 3, 2023. The DBC considered various inputs including: the final reviews completed by the CADTH CRR on February 07, 2023, which included clinical and pharmacoeconomic evidence review material and the CADTH recommendations. The DBC received no Patient Input Questionnaire responses from patients, caregivers, or patient groups, and instead considered patient input provided to the CRR, as well as a Budget Impact Assessment.
Drug Coverage Decision	**Non-Benefit**

Date	March 14, 2024
Reason	• This drug coverage decision is consistent with the CDEC recommendation to reimburse Ferriprox for the treatment of patients with transfusional iron overload due to SCD or other anemias, only if the cost of Ferriprox does not exceed the drug program cost for the lowest cost iron chelation therapy used to treat transfusional iron overload associated with the treatment of SCD or other anemias. • This drug coverage decision is also consistent with the DBC recommendation not to list Ferriprox for the treatment of patients with transfusional iron overload due to SCD or other anemias. • Evidence from a clinical trial and an indirect comparison suggested that Ferriprox was similarly effective compared to deferoxamine (DFO) and deferasirox (DFX) for reducing the concentration of iron in the liver of patients with transfusional iron overload. • At the manufacturer-submitted price for Ferriprox and publicly listed prices for DFO and DFX, Ferriprox was more costly than both other options. • Based on CDEC's review, Ferriprox is not cost-effective. There is insufficient evidence to justify a greater cost for Ferriprox compared with DFO and DFX. • The pan-Canadian Pharmaceutical Alliance (pCPA) was involved in negotiations with the manufacturer for Ferriprox, but on October 27, 2023, the negotiations concluded without an agreement. BC did not participate in the pCPA negotiations because of the DBC recommendation not to list.
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

Deferiprone (Ferriprox™)

Chiesi Canada Corp.

Description:

Drug review of **deferiprone (Ferriprox™)** for the following Health Canada approved indications:

For the treatment of patients with transfusional iron overload due to sickle cell disease (SCD) or other anemias.

In their review, the DBC considered the following: the final reviews completed by the Canadian Agency for Drugs and Technologies in Health (CADTH) on February 07, 2023, which included clinical and pharmacoeconomic evidence review material and the CADTH recommendations. The DBC received no Patient Input Questionnaire responses from patients, caregivers, or patient groups, and instead considered patient input provided to the CDR, as well as a Budget Impact Assessment.

Dosage Forms:

Ferriprox™ is available as deferiprone 1000 mg oral tablet and 100 mg/mL oral solution.

Recommendations:

1. The Drug Benefit Council (DBC) recommends not to list deferiprone (Ferriprox™).

Reasons for the Recommendation:

1. Summary

- Results from one 12-month, open-label, randomized, pivotal trial demonstrated that orally administered deferiprone was noninferior to subcutaneously (SC) administered deferoxamine for change from baseline in liver iron concentration (LIC) and serum ferritin (SF) in patients with SCD and other anemias who require iron chelation therapy for transfusional iron overload.
- Treatment with defiriprone may be associated with rare but serious adverse events (SAEs) (i.e., severe neutropenia and agranulocytosis) as well as with an increased number of other SAEs compared with deferoxamine, including sickle cell crisis and neutropenia.
- At the manufacturer-submitted price for deferiprone and publicly listed prices for deferasirox and deferoxamine, deferiprone was more costly than both other options.

2. Clinical Efficacy

- The DBC considered the CADTH clinical review, which included two studies: FIRST (N = 213) and Calvaruso et al. (2014) (N = 60).
- FIRST was a pivotal, late-phase (phase IV in the US, phase IIIb in other countries), multicentre, randomized, open-label, noninferiority study comparing the efficacy and safety of deferiprone versus deferoxamine in patients with SCD or other transfusion-dependent anemias. The primary end point of FIRST was change from baseline in LIC after 12 months. For noninferiority, the upper limit of the 96.01% CI could be no more than 2 mg/g dw. Secondary outcomes included changes in cardiac iron concentration (CIC), SF, and health-related quality of life (HRQoL).
- Calvaruso et al. (2014) was a 5-year multicentre open-label randomized controlled trial (RCT) to compare the safety and efficacy of deferiprone versus deferoxamine in Italian patients. Eligible patients were randomized (1:1) to receive either deferiprone or deferoxamine for up to 12 months. The primary outcome was a reduction in SF and patients were considered responders if their SF values < 400 ng/mL.
- CDEC noted there were serious limitations with Calvaruso et al. (2014), including concerns about generalizability of the study population to the Canadian setting, the small sample size, and considerable loss to follow-up.
- Results from FIRST demonstrated that orally administered defiriprone was non-inferior to SC administered deferoxamine for change from baseline in LIC, SF, and cardiac iron in patients with SCD and other anemias who require iron chelation therapy for transfusional iron overload.
- For detailed information on the systematic review of deferiprone please see the CDEC Final Recommendation at: https://www.cadth.ca/deferiprone-0.

3. Safety

- In FIRST, at least 1 adverse event (AE) was reported for 88.2% of patients in the defiriprone group and 88.2% of patients in the deferoxamine group.
- At least one SAE was reported for 26.3% of patients in the defiriprone group and 18.4% of patients in the deferoxamine group. The most frequent SAE was sickle cell crisis, experienced by 10.5% of defiriprone patients and

5.3% of deferoxamine patients; followed by pyrexia in 3.3% and 3.9%, respectively; neutropenia in 2.6% and 1.3% respectively, abdominal pain in 2.0% and 1.3% respectively, and acute chest syndrome in 2.0% and 0.0% respectively.

- In FIRST, 12 patients withdrew due to AEs, 5.9% versus 3.9% in the defiriprone and deferoxamine groups, respectively. 5 of 12 withdrawals were considered to be at least possibly related to study treatment, 4 were in the defiriprone group: 1 event of agranulocytosis, 1 of mild neutropenia that lasted beyond 14 days, and 2 of abdominal pain and vomiting (both moderate in 1 patient, both severe in the other). The 1 case in the deferoxamine group was due to severe nausea.
- Of notable harms, agranulocytosis occurred in 1 patient in the defiriprone group, compared to zero (0) patients in the deferoxamine group. Neutropenia occurred in 4 patients in the defiriprone group, compared to 1 patient in the deferoxamine group.
- For detailed information on the safety and tolerability of deferiprone, please see the CDEC Final Recommendations at the links above.

4. Economic Considerations

- At the manufacturer-submitted price for deferiprone and publicly listed prices for deferasirox and deferoxamine, deferiprone was more costly than both deferoxamine and deferasirox.
- As deferiprone is considered noninferior to deferoxamine, CADTH recommended that the total drug cost of deferiprone should not exceed the total drug cost of deferoxamine and deferasirox;.

5. Of Note

- Renal dysfunction was highlighted as a common complication in patients with SCD and consequently some patients may experience intolerance to deferasirox. For others, the SC or IV administration of deferoxamine may not be a feasible treatment option.