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	**iron isomaltoside 1000**
Brand Name	Monoferric®
Dosage Form(s)	100 mg/mL solution for intravenous (IV) administration
Manufacturer	Pfizer Canada Inc.
Submission Type	**New Submission**
Use Reviewed	Treatment of Iron Deficiency Anemia (IDA)
Common Drug Review (CDR)	Yes, CDR recommended: **Reimburse**. Visit the CDR website for more details: https://www.cadth.ca/sites/default/files/cdr/complete/SR0622%20Monoferric%20-%20CDEC%20Final%20%20Recommendation%20March%2027%2C%202020%20for%20posting.pdf
Drug Benefit Council (DBC)	The DBC met on June 1, 2020, and considered various inputs including: the final reviews completed by the Common Drug Review (CDR) on March 25, 2020, 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 2 patients and 4 caregivers, a summary of CDR Patient Group Input, an Other Drug Agencies Review Recommendations document prepared by the Canadian Agency for Drug and Technologies in Health (CADTH), an Abbreviated Formulary Drug Review by British Columbia Health Authorities Pharmacy and Therapeutics (BCHA P&T), Clinical Practice Reviews from one specialist, and a Budget Impact Assessment. • See Appendix for DBC Recommendation and Reasons
Drug Coverage Decision	**Limited Coverage Benefit. Access the iron isomaltoside criteria from www.gov.bc.ca/pharmacarespecialauthority**

Date	October 6, 2021
Reason(s)	**Consistent with the recommendations of CDEC and DBC.** • Iron isomaltoside is similar to iron sucrose (Venofer) with respect to efficacy, safety and quality of life in adult patients with IDA who have intolerance or unresponsiveness to oral iron therapy. • Based on the submitted product price, iron isomaltoside was more expensive than iron sucrose, and according to the CDR review, the cost-effectiveness of iron isomaltoside compared to iron sucrose is uncertain. • The Ministry participated in the pan-Canadian Pharmaceutical Alliance negotiations with the manufacturer which were able to address some of the concerns identified by the CDEC with respect to the uncertainty in the cost-effectiveness and value for money. • On October 6, 2021 the Ministry will list iron isomaltoside as a Limited Coverage benefit with criteria, and at the same time modify iron sucrose to be Limited Coverage benefits with the same criteria.
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 Common Drug Review (CDR)
- 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: DBC Recommendation and Reasons

Drug Benefit Council (DBC) Recommendation and Reasons for Recommendation

FINAL

Iron Isomaltoside 1000 (Monoferric)
Pfizer Canada Inc.

Description:

Drug review of **iron isomaltoside 1000 (Monoferric)** for the following Health Canada approved indications:

> For the treatment of iron deficiency anemia (IDA) in adults who have an intolerance or unresponsiveness to oral iron.

In their review, the DBC considered the following: the final reviews completed by the Common Drug Review (CDR) on March 25, 2020, 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 2 patients and 4 caregivers, a summary of CDR Patient Group Input, an Other Drug Agencies Review Recommendations document prepared by the Canadian Agency for Drug and Technologies in Health (CADTH), an Abbreviated Formulary Drug Review by British Columbia Health Authorities Pharmacy and Therapeutics (BCHA P&T), Clinical Practice Reviews from one specialist, and a Budget Impact Assessment.

Dosage Forms:

Monoferric is available as iron isomaltoside 100 mg/mL elemental iron solution for injection.

Recommendations:

1. The Drug Benefit Council (DBC) recommends not to list iron isomaltoside 1000 (Monoferric) at the submitted price.

Of Note:

- If the price of iron isomaltoside 1000 is reduced to the same or lower than that of iron sucrose, the Ministry should consider listing iron isomaltoside 1000 as per the CDEC recommendation.

Reasons for the Recommendation:

- Evidence from four randomized controlled trials (RCTs) showed that iron isomaltoside 1000 was non-inferior to iron sucrose in raising and/or maintaining hemoglobin (Hb) levels.
- At the manufacturer submitted price, iron isomaltoside 1000 was more costly than iron sucrose.

1. Summary

- The CDR review of four randomized controlled trials (RCT) found that iron isomaltoside 1000 was non-inferior to iron sucrose in raising and/or maintaining hemoglobin (Hb) levels.
- At the manufacturer submitted price, iron isomaltoside 1000 is significantly more costly than the publicly available price of iron sucrose.
- Limitations in the manufacturer's pharmacoeconomic analysis increased the uncertainty regarding the cost-effectiveness of iron isomaltoside 1000.

2. Clinical Efficacy

- The DBC considered the CDR review, which included four Phase III, multi-centre, open-label, parallel group, active-control, non-inferiority, randomized controlled trials (RCTs) (PROPOSE, FERWON-Nephro, PROVIDE and FERWON-IDA) comparing iron isomaltoside 1000 to iron sucrose in patients with IDA.
- All four trials showed iron isomaltoside 1000 to be non-inferior to iron sucrose in raising and/or maintaining hemoglobin (Hb) levels.
- In PROVIDE trial, the majority of patients required a greater mean cumulative iron dose with iron isomaltoside 1000 compared to iron sucrose (1640.20 mg vs. 1127.9 mg); this reduces some of the health system benefits of iron isomaltoside.
- The health related quality of life outcomes of energy, fatigue and overall quality of life were found to not be different for either iron sucrose or iron isomaltoside across the majority of included trials.
- For detailed information on the systematic review of iron isomaltoside 1000 please see the CDEC Final Recommendation at: https://www.cadth.ca/iron-iii-isomaltoside-1000.

3. Safety

- The safety profile of iron isomaltoside 1000 and iron sucrose were similar in three of the four included trials. Iron isomaltoside 1000 participants in the PROPOSE trial had a slightly higher frequency of treatment-emergent adverse events, serious adverse events and withdrawals due to adverse events compared to iron sucrose.
- Adverse event rates for iron isomaltoside are either numerically higher or similar to iron sucrose in the published clinical trials.
- As per information provided by the BCHA P&T review, the relative safety of iron isomaltoside versus iron sucrose remains uncertain. Post-marketing surveillance data in Australia and European countries has raised safety concerns.
- The product monographs and prescriber information for both iron isomaltoside and iron sucrose contain serious warnings regarding reports of serious hypersensitivity reactions including life threatening and fatal anaphylactic/anaphylactoid reactions.
- For detailed information on the safety and tolerability of iron isomaltoside 1000, please see the CDEC Final Recommendations at the links above.

4. Economic Considerations

- At the manufacturer-submitted price, iron isomaltoside 1000 is more costly than the publicly available price of iron sucrose.
- The CDEC reanalysis of the manufacturer's pharmacoeconomic submission found that differences in infusion time and frequency may lead to savings in total costs with iron isomaltoside 1000 compared with

iron sucrose (e.g., from reduced supplies, and shorter chair time and nursing time), which may benefit some budget holders (i.e., hospitals), while other payers may observe increased costs (i.e., public drug plans).
- Limitations in the manufacturer's pharmacoeconomic analysis (particularly the exclusion of adverse events from the analysis) increased the uncertainty regarding the cost-effectiveness of iron isomaltoside 1000.

5. Of Note
- Other IV iron products for treatment of IDA include: iron sucrose (Venofer), indicated for treatment of IDA in non-dialysis-dependent chronic kidney disease (NDD-CKD) with or without erythropoietin, hemodialysis-dependent (HDD)-CKD with erythropoietin, and peritoneal-dialysis-dependent (PPD)-CKD patients with erythropoietin; and sodium ferric gluconate complex in sucrose (Ferrlecit), indicated for the treatment of IDA in chronic HDD-CKD patients receiving erythropoietin.
- In 2016 and 2020 respectively, the iron dextran products Infufer and Dexiron were discontinued by the manufacturers.
- On Jan 17, 2020, the Ministry listed iron sucrose as a regular benefit to ensure at least one IV iron product would be available.

DBC Meeting – June 1, 2020
DBC Recommendation and Reasons for Recommendations