BRITISH COLUMBIA | Ministry of Health

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	**mecasermin**
Brand Name	Increlex®
Dosage Form(s)	10 mg/mL sterile solution for subcutaneous injection in 5 mL (40mg/4mL) multi-dose vials
Manufacturer	Ipsen Biopharmaceuticals Canada Inc.
Submission Type	**New Submission**
Use Reviewed	Treatment of growth failure in children and adolescents from 2 to 18 years with confirmed severe primary insulin-like growth factor-1 deficiency (SPIGFD).
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.
Drug Benefit Council (DBC)	The DBC met on March 7, 2022. In their review, the DBC considered the following: the final reviews completed by the CRR of the CADTH on January 21, 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 thus considered patient input provided to the CRR, Clinical Practice Reviews from a specialist, and a Budget Impact Assessment. The DBC recommended that mecasermin not be listed for the treatment of growth failure in children and adolescents from 2 to 18 years with confirmed severe primary insulin-like growth factor-1 deficiency (SPIGFD).

mecasermin (Increlex®)

Drug Coverage Decision	**Non-Benefit; Exceptional Case-by-Case Coverage through the Expensive Drugs for Rare Diseases (EDRD) Process**
Date	April 27, 2023
Reason(s)	**Drug coverage decision is consistent with the CADTH recommendations.** • Mecasermin demonstrated a statistically significant benefit on increased height velocity in children with open epiphyses and diagnosed growth failure due to SPIGFD. • There is an unmet need for drug therapy indicated for growth failure in children and adolescents with confirmed SPIGFD. • Limitations of the trial meant no conclusions could be made on the effects of mecasermin on important subsequent endpoints, such as functional status and health-related quality of life. • Based on economic considerations and the submitted product price, the drug was not cost-effective and did not offer optimal value for money. • The Ministry of Health participated in the pan-Canadian Pharmaceutical Alliance (pCPA) negotiations with the manufacturer and the pCPA was able to address the concerns identified by CADTH with respect to the cost-effectiveness and value for money.
Other Information	See the DBC Recommendation & Reasons.

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

Mecasermin (Increlex®)
Ipsen Biopharmaceuticals Canada Inc.

Description:

Drug review of **mecasermin (Increlex®)** for the following Health Canada approved indications:

> For the treatment of growth failure in children and adolescents from 2 to 18 years with confirmed severe primary insulin-like growth factor-1 deficiency (SPIGFD).

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 January 21, 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 thus considered patient input provided to the CDR, Clinical Practice Reviews from a specialist, and a Budget Impact Assessment.

Dosage Forms:

Increlex® is available as mecasermin 5 mL multi-dose vial, with each vial containing 4 mL (40 mg) of solution.

Recommendations:

1. The Drug Benefit Council (DBC) recommends not to list mecasermin (Increlex®).

Reasons for the Recommendation:

1. **Summary**

- Results from one phase III, multi-centre, single arm, open-label trial demonstrated that mecasermin increases height velocity in children with open epiphyses and diagnosed growth failure due to SPIGFD.
- Limitations in the trial design mean it is not possible to establish a causal link between the treatment and the growth outcomes and harms, nor is it possible to draw any conclusions regarding the potential benefit of mecasermin on quality of life or on other clinical outcomes identified as being important to patients.

- The cost-effectiveness of mecasermin is highly uncertain given we are unable to establish a causal link between treatment and outcomes. Exploratory analyses conducted by CADTH estimated a reduction in price of at least 92% would be required for mecasermin to achieve an incremental cost-effectiveness ratio (ICER) of $50,000 per quality-adjusted life year (QALY).

2. Clinical Efficacy

- The DBC considered the CDEC systematic review, which included one phase III, multi-centre, single arm, open-label trial (Study 1419, N = 92) in children with open epiphyses and diagnosed with growth failure due to SPIGFD associated with either growth hormone (GH) receptor defects or GH-deletion defects and anti-GH antibodies.
- The primary efficacy outcomes of Study 1419 were height velocity, near-adult height, and estimated improvement in near-adult height. Secondary efficacy outcomes were height velocity standard deviation (SD) score, height SD score, change in bone age relative to change in chronological age, and body mass index (BMI) SD score.
- During year 1 of mecasermin treatment, there was an increase in mean (SD) height velocity from 2.6 (1.7) cm per year at baseline to 8.0 (2.3) cm per year. Height velocities for years 2 through 8 of treatment remained greater than baseline (i.e., 5.9 [1.7] cm per year in year 2 and 4.4 [1.5] cm per year in year 8).
- Due to the rare and severe nature of SPIGFD, a randomized control group may not have been feasible or ethical. As a result, the findings are at high risk of confounding and is not possible to establish a causal link between the treatment and the growth outcomes and harms.
- Due to the design limitations of Study 1419, it is not possible to determine with certainty the clinical significance of changes in height on treatment, and how the observed changes in height and height velocity would differ from untreated patients.
- Clinical outcomes other than height were not assessed in Study 1419; therefore, it is not possible to draw any conclusions pertaining to the potential benefit of mecasermin on other clinical outcomes such as heart strength, lung capacity, and bone strength, which are outcomes identified as important to patients.
- Health-related quality of life (HRQoL) was not measured in Study 1419; therefore, it is not possible to draw any conclusions pertaining to the potential benefit of mecasermin on HRQoL.
- A large proportion of patients (62%) discontinued treatment early, many (33%) of whom were lost to follow-up before attaining near-adult height. There is a high risk that the long-term efficacy and harms data could be biased due to missing outcomes for these patients.
- For detailed information on the systematic review of mecasermin please see the CDEC Final Recommendation at: https://www.cadth.ca/sites/default/files/DRR/2022/SR0692REC-Increlex_JH_BF-meta.pdf

3. **Safety**

- Seventy-six (83%) patients in Study 1419 had at least 1 adverse event (AE). The most reported AEs included metabolism and nutrition disorders, general disorders and administration site conditions, infections and infestations, respiratory, thoracic, and mediastinal disorders, gastrointestinal disorders, nervous system disorders, and musculoskeletal and connective tissue disorders.
- Eighteen (20%) patients had at least 1 serious adverse event (SAE) that required hospitalization. No patient withdrew from the study due to an AE and no patient died during the study. The most frequently reported notable harms included hypoglycemia, lipohypertrophy at the injection site, tonsillar hypertrophy, and adenoidal hypertrophy.
- For detailed information on the safety and tolerability of mecasermin, please see the CDEC Final Recommendations at the links above.

4. **Economic Considerations**

- The cost-effectiveness of mecasermin is highly uncertain due to the lack of robust clinical and safety data in comparison with best supportive care (BSC), as well as uncertainty in the impact of the predicted gain in height on patient quality of life over their lifetime.
- Exploratory analyses conducted by CADTH determined the ICER was likely closer to the estimate of $624,249 per QALY gained. Mecasermin is not cost-effective at a $50,000 per QALY willingness-to-pay threshold.
- A price reduction of at least 92% for mecasermin would be required for mecasermin to achieve an ICER of $50,000 per QALY compared to best supportive care (BSC).

5. **Of Note**

- SPIGFD is a rare disease, with an estimated 4.9 cases per year in BC, of which up an estimated 2 patients would be candidates for treatment. Mecasermin is the first Health Canada-approved treatment for SPIGFD.
- A patient group submission to CADTH from the International Coalition of Organizations Supporting Endocrine Patients (ICOSEP) indicated that although short stature is the most visible symptom of SPIGFD, it also affects everyday activities like getting out of bed, playing with others, and concentrating on tasks.
- The patient group submission to CADTH identified the need for a treatment that would also improve heart strength, lung capacity, and bone strength.