INESSS
LE SAVOIR PREND FORME

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Glassia™ – Congenital alpha$_1$-antitrypsin deficiency

English summary

Une production de l'Institut national d'excellence en santé et en services sociaux (INESSS)

Québec

SUMMARY

Glassia™ – Congenital alpha$_1$-antitrypsin deficiency

Mandate

At the request of the manufacturer, Takeda Canada Inc., the Institut national d'excellence en santé et en services sociaux (INESSS) assessed Glassia™, a human alpha$_1$-proteinase inhibitor. In Canada, Glassia™ is indicated for chronic augmentation and maintenance therapy in adults with clinically evident emphysema due to severe hereditary deficiency of alpha1-PI, also known as alpha$_1$- antitrypsin deficiency. The indication requested from INESSS was the same.

INESSS conducted simultaneous assessments of Prolastin™-C Liquid, Zemaira™ and Glassia™, all human plasma alpha$_1$-antitrypsin products. Recommendations for these 3 products were published at the same time.

Assessment Approach

A review of data from the literature and those provided by the manufacturer was conducted to document the efficacy, safety, and cost-effectiveness of Glassia™. In addition, contextual and experiential data from expert consultation were mobilized and integrated. Efficiency and budget impact analyses were developed by INESSS.

Population Dimension

Alpha$_1$-proteinase inhibitor deficiency, or alpha$_1$-antitrypsin deficiency (DAAT), is a rare genetic condition with variable presentation that can lead to severe pulmonary (emphysema, chronic bronchitis, and bronchiectasis) and hepatic symptoms, often with a slow progression. Due to the heterogeneous and often delayed clinical manifestations as well as the discovery of new pathogenic variants associated with the disease, DAAT is an under-diagnosed condition. Usual treatments are aimed at alleviating respiratory symptoms and include inhaled medications, pulmonary rehabilitation and, for some patients, augmentation therapy consisting of weekly intravenous administration of plasma-derived alpha$_1$-antitrypsin (AAT). Augmentation therapy aims to slow the progression of emphysema in individuals with DAAT. Currently, only Prolastin™-C is available in Quebec, and public reimbursement is possible only through the “mesure du patient d’exception”.

Treatments that halt or slow the progression of emphysema and the deterioration of lung and liver function would meet current healthcare needs, especially if they were to improve the quality of life of affected individuals and their families. Facilitating access to augmentation therapy is also desired.

Clinical Dimension

Assessment of the therapeutic value of Glassia™ was based on 1 bioequivalence study with Prolastin™ and a *post hoc* analysis of the same study.

Efficacy

- In individuals with DAAT, the human plasma ATT Glassia™ product is considered bioequivalent to Prolastin™ since it has a comparable pharmacokinetic profile.
- No data on the ability of Glassia™ to slow the progression of emphysema in individuals with DAAT have been submitted by the manufacturer or reported in the literature.

Safety

- The safety profile of Glassia™ is considered acceptable and comparable to that of Prolastin™.

Organizational Dimension

Coverage for human plasma AATs is currently provided by the RAMQ through the *mesure du patient d'exception* and private insurance plans. From now on, plasma AATs will have to be registered on the *Liste des produits du système du sang du Québec* and win a tender by Héma-Québec before they can be distributed. During this management change, it would be prudent to avoid treatment interruptions and minimize the consequences that could be associated with them.

Economic Dimension

Efficiency Analysis

At the submitted price, Glassia™ would generate savings of $ [redacted] per week compared with Prolastin-C™, whose efficiency has not been evaluated prior to this assessment.

Budget Impact Analysis

Should Glassia™ be added to the *Liste des produits du système du sang du Québec,* an increase in the number of patients can be expected due to patients currently using Prolastin™-C through the private drug insurance plan to continue their AAT inhibitor treatment through the public plan. This increase in the number of people covered by the public system ([redacted] %) would translate into additional costs estimated at over $ 8 million over 3 years.

Socio-Cultural Dimension

In 2022, Quebec adopted a policy aimed at optimizing access to quality health care and services that are adapted to the specific needs of culturally sensitive patients with rare diseases. Some experts recognize that Quebec is at the forefront of care for several rare diseases, including DAAT, compared to other Canadian provinces.

Therapeutic Value Decision

INESSS recognizes the therapeutic value of Glassia™ for chronic augmentation and maintenance therapy in adults with clinically evident emphysema due to severe hereditary deficiency of alpha1-PI, also known as alpha$_1$- antitrypsin deficiency. The reasons for this recognition are as follows:

- The importance of the health needs for this rare condition is recognized for the treatment of emphysema secondary to DAAT.
- Glassia™ is considered bioequivalent to Prolastin™. It should be noted that the therapeutic value of AATs Prolastin™, Prolastin™-C and Prolastin™-C Liquid has been recognized by INESSS.
- The safety profile of Glassia™ appears to be comparable to that of Prolastin™ based on frequencies of adverse events between groups in the bioequivalence study.
- There is concern about under-diagnosis of the condition and suboptimal management of a less severely affected population that could also benefit from treatment.

Overall Assessment

INESSS is of the opinion that it is fair and reasonable to add Glassia™ to the *Liste des produits du système du sang du Québec* for chronic augmentation and maintenance therapy in adults with clinically evident emphysema due to severe hereditary deficiency of alpha1-PI, also known as alpha$_1$- antitrypsin deficiency. The reasons for this position are as follows:

- The therapeutic value of Glassia™ is recognized solely based on a conclusion of bioequivalence with Prolastin™.
- Although Glassia™ is [redacted] than Prolastin™-C at the price submitted by the manufacturer, neither of these AATs is effective compared to best supportive care. Based on recent assessments (Zemaira™ and Prolastin™-C Liquid) for the treatment of severe AAT deficiency, augmentation therapy in addition to best supportive care (BSC) compared to BSC alone would require a price reduction of between 86 % and 90 % or between 70 % and 75 % to achieve efficiency thresholds of $ 50,000 and $ 100,000 per QALY, respectively.
- The increase in the budgetary impact due to individuals with DAAT switching from private insurance coverage to public management by Héma-Québec is significant.
- The burden of administering a weekly intravenous product in specialized clinics is recognized. The implementation of a home administration program for patients who want so would be desirable and would improve their quality of life and reduce the use of specialized resources.

- It is important to ensure overlap between the current RAMQ access model and the future Héma-Québec model, in order to avoid treatment disruption for these patients.
- In a competitive tendering context, the addition of Glassia™ to the *Liste des produits du système du sang du Québec* represents a therapeutic alternative to other AAT products on the *Liste des produits du système du sang* for the population targeted by the indication.

INESSS RECOMMENDATION FOR Glassia™

In light of the available data, INESSS recommends the addition of Glassia™ to the *Liste des produits du système du sang du Québec* for chronic augmentation and maintenance therapy in adults with clinically evident emphysema due to severe hereditary deficiency of alpha1-PI, also known as alpha$_1$- antitrypsin deficiency.

Recommendation Clarification

Considering the claims of bioequivalence between Prolastin™-C Liquid, Zemaira™ and Glassia™, reimbursement of Glassia™ for the requested indication would be a responsible, fair, and equitable decision, if its cost were the lowest during the next call for tenders by Héma-Québec.

Clarification for Decision-Makers

In Héma-Québec's next call for tenders for AATs, the indications for the 3 products Prolastin™-C Liquid, Zemaira™ and Glassia™ could be grouped under the common indication "for the treatment of emphysema in adults with AATs."

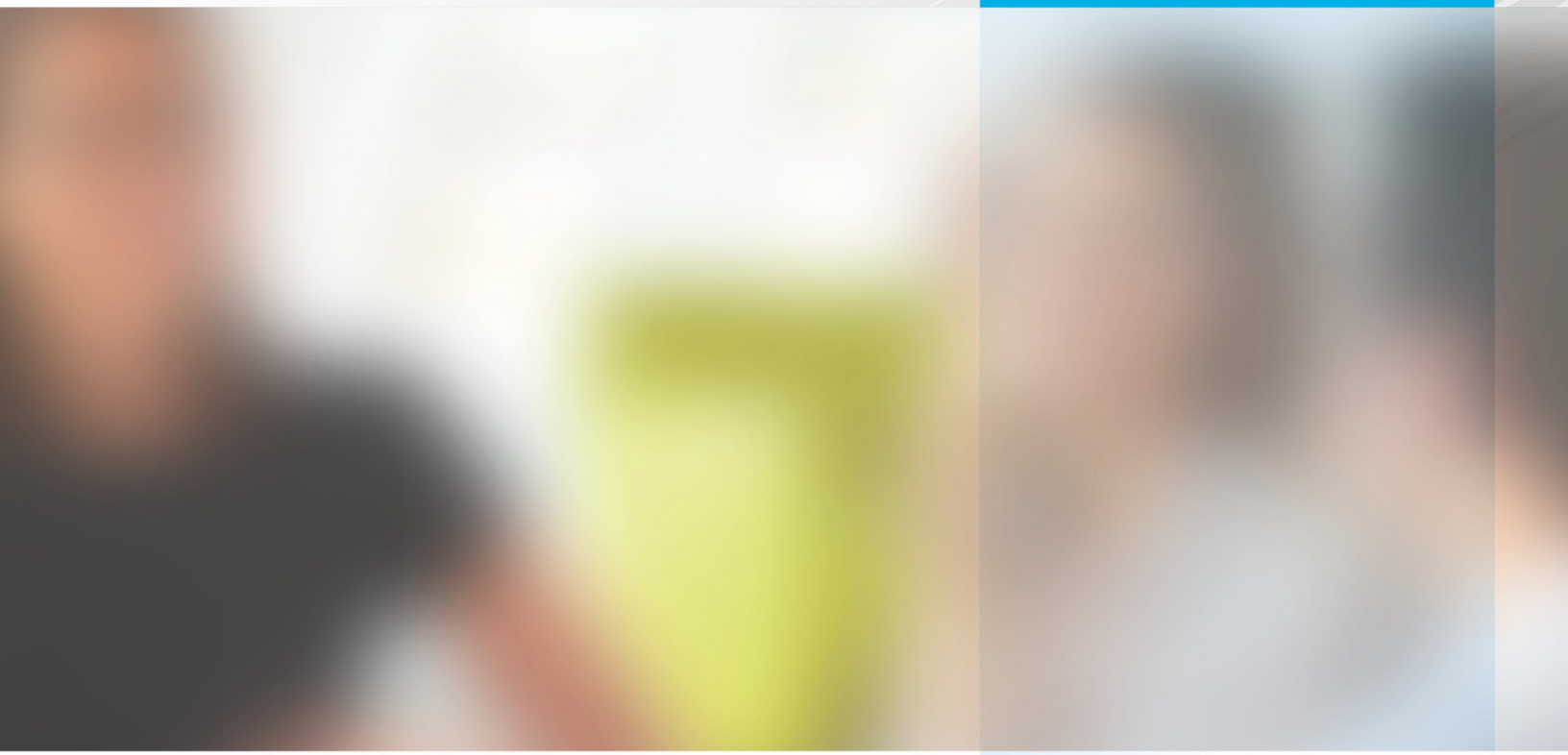
Consistent with the recommendations of the Canadian Thoracic Society, the historical access criteria of the *mesure du patient d'exception* for Prolastin™-C and the perspectives of the experts consulted, as well as in the interest of optimal use of human blood-derived products, INESSS considers that plasma alpha$_1$-antitrypsin on the *Liste des produits du système du sang* should be reserved for the following population:

- for the treatment of emphysema in adults:
  - with a clinical presentation of progressive lung disease;

    and
  - with FEV_1 between 25 % and 80 % of predicted value;

    and
  - with demonstrated alpha$_1$-antitrypsin deficiency (plasma concentration ≤ 11 µmol/L or clinically relevant genotype) ;

    and
  - under optimal pharmacological and non-pharmacological treatment.



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