CADTH

CADTH REIMBURSEMENT REVIEW

Stakeholder Feedback on Draft Recommendation

Alpha1-proteinase inhibitor (Human) (Zemaira)

(CSL Behring Canada, Inc.)

Indication: Severe Alpha1-proteinase inhibitor deficiency

March 31, 2022

CADTH

CADTH Reimbursement Review

Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	ST0702
Name of the drug and Indication(s)	Alpha1-proteinase inhibitor (human) (Zemaira) for maintenance treatment in adults with severe A1-PI deficiency (e.g. genotypes PiZZ, PiZ(null), Pi(null,null), PiSZ) and clinical evidence of emphysema
Organization Providing Feedback	FWG

1. Recommendation revisions
Please indicate if the stakeholder requires the expert review committee to reconsider or clarify its recommendation.

Request for Reconsideration	**Major revisions:** A change in recommendation **category** or patient **population** is requested	☐
	Minor revisions: A change in reimbursement **conditions** is requested	☐
No Request for Reconsideration	**Editorial revisions:** Clarifications in recommendation **text** are requested	☒
	No requested revisions	☐

2. Change in recommendation category or conditions
Complete this section if major or minor revisions are requested

Please identify the specific text from the recommendation and provide a rationale for requesting a change in recommendation.

3. Clarity of the recommendation
Complete this section if editorial revisions are requested for the following elements

a) Recommendation rationale

Please provide details regarding the information that requires clarification.

b) Reimbursement conditions and related reasons

Please provide details regarding the information that requires clarification.

1) Page 4, table 1, prescribing condition 5:
"Reimbursement of Zemaira should not be associated with a limitation on dosing"
Suggest changing the text as follows:
"Reimbursement of Zemaira should allow to compensate for missed doses"
If overall dose per patient remains same, there is no reason to highlight a negative condition.
The recommended text captures clinical experts' rationale on dosing more appropriately. Also, it

would be reasonable to move this text to discussion point rather than having a condition that conflicts with the product monograph recommended dosing and frequency.

c) Implementation guidance

Please provide high-level details regarding the information that requires clarification. You can provide specific comments in the draft recommendation found in the next section. Additional implementation questions can be raised here.

1) Page 5 Discussion points, fourth bullet – Please explain why percent reduction is different than what is mentioned in the table 1 i.e., 93% vs 84%.

2) Please explain the role of the Patient Support Program if product will be given/administered in the hospital?

3) In 4.2 Prescribing implementation guidance:
Suggest Removal of the following statement: Access to Zemaira may require coordination amongst the public drug plans and hospital physicians as respirologists managing these patients may not have prescribing privileges in the hospital or health jurisdiction where the patient may be getting their infusion.
Rationale: Drug Plans do not coordinate access to products through CBS.

Outstanding Implementation Issues

In the event of a positive draft recommendation, drug programs can request further implementation support from CADTH on topics that cannot be addressed in the reimbursement review (e.g., concerning other drugs, without sufficient evidence to support a recommendation, etc.). Note that outstanding implementation questions can also be posed to the expert committee in Feedback section 4c.

Algorithm and implementation questions
1. Please specify sequencing questions or issues that should be addressed by CADTH (oncology only)
1. 2.
2. Please specify other implementation questions or issues that should be addressed by CADTH
1. Page 4, Table 1, Initiation – reimbursement condition: need implementation guidance on following condition as we can not operationalize this in its current state: "Zemaira should be reimbursed in adults with severe A1-PI deficiency (e.g. genotypes PiZZ, PiZ(null), Pi(null,null), PiSZ) and clinical evidence of emphysema " According to clinical experts and as mentioned in the table 2, lab tests and genetic tests are available in all or most provinces. Therefore, we need guidance on how to use these test results to confirm severe A1-PI deficiency. Also, we need guidance on how to measure clinical evidence of emphysema.

Support strategy
3. Do you have any preferences or suggestions on how CADTH should address these issues?
May include implementation advice panel, evidence review, provisional algorithm (oncology), etc. 1. Recommendation on implementation guidance A) To confirm severe A1-PI deficiency: - lab test cut-off for serum AAT level, for e.g., <11 micromol/L before start of the treatment, and - Guidance for genetic test, e.g., documented genotype of PiZZ, PiZ (null), or Pi (null, null), PiSZ AAT deficiency or other equivalent rare genotypes associated with serum AAT concentrations of less than 11 micromol/L B) To confirm clinical evidence of emphysema, provide threshold to measure Forced expiratory volume in 1 second (FEV1).

Alpha-1 Canada Response to the CADTH Draft Recommendation: Stakeholder Feedback on Alpha1-proteinase inhibitor (human) (Zemaira)

Alpha-1 Canada welcomes the opportunity to provide stakeholder feedback regarding the Zemaira CADTH draft recommendation. On behalf of our staff, board of directors and the patient community that we serve, we would like to thank the Canadian Agency for Drugs and Technologies in Health (CADTH) for conducting a rigorous review and for the thorough engagement with our organization throughout the process.

Alpha-1 Canada was reassured that the Canadian Plasma-Related Expert Committee (CPEC) used data from clinical studies proving that augmentation therapy can maintain protective levels of AAT; moreover, that augmentation formulations are disease-modifying plasma protein therapies to treat severe alpha-1 deficiencies, limited to SZ, ZZ, and null genotypes, and some of the rare variants that are considered equivalent.

Alpha-1 Canada is pleased with the CADTH draft recommendation and deems the criteria outlined in the recommendation as satisfactory and the groundwork for establishing a new category/class on the Canadian Blood Services national formulary. Establishing a dedicated augmentation therapy category on the Canadian Blood Services Plasma Protein & Related Products Formulary, to protect the health of Canadian alpha-1 patients, will contribute to an increased quality of life for Canadian alpha-1 patients and reduce the cost on the broader health care system.

The Canadian Plasma-Related Expert Committee agreed with the clinical experts that reimbursement criteria should be identical for both Zemaira and Prolastin-C, which warrants a broader examination regarding how additional brands of augmentation therapy can be listed and accessed through the nation's blood operator, recognizing that acute shortages can, and have occurred in the supply of IG and PPPs over the past few decades. This will also ensure business continuity for the nation's blood operator and uninterrupted supply for Canadian patients.

Due to alpha-1 antitrypsin deficiency being a rare disease and the only specific treatment being a plasma-protein augmentation therapy, there is a high cost associated with the treatment. This is not dissimilar to other rare disease treatments and other plasma protein products that are listed with the nation's blood operator; hence, the suggested reduction in price of Zemaira at 93% is not aligned with other PPPs. The costs associated with providing augmentation therapies should be commensurate with other plasma protein products considering the comparable fractionation processes involved. PPPs are high-cost therapies for rare blood disorders; hence, listing and purchasing PPPs through Canadian Blood Services' pan-Canadian approach gives provincial and territorial health systems bulk-buying power; however, a 93% reduction in price for Zemaira is not feasible, considering it is a biologic.

Alpha-1 Canada values the Canadian Plasma-Related Expert Committee's assessment of Zemaira for the treatment of severe alpha-1 antitrypsin deficiency. The nefarious nature of this disease has no bounds and therefore cannot be properly managed in a country where there has been such an unpredictable patchwork of care. The historical inequities in access to augmentation therapy, both with public and private payers has been dire for severely affected alpha-1 patients in Canada; therefore, our organization commends CADTH and the CPEC for validating the benefits of augmentation therapy, so we can now move forward with establishing an equitable pathway for Canadian alpha-1 patients to access the only specific therapy to treat this genetic disease.

Angela Diano, Executive Director
Submitted March 31, 2022