CADTH

CADTH REIMBURSEMENT REVIEW

Stakeholder Feedback on Draft Recommendation

ASPARLAS (calaspargase pegol)

(**Servier Canada Inc.**)

Indication: A component of a multi-agent chemotherapeutic regimen for the treatment of acute lymphoblastic leukaemia (ALL) in pediatric and young adult patients age 1 to 21 years.

December 14, 2023

CADTH

CADTH Reimbursement Review

Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0321
Name of the drug and Indication(s)	Calaspargase pegol as a component of a multi-agent chemotherapeutic (MAC) regimen for the treatment of acute lymphoblastic leukemia (ALL) in pediatric and young adult patients age 1 to 21 years
Organization Providing Feedback	PAG

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	X
	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.

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Publication Date: TBC
Report Length: 2 Pages

b) Reimbursement conditions and related reasons
Please provide details regarding the information that requires clarification.
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. PAG requested adding mixed or biphenotypic leukemia under Considerations for initiation of therapy. In the discussion point, pERC agreed to extend to Ph+, Down syndrome, and T-cell ALL. PAG requested adding these 3 indications and the mixed/biphenotypic leukemia to Table 2 (p.9).

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. 2.
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.

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0321-000-000
Brand name (generic)	calaspargase pegol (Asparlas)
Indication(s)	A component of a multi-agent chemotherapeutic regimen for the treatment of acute lymphoblastic leukaemia (ALL) in pediatric and young adult patients aged 1 to 21 years.
Organization	The Leukemia & Lymphoma Society of Canada (LLSC)
Contact information[a]	Name: Colleen McMillan, Advocacy Lead [redacted]

Stakeholder agreement with the draft recommendation		
1. Does the stakeholder agree with the committee's recommendation.	Yes	☒
	No	☐
We agree with the committee's recommendation as this treatment may meet patients' need for effective treatments that have manageable side effects, improve quality of life, and ensure a more reliable drug supply and less frequent drug administration while offering a manageable toxicity profile, and less frequent drug administration, as well as an extended shelf life, which may support a more stable supply. We thank CADTH very much for this recommendation.		
Expert committee consideration of the stakeholder input		
2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☒
	No	☐
Clarity of the draft recommendation		
3. Are the reasons for the recommendation clearly stated?	Yes	☒
	No	☐
4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☒
	No	☐
5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☒
	No	☐

[a] CADTH may contact this person if comments require clarification.

Appendix 1. Conflict of Interest Declarations for Patient Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.

A. Patient Group Information	
Name	*Colleen McMillan*
Position	*Advocacy Lead*
Date	*07-12-2023*
☒	I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

B. Assistance with Providing Feedback		
1. Did you receive help from outside your patient group to complete your feedback?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
2. Did you receive help from outside your patient group to collect or analyze any information used in your feedback?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		

C. Previously Disclosed Conflict of Interest		
1. Were conflict of interest declarations provided in patient group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section D below.	No	☒
	Yes	☐

D. New or Updated Conflict of Interest Declaration

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Servier Canada Inc.	☒	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0321
Brand name (generic)	ASPARLAS® (calaspargase pegol)
Indication(s)	A component of a multi-agent chemotherapeutic regimen for the treatment of acute lymphoblastic leukaemia (ALL) in pediatric and young adult patients age 1 to 21 years.
Organization	Servier Canada Inc. (Servier)
Contact information[a]	[redacted]

Stakeholder agreement with the draft recommendation		
1. Does the stakeholder agree with the committee's recommendation.	Yes	☒
	No	☐

Servier agrees with the committee's recommendation that ASPARLAS be reimbursed as a component of a multi-agent chemotherapeutic (MAC) regimen for the treatment of acute lymphoblastic leukemia (ALL) in pediatric and young adult patients age 1 to 21 years, in line with the reimbursement conditions outlined in Table 1 of the recommendation document.

ONCASPAR (pegaspargase) is the established standard of care (SOC) *E. coli*-derived pegylated asparaginase product, incorporated across Canada as part of standard clinical practice and clinical trials. Gains in overall survival (OS), along with the demonstrated importance of completing planned asparaginase therapy to reach optimal disease outcome, underscores the importance of securing availability for patients.

ASPARLAS is closely related to ONCASPAR, and its clinical safety and efficacy was built on ONCASPAR. The primary objectives of the clinical development program for ASPARLAS were focused on feasibility of use and safety, as well as pharmacokinetic (PK)/pharmacodynamic (PD) comparability versus ONCASPAR. DFCI 11-001 demonstrated that, at the same dosage, every 3-week ASPARLAS has similar efficacy and toxicity outcomes compared to every 2-week ONCASPAR administration during induction phase and post-induction treatment in an asparaginase-intense regimen. COG AALL07P4 concluded that, despite the significantly longer asparagine depletion period observed in ASPARLAS-treated patients, comparable toxicity was shown, compared to ONCASPAR i.e., direct replacement of ONCASPAR with ASPARLAS at the same dosage of 2,500 IU/m^2 is feasible, as part of COG high-risk backbone regimens. These conclusions are echoed by the committee in their Rationale for the Recommendation on pg. 3: *"Evidence from 2 phase II, multicentre, open-label trials […] demonstrated that treatment with calaspargase pegol as a component of a MAC regimen may result in similar clinical benefit when compared to pegaspargase in pediatric and young adult patients with ALL."*

As noted in Servier's submission package, the short shelf-life of ONCASPAR limits the stocking option and poses a serious risk to the supply chain's ability to adjust to changes and disruptions. Any potential drug shortage is time consuming to manage for the healthcare team and creates anxiety among patients and health care professionals. ASPARLAS provides a solution to secure appropriate

supply. Servier is please to see that the committee has recognized this during its deliberation (Discussion Point #1 on pg. 5).

Expert committee consideration of the stakeholder input

2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☐
	No	☒

The recommendation demonstrates that the committee has considered the majority of the input that Servier had provided to CADTH. However, Servier would like to note that post-NOC comments related to the budget impact analysis (BIA) were not considered. The CADTH re-analysis of the BIA does not correctly reflect the final indication. Rather, it includes pediatric and adult patients of all ages. As per the post-NOC materials provided to CADTH:

- It is estimated that ASPARLAS will capture 50% of ONCASPAR market share of patients aged 1 to 21 years in Year 1, and 100% of ONCASPAR market share of patients 1 to 21 years in Years 2 and 3.
- It is estimated that 91.0% of the aforementioned pediatric incident population would be between the ages of 1 to 19 years, and that 2.6% of the aforementioned adult incident population would be between the ages of 20 to 21 years.
- This translates to a capture of 45.5% and 1.3% of pediatric and adult ONCASPAR market share, respectively, in Year 1, as well as 91.0% and 2.6% of pediatric and adult ONCASPAR market share, respectively, in Years 2 and 3.

Considering the assumptions above and updating the distribution of the trial protocol for the pediatric population to align with the COG AALL07P4 trial (as per the CADTH re-analysis), the pan-Canadian budget impact is estimated to be $540,964 in Year 1, $1,085,714 in Year 2, and $1,089,527 in Year 3 (3-year total = $2,716,205). A comparison of these values and the current CADTH re-analysis values are summarized in the table below:

Estimated pan-Canadian budget impact:				
	Year 1	**Year 2**	**Year 3**	**3-Year Total**
CADTH re-analysis in draft recommendation (based on draft indication)	$913,376	$1,841,318	$1,856,090	$4,610,784
Servier updated re-analysis (based on final indication)	$540,964	$1,085,714	$1,089,527	$2,716,205

CADTH noted to Servier during the draft recommendation review and validation process that, in order to avoid a lengthy delay with the review timelines for CADTH to revise the BIA numbers based on the target population in the approved indication, the economic report would not be revised and CADTH would proceed with the draft recommendation.

This information is being provided for context only, and no revision to the recommendation is being requested.

Clarity of the draft recommendation

3. Are the reasons for the recommendation clearly stated?	Yes	☒
	No	☐

No additional comments.

4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☒
	No	☐
No additional comments.		
5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☒
	No	☐
Servier agrees that the reimbursement conditions are clearly stated and the rationale for the conditions are provided in the recommendation. However, Servier would like to comment on the pricing condition that "[ASPARLAS] should be negotiated so that it does not exceed the drug program cost of treatment with [ONCASPAR]" (pg. 4). While the committee notes that there is insufficient clinical evidence to justify a cost premium for ASPARLAS over ONCASPAR, Servier believes it is important to consider that the price premium (incremental cost) for ASPARLAS compared with ONCASPAR could be justified by attributing value to bringing a solution and innovation though investment in clinical programs in order to improve/optimize the supply chain's ability to adjust to changes and disruptions. Moreover, at the point of care, ASPARLAS offers a solution to reduce stock management problems. ASPARLAS will serve the same population as ONCASPAR, with a reliable supply, comparable overall survival benefit, manageable adverse events profile, and with a modest budget impact. ASPARLAS also provides equity in access using a high-quality formulation of asparaginase. This information is being provided for context only, and no revision to the recommendation is being requested.		

[a] CADTH may contact this person if comments require clarification.