CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0711-000
Brand name (generic)	ALBRIOZA (sodium phenylbutyrate and ursodoxicoltaurine)
Indication(s)	For the treatment of patients with amyotrophic lateral sclerosis (ALS)
Organization	ALS Society of Canada

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

The ALS Society of Canada agrees with the committee's draft recommendation to reimburse sodium phenylbutyrate and ursodoxicoltaurine (PB-TURSO) with conditions. However, we are very concerned that the following initiation criteria may result in inequitable access for people living with ALS.

1.1. Have a diagnosis of definite ALS
1.2. Have had ALS symptoms for 18 months or less

Equitable access to innovative therapies is a critical issue for people and families affected by ALS across Canada. We recommend the following editorial revisions to initiation criterion 1.1. and 1.2. in order to align them with the realities of the diagnosis and treatment of ALS.

1.1 Have a diagnosis of definite ALS, *as determined by a Canadian ALS clinician, using any medically accepted diagnosis criteria.*
1.2 Have had ALS symptoms for 18 months or less, *with flexibility by a Canadian ALS clinician to prescribe where the time to diagnosis exceeds 18 months.*

Our rationale for the suggested wording changes to 1.1 and 1.2 are as follows:

It is important to clarify that a definite diagnosis does not have to be made using the revised El Escorial criteria. ALS clinicians should be able to use any medically accepted diagnosis criteria to confirm the diagnosis. Canadians living with ALS should not need to wait until their progression reaches a specific state before being allowed access to a therapy.

- People living with ALS measure time by loss – **loss of function and loss of life.** No person should lose their life while waiting to access a proven therapy. Given how quickly ALS can progress, requiring a specific level of progression before enabling access to a therapy **does not align with the right to health and life of Canadians.**
- In our initial submission, most **patients taking PB-TURSO** (80%) and **caregivers** (89%) of people on the treatment would recommend that it be made accessible to people living with ALS.

- As one patient stated, ***"I would like to see everyone in the ALS community get it,"*** while another shared that **"*many patients before us have died because time 'ran out' for them. You must understand that delaying the availability of potential drugs can be a death sentence for us."***
- The input from the clinical expert consulted by CADTH noted that **all patients diagnosed with ALS would be suitable for treatment with PB-TURSO**. Furthermore, the clinical expert suggested that **patients who are most suitable for treatment be decided based on clinician judgement** rather than functional rating scores or pulmonary function tests.
- Lastly, the clinical expert stated **there is no physiological or pharmacological reason to predict that patients at other levels of the El Escorial diagnostic criteria (i.e., "probable" or "possible") would not respond to the treatment** – a point that the CDEC agreed with.

With no confirmed biomarkers, and given the heterogeneity of ALS, current methods for diagnosing ALS involve ruling out other diseases that share similar symptoms – timelines for which can differ depending on the province you live in and how readily available appropriate medical testing is. Time-to-diagnosis criterion does not reflect the real-world experience of ALS and should not become a barrier to access.

- Four provinces within Canada have a time-to-diagnosis **that is longer than 18 months**, representing a large population of where people affected by ALS live[1].
- Given the heterogeneity of the disease, people living with ALS have shared that often symptoms – especially those early in the diagnosis process – may not have been attributed to ALS, but rather other health issues. As a result, it took **years before a diagnosis of ALS was confirmed despite having early symptoms**.
- Many people affected by ALS have **expressed great concern over criterion 1.2**. The anticipated impact is that an 18-month timeframe will **deny access to the majority of people affected by ALS.**
- A diagnosis of ALS and the realities of living with the disease already have a profound and pervasive effect on the lives of those who are struck by this devastating disease. People living with ALS should not lose access to a new therapy **because the province they live in has inequitable access to resources needed to confirm a diagnosis in less than 18 months**.

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	☒

In our opinion, two of the initiation criteria in particular (1.1. and 1.2.) do not address the urgency or impact of the disease we communicated, and therefore the recommendation does not demonstrate that the committee considered the entirety of our patient group input submission.

Clarity of the draft recommendation

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

The reasons for the recommendation are clearly stated, but as noted above, contradict to some extent the advice provided by the clinical expert consulted by CADTH and agreed upon by the CDEC.

[1] Hodgkinson, V. L., Lounsberry, J., Mirian, A., Genge, A., Benstead, T., Briemberg, H., Grant, I., Hader, W., Johnston, W. S., Kalra, S., Linassi, G., Massie, R., Melanson, M., O'Connell, C., Schellenberg, K., Shoesmith, C., Taylor, S., Worley, S., Zinman, L., & Korngut, L. (2018). Provincial Differences in the Diagnosis and Care of Amyotrophic Lateral Sclerosis. The Canadian journal of neurological sciences. Le journal canadien des sciences neurologiques, 45(6), 652–659. https://doi.org/10.1017/cjn.2018.311

4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☒
	No	☐

While they have been clearly articulated, the following implementation issues have not been adequately addressed in the recommendation:

- There is no physiological or pharmacological reason to predict that patients at other levels of the El Escorial diagnostic criteria (i.e., “probable” or “possible”) would not respond to the treatment – yet the initiation criterion is limited to patients with a diagnosis of definite ALS.
- According to the clinical expert consulted by CADTH, it is expected that PB-TURSO would be offered as add-on therapy in addition to riluzole and/or edaravone – yet the initiation criteria for the various therapies do not align. These differences in reimbursement criteria could lead to people living with ALS being unable to access a treatment regiment that best meets their needs.

5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☒
	No	☐

The reimbursement conditions are clearly stated and the rationale for the conditions are provided in the recommendation. However, as noted above, the initiation criteria 1.1. and 1.2. do not reflect the reality of people living with ALS and should be modified as suggested.

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