CADTH

CADTH REIMBURSEMENT REVIEW

Stakeholder Feedback on Draft Recommendation

risperidone (Perseris)

HLS Therapeutics Inc.

Indication: Treatment of schizophrenia in adults.

August 26, 2021

CADTH

CADTH Reimbursement Review

Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0671
Name of the drug and Indication(s)	Perseris (risperidone) for the treatment of schizophrenia
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	X

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

3. Clarity of the recommendation Complete this section if editorial revisions are requested for the following elements
a) Recommendation rationale
N/A
b) Reimbursement conditions and related reasons
N/A
c) Implementation guidance
N/A

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0671 Perseris
Brand name (generic)	PERSERIS® (risperidone for extended-release injectable suspension)
Indication(s)	PERSERIS® is indicated for the treatment of schizophrenia in adults
Organization	HLS Therapeutics Inc.
Contact information[a]	Name: [redacted]

Stakeholder agreement with the draft recommendation		
1. Does the stakeholder agree with the committee's recommendation.	Yes	☒
	No	☐
The sponsor agrees with the overall recommendation but objects to the inconsistencies when referring to the price of the product versus its comparators. Details are provided under section 3 below.		

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	☐
If not, what aspects are missing from the draft recommendation?		

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

We noted several inconsistencies and inaccuracies when referring to the price of the product versus other LAIs. These are:

p.2, Rationale for the recommendation, 2nd paragraph, "*risperidone ER was more costly compared with most other long-acting injectable (LAI) atypical antipsychotics (AAPs), and risperidone ER is assumed to be similarly effective as other LAI AAPs. As such, risperidone ER should be no more costly than the least costly reimbursed LAI AAP for adults with schizophrenia.*"

p.3, Table 1, Pricing, Reason, "*At the submitted price, Risperidone ER is more costly than some other atypical antipsychotic long-acting injectable antipsychotic agents (especially at the higher dosing regimens).*"

p.8, Economic evidence, 2nd paragraph, "*At the submitted prices of $456.18 (90 mg dose) and $608.22 (120 mg dose), the annual cost of risperidone ER is $5,474 to $7,299 per patient. This annual cost is more expensive than that of risperidone tablets ($349 to $524 per patient annually) but within the range of other long-acting injectable AAPs ($3,815 to $8,877 per patient annually).*"

The statements on p.2 and p.3 are inaccurate and contradict what is stated on p.8. In actual fact, Risperidone ER is no more costly than all other LAIs at their most frequently prescribed doses, except for the 120mg when compared to the highest dose of only one other LAI (aripiprazole LAI). Furthermore, aripiprazole is not a relevant comparator as it is not risperidone based.

We request that the statements on p.2 and p.3 be revised to reflect this language and become consistent with the statement on p.8, as follows:

The statement on p.2 should read: "risperidone ER was priced within the range of other long-acting injectable (LAI) atypical antipsychotics (AAPs), and risperidone ER is assumed to be similarly effective as other LAI AAPs. As such, risperidone ER should be no more costly than the least costly reimbursed risperidone-based LAI AAP for adults with schizophrenia."

The statement on p.3. should read: "At the submitted price, Risperidone ER is within the range of other long-acting injectable (LAI) atypical antipsychotics (AAPs)."

Also on p. 3, Table 1, (Pricing section, 2nd bullet) the statement: "*There is insufficient evidence to justify a cost premium for risperidone ER over the least expensive long-acting injectable atypical antipsychotic reimbursed for schizophrenia."* is misleading as risperidone ER is not premium-priced. We request that it be changed to: "At the submitted price, risperidone ER is within the range of other long-acting injectable (LAI) atypical antipsychotics (AAPs). It is no more costly than the least costly reimbursed risperidone-based LAI AAP for adults with schizophrenia.

Furthermore, the statement on p.8 contains information which is not relevant in the cost comparison of this risperidone long-acting formulation, such as the reference to its price versus the tablet formulations or to aripiprazole, a non-risperidone-based LAI. Risperidone ER should be compared to other risperidone-based LAI, namely Risperdal Consta and Invega Sustenna and Trinzia. Consequently, the statement on p.8 should read: "At the submitted prices of $456.18 (90 mg dose) and $608.22 (120 mg dose), the annual cost of risperidone ER is $5,474 to $7,299 per patient. This annual cost is within the range of other long-acting injectable AAPs ($3,815 to $8,877 per patient annually)."

In addition, the following statement on page 8 is misleading: *"In order for the cost of the highest recommended dose of risperidone ER to equal that of the least expensive comparator at its highest recommended dose (aripiprazole LAI), the price of risperidone ER 120 mg would need to be reduced by 25%."* It ignores the cost savings related to the inherent advantages of risperidone ER such as not requiring a loading dose nor supplemental oral risperidone dosing (reducing required monitoring intensity for outpatients, or length of stay for inpatients when initiating long-acting injectable AAPs), despite the fact that these statements were part of the CADTH review report.

The current recommendation also contradicts the CADTH assessment of the Budget Impact Analysis of reimbursing risperidone ER which predicts cost savings at the proposed price. We also wish to point out an error in the Budget Impact paragraph of the recommendation. It should state: "Based on CADTH reanalysis, the budgetary impact of reimbursing risperidone ER for patients with schizophrenia is expected to result in savings of $1,171 in Year 1, $32,179 in Year 2, and of $298,205 in Year 3, for a three-year cumulative budgetary savings of $331,555.

Finally, we object to the following statement in the Critical Appraisal section of the recommendation. Page 7, 4th paragraph: *"… the CADTH clinical expert indicated that while further studies are needed to assess the long-term efficacy (e.g., relapse, remission, hospitalization etc.)"* Although additional studies are always useful, the recommendation fails to acknowledge that the sponsor' s submission included Study 13-0005, a 52-week, multicenter, phase 3, open-label, single arm study. The primary objective of this study was to assess the long-term safety and tolerability of risperidone ER injections in subjects with schizophrenia. The secondary objective of this study was to continue collecting clinical outcome data with PERSERIS injections in subjects with schizophrenia using the PANSS and CGI-S scale. This study provides important efficacy and safety information on the long-term use of risperidone ER in 500 patients. We request the following sentence be added to the end of that paragraph, "*It should be noted that a long-term open label trial, Study 13-0005, was completed by the sponsor to provide evidence of safety and tolerability up to 52 weeks."*

4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☐
	No	☒
Inconsistencies remain as described in section 3, above.		
5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☐
	No	☒
Inconsistencies remain as described in section 3, above.		

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