CADTH

CADTH REIMBURSEMENT REVIEW

Stakeholder Feedback on Draft Recommendation

budesonide (Jorveza)

(AVIR Pharma Inc.)

Indication: For the induction and maintenance of clinico-pathological remission in adults with eosinophilic esophagitis (EoE), as per Health Canada indication.

July 22, 2021

CADTH

CADTH Reimbursement Review

Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0666
Name of the drug and Indication(s)	Budesonide (Jorveza) For the induction and maintenance of clinico-pathological remission in adults with eosinophilic esophagitis (EoE).
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	X
	No requested revisions	☐

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

3. Clarity of the recommendation Complete this section if editorial revisions are requested for the following elements
a) Recommendation rationale
b) Reimbursement conditions and related reasons
Suggest minor revision to wording: “Response to treatment should be assessed 3 months after initiating maintenance treatment with budesonide, then every 12 months thereafter.”
c) Implementation guidance

For Implementation Guidance 2, suggest removal of *"across jurisdictions*". Since the CDEC recommendation for Jorveza for induction therapy indicates a maximum duration of authorization of 6 weeks, this indication is still under pCPA negotiation and it is currently unknown what max duration will be funded by the jurisdictions, this statement may cause confusion if included.

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0666
Brand name (generic)	Budesonide (Jorveza)
Indication(s)	Maintenance of eosinophilic esophagitis (EoE) in adults
Organization	Food Allergy Canada
Contact information[a]	[redacted]

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

Please explain why the stakeholder agrees or disagrees with the draft recommendation. Whenever possible, please identify the specific text from the recommendation and rationale.

Generally, we agree that budesonide should be reimbursed for the maintenance of clinico-pathological remission in adults with EoE, and the rationale that budesonide has the potential to address the needs of patients seeking a treatment that provides sustained disease control and symptom relief. We are unclear, however, about the course of action for patients who respond to the drug, but then become non-adherent and relapse.

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	☐

If not, please provide details regarding the information that requires clarification.

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

If not, please provide details regarding the information that requires clarification.

We are uncertain about how this point can be addressed and what it means for patients: "There is insufficient evidence to demonstrate whether patients who relapse while receiving budesonide for the maintenance of remission would respond to a subsequent reinduction course of treatment with budesonide or in the same manner as they responded to the initial treatment course."

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

While there are positive elements in the recommendation, we have a concern around the discontinuation condition as it relates to patients who experience clinical relapse.

As we understand it, those who do not adhere to the therapy, for any reason, are included in this category and would no longer qualify for coverage of maintenance or a second course of induction. We find this worrisome for patients with EoE who respond to the drug, but then become non-adherent and relapse. At such a point, what options would these patients have?

For patients dealing with chronic conditions, medication adherence is a documented challenge, with reports of approximately 50% not taking medications as prescribed. There are different reasons why this happens, including either intentional or unplanned actions on the part of patients, beyond stopping treatment because their symptoms are lessened. As such, it seems unreasonable that non-adherence is a basis for EoE patients to not receive future coverage. We are aware of other conditions, such as asthma, in which intermittent treatment is allowed when it recurs, whether for non-adherence or other reasons, and wonder about considerations of Jorveza (budenoside) for EoE patients.

[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	*Jennifer Gerdts*
Position	*Executive Director*
Date	*20-07-2021*
☒	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**
AVIR Pharma Inc.	☐	☐	☒	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0666
Brand name (generic)	Budesonide (Jorveza)
Indication(s)	Maintenance of Eosinophilic esophagitis in adults
Organization	EOS Network
Contact information[a]	[redacted]

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

We are delighted to read your recommendation for Budesonide (Jorveza) to become the first maintenance treatment for adults affected by Eosinophilic Esophagitis.

This recommendation could improve the health and quality of life for many adult EoE patients.

Please find below our 2 suggested amendments for the draft conditions.

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?

Whilst the recommendation reflects that the committee has correctly considered the need for a long-term maintenance therapy it does not reflect that some patients face additional challenges such as symptoms and histology not corelating or the difficulties of lifelong daily treatment compliance.

See comments below

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

If not, please provide details regarding the information that requires clarification.

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

If not, please provide details regarding the information that requires clarification.

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

A) <u>Discontinuation</u>

We would request that you consider removing the discontinuation recommendation:

Otherwise, patients who experience clinical relapse, histological relapse, food impaction which needed endoscopic intervention, or need for an endoscopic dilation while receiving budesonide as maintenance therapy would no longer be able to access the only recommended treatment for EoE which would then cause increased burden on the patient and healthcare system.

As a chronic disease compliance of lifelong twice daily maintenance may wane in some patients possibly due to personal circumstances, age related (transitional selfcare/independence) or through wanting a break from daily steroid usage. This should not remove or exempt patients from accessing Budesonide (Jorveza) treatment.

For Example: An asthmatic patient with returning symptoms would not be refused/discontinued an asthma pump just because they forgot to use it compliantly or had a period of time where they needed a break from treatment.

It has been reported by some of our patient community that once their EoE is under control it is easy to forget the severity of their condition. EoE symptoms increase slowly once stopping the medication or if skipping doses.
This only then becomes a concern once they have dysphagia or food impaction again.

This is further complicated when histology and symptoms do not correlate ie the histology can be increasing but no symptoms meaning the EoE is silently increasing in severity.

As per the clinical input on page 6 of your recommendation it also important to note that some patients may have an increase in symptoms or histology when on low dose maintenance which then needs to be increased for remission induction again.

B) Prescribing

Due to the current limited experienced expertise, **we would request your recommendation to be amended to:**

A patient must be under the care of a gastroenterologist to monitor the EoE histology though endoscopy and manage their long-term care.

We agree that it is preferential for all EoE patients to be under the care of a specialist with experience in the diagnosis and management of EoE but as a patient organisation with a global healthcare professional network that reaches over 30 countries, we aware of a global shortage of expertise resulting in diagnosis delay.

EOS community survey April 2021 – 163 participants averaged 9 years of symptoms to diagnosis

EoE is a rare disease, as an organisation we continue to raise awareness and improve education which we hope will be aided with a recommended treatment such as Budesonide (Jorveza).

Amending this recommendation would allow an opportunity to increase HCP experience and education through the adoption of the latest guidelines which would improve patient access to care.

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

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- 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	*Amanda Cordell*
Position	*Chair and Founder*
Date	*22-07-2021*
☒	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**
Avir: I provided a zoom presentation to educate staff on the patients experience of living with Eosinophilic Esophagitis	☒	☐	☐	☒
Dr Falk: *I provided a zoom presentation to educate a focus group on the patients experience of living with Eosinophilic Esophagitis Food bolus obstruction and development of*	☒	☐	☐	☐

various patient educational resources projects				
Astra Zeneca: Ongoing participation in a global working group to improve patient outcomes for those with Eosinophilic driven diseases	☒	☐	☐	☐
Regeneron Sanofi: EOS organisation growth project		x		

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0666-000
Brand name (generic)	JORVEZA (budesonide)
Indication(s)	Indicated for the induction and maintenance of clinico-pathological remission in adults with eosinophilic esophagitis (EoE).
Organization	AVIR Pharma Inc.
Contact information[a]	[redacted]

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

Please explain why the stakeholder agrees or disagrees with the draft recommendation. Whenever possible, please identify the specific text from the recommendation and rationale.

Overall, AVIR Pharma Inc. is pleased with the Canadian Drug Expert Committee's recommendation that budesonide should be reimbursed for the maintenance of clinico-pathological remission in adults with eosinophilic esophagitis (EoE). Although we understand most of the reimbursement conditions put forth, we believe that the following condition merits clarification *(page 3)* *''Patients who experience clinical relapse, histological relapse, food impaction which needed endoscopic intervention, or need for an endoscopic dilation while receiving budesonide as maintenance therapy, should discontinue budesonide.''* which implies that all relapsing patients, including a significant proportion due non-adherence to treatment as well as another proportion of patient who experience stricture, to discontinue budesonide and not be allowed for re-treatment, although they are not considered non-responders.

- According to our understanding of the recommendation, these patients (responders to therapy but non-adherent) may be forced to discontinue treatment with budesonide even though they previously responded during the induction phase and during maintenance therapy. Patient adherence to treatment is a common challenge in chronic disease therapies. Discontinuation may have occurred either because the resolution of symptoms and the patient felt they were doing better, by instruction from their physician to reduce long-term exposure to corticosteroids or to evaluate if they would relapse further to treatment discontinuation. Indeed, the cause of the relapse for a non-adherent patient differs from the cause in a patient who simply does not respond to therapy. Clinical experts have previously indicated on many occasions that given the chronicity of EoE, patients will eventually relapse, and require access to budesonide orodispersible tablets to treat recurrences and prevent future recurrences : (page 6) 1- *''The clinical experts also indicated while maintenance therapy, in general, would imply continuous treatment, in clinical practice, treatment might be titrated, intermittent, persistent, or stopped, the decision is impacted by symptoms, complications, strictures, and persistent inflammation on endoscopy.''* (page 6) *2- ''The clinical experts indicated that they would try first to maintain the remission using the budesonide 0.5 mg twice daily dosage; if the patient relapse, then re-induction of remission using the budesonide 1mg twice daily dosage will be tried. After achieving remission again using the 1 mg budesonide twice daily dose, patients would be switched back to the 0.5 mg budesonide twice daily for maintenance of remission.''* (page 6) *3- ''Patients who relapse again while on the 0.5 mg budesonide twice daily would have their*

dosage increased to 1 mg budesonide twice daily for re-induction of remission. After achieving remission on the 1 mg budesonide twice daily dose, patients would remain on the 1 mg budesonide twice daily for the maintenance of remission." (page 6)4- '' The clinical experts think that patients with a history of severe disease as manifested by food impactions or significant fibrosis need to stay on 0.5 mg budesonide orodispersible tablets twice daily for a long period. Indeed, they have indicated that while maintenance therapy in general would imply continuous treatment, in clinical practice treatment might be titrated, intermittent, persistent, or stopped, the decision is impacted by symptoms, complications, strictures, and persistent inflammation on endoscopy. According to physicians consulted, patients who relapse while receiving budesonide 0.5 mg for the maintenance of remission, especially if non-adherent, are expected to respond to a subsequent treatment course in the same manner as they responded to the initial treatment course with budesonide 1 mg.

- Some clinical experts have also reported that, although small, a proportion of patients with an advanced fibrostenotic phenotype might still require an endoscopic stricture dilation independently of treatment success with Jorveza, ie. histological remission. These patients should be allowed to continue their treatment with Jorveza since the need for such dilation is not indicative of treatment failure. Furthermore, treatment discontinuation would lead to a loss of anti-inflammatory effect and may contribute to a downward spiral of patients' conditions.
- Finally, as with other chronic inflammatory diseases, a proportion of patients are expected to discontinue treatment when they stop experiencing symptoms amongst other reasons. Unfortunately, with this reimbursement condition for the maintenance treatment, these patients would be left without any treatment options, unless we misunderstood the recommendation to be intended for patients that relapse while receiving treatment (i.e. that are considered non-responders). If the condition applies to all patients relapsing while on maintenance therapy, regardless of their responder/adherence status, it is unclear to us why it would be preferable to switch these patients back to off-label medications especially when clinical experts stated that their preference would be to re-initiate these patients with budesonide orodispersible tablets as they would not be considered non-responders.

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	☐
If not, please provide details regarding the information that requires clarification.		
4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☐
	No	☒
If not, please provide details regarding the information that requires clarification. Please refer to comments under Point 1		
5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☒
	No	☐
If not, please provide details regarding the information that requires clarification.		

[a] CADTH may contact this person if comments require clarification. Contact information will not be included in any public posting of this document by CADTH.