

CADTH Reimbursement Review Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0723-000
Brand name (generic)	Orladeyo (Berotralstat)
Indication(s)	hereditary angioedema (HAE)
Organization	Hereditary Angioedema Canada (HAEC)
Contact information ^a	Name: [REDACTED] tel: [REDACTED] email: [REDACTED]
Stakeholder agreement with the draft recommendation	
1. Does the stakeholder agree with the committee's recommendation.	Yes <input type="checkbox"/> No <input checked="" type="checkbox"/>
<p>Please explain why the stakeholder agrees or disagrees with the draft recommendation. Whenever possible, please identify the specific text from the recommendation and rationale.</p> <p>In the CDEC recommendation, it stated that "...other patient-identified unmet needs do not seem to be met by berotralstat."</p> <p>HAEC does not believe that CDEC has considered the full spectrum of areas of unmet need for treatments for HAE.</p> <p>Importantly, there is no current way to predict who will respond best to any current treatment for HAE, and while some patients respond extremely well to certain treatments, others do not. This heterogeneity in response to treatment drives an urgent need for treatment options for Long-term Prophylaxis (LTP).</p> <p>And, as stated in our patient input submission, other important areas of unmet need (that are met by berotralstat) include patients who experience damage to their veins or worry about future damage to their veins. This need is very different than simply preferring an easier to administer treatment, as many patients experience severe damage to their veins making IV treatments untenable. Also, many patients using LTP have a pragmatic concern about maintaining the integrity of their veins because a commonly used, and nationally accessible, acute treatment requires a healthy vein to receive the treatment.</p> <p>CDEC seems to also not understand the underlying rationale for what drives HRQoL. As reported in our patient input submission, the majority of our surveyed patients/caregivers report having regular fear of unpredictable attacks. These patients experience generalized anxiety and stress along with many other emotional and cognitive impacts. Recognizing that over 20% of patients we have surveyed (n=113) are currently very dissatisfied or dissatisfied with the effectiveness of their current treatment used to prevent attacks, and recognizing the general anxiety caused by living with HAE, even a treatment that significantly reduces the number of attacks is not going to significantly improve a patient's HRQoL.</p>	

HAE Canada is a part of HAE International (HAEi), a global non-profit network of 95 patient-led member organizations dedicated to improving the lives of people suffering from hereditary angioedema (HAE) – a serious, debilitating, and life threatening chronic, rare genetic condition. HAEi is a company and product neutral organization that enthusiastically supports drug discovery research aimed at approval for and reimbursement of a variety of options that allow patients and physicians to choose a therapy that best fits individual needs. HAEi views HAE Canada as one of the most important and accomplished members and serves as a role model to HAE groups in other countries looking to improve the lives of people suffering from HAE.

The following is commentary from HAEi in response to the recent CADTH recommendation that berotralstat not be reimbursed for routine prevention of attacks of HAE.

HAEi is surprised and disappointed by CADTH’s position. While we have serious issues with the analysis and tone in the CADTH report, we will leave the technical critiques to medical professionals and scientists. We have, however, asked our Chief Medical Advisor (and one of the world’s leading HAE Key Opinion Leaders) Professor Marcus Maurer (see full vitae at <http://www.marcus-maurer.com>) to weigh in on the CADTH report. Professor Maurer notes,

“I have reviewed the CADTH report and take issue with its conclusions regarding the clinical relevance of berotralstat’s reduction in HAE attacks and impact on patient quality of life. It is unfortunate that CADTH ignores recent data gleaned from the company’s APex-2 and APeX-S clinical trials that provides evidence of continued attack reduction and sustained improvement in quality of life.”

HAEi is perplexed by the decision that puts Canada—a sophisticated country with one of world’s leading health care systems—out of step with the other countries that have approved berotralstat for reimbursement: European Union, Israel, Japan, Saudi Arabia, and the USA. Each of these entities recognized that this first non-steroidal oral prophylaxis treatment,

- met its clinical trial endpoints,
- represents a significant advantage by reducing the treatment burden, and
- demonstrates an efficacy profile that provides substantial benefit.

Finally, it is important that any entity reviewing an HAE medicine understands something that we at HAEi always hear during our countless interactions with the global patient community. There is no one medicine that works for everyone, and having choices is crucial for giving patients a chance for reasonable disease control.

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	<input type="checkbox"/>
	No	<input checked="" type="checkbox"/>

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

HAE is a highly complex disease with patients demonstrating wide heterogeneity in response to existing available treatments.

Additionally, the patients that live with HAE, even when they have a clinically-meaningful response to prophylactic treatment, live with ever-present anxiety and fear due to unpredictable attacks that dramatically impact their ability to work, pursue education, travel, exercise, do household chores, and socialize with family and friends.

These insights, presented in great detail in the HAEC patient input submission, do not appear to be clearly understood or acknowledged by CDEC.

Clarity of the draft recommendation

3. Are the reasons for the recommendation clearly stated?	Yes	<input checked="" type="checkbox"/>
	No	<input type="checkbox"/>
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	<input type="checkbox"/>
	No	<input type="checkbox"/>
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	<input type="checkbox"/>
	No	<input type="checkbox"/>
If not, please provide details regarding the information that requires clarification.		

^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	<i>Please state full name</i>			
Position	<i>Please state currently held position</i>			
Date	<i>Please add the date form was completed (DD-MM-YYYY)</i>			
<input type="checkbox"/>	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	<input type="checkbox"/>
			Yes	<input type="checkbox"/>
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	<input type="checkbox"/>
			Yes	<input type="checkbox"/>
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	<input type="checkbox"/>
			Yes	<input type="checkbox"/>
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
<i>Add company name</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<i>Add company name</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<i>Add or remove rows as required</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Appendix 2. Conflict of Interest Declarations for Clinician 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.
- For conflict of interest declarations:
 - Please 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.
 - Please note that declarations are required for each clinician that contributed to the input.
 - If your clinician group provided input at the outset of the review, only conflict of interest declarations that are new or require updating need to be reported in this form. For all others, please list the clinicians who provided input are unchanged
 - Please add more tables as needed (copy and paste).
 - All new and updated declarations must be included in a single document.

A. Assistance with Providing the Feedback		
2. Did you receive help from outside your clinician group to complete this submission?	No	<input type="checkbox"/>
	Yes	<input type="checkbox"/>
If yes, please detail the help and who provided it.		
3. Did you receive help from outside your clinician group to collect or analyze any information used in this submission?	No	<input type="checkbox"/>
	Yes	<input type="checkbox"/>
If yes, please detail the help and who provided it.		
B. Previously Disclosed Conflict of Interest		
4. Were conflict of interest declarations provided in clinician group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section C below.	No	<input type="checkbox"/>
	Yes	<input type="checkbox"/>
If yes, please list the clinicians who contributed input and whose declarations have not changed: <ul style="list-style-type: none"> Clinician 1 Clinician 2 Add additional (as required) 		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	Please state full name
Position	Please state currently held position
Date	Please add the date form was completed (DD-MM-YYYY)
<input type="checkbox"/>	I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.
Conflict of Interest Declaration	

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
Add company name	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Add company name	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Add or remove rows as required	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

New or Updated Declaration for Clinician 2	
Name	Please state full name
Position	Please state currently held position
Date	Please add the date form was completed (DD-MM-YYYY)
<input type="checkbox"/>	I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
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
Add company name	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Add company name	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Add or remove rows as required	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

New or Updated Declaration for Clinician 3	
Name	Please state full name
Position	Please state currently held position
Date	Please add the date form was completed (DD-MM-YYYY)
<input checked="" type="checkbox"/>	I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
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
Add company name	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Add company name	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Add or remove rows as required	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

New or Updated Declaration for Clinician 4				
Name	<i>Please state full name</i>			
Position	<i>Please state currently held position</i>			
Date	<i>Please add the date form was completed (DD-MM-YYYY)</i>			
<input type="checkbox"/>	I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.			
Conflict of Interest Declaration				
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
<i>Add company name</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<i>Add company name</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<i>Add or remove rows as required</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

New or Updated Declaration for Clinician 5				
Name	<i>Please state full name</i>			
Position	<i>Please state currently held position</i>			
Date	<i>Please add the date form was completed (DD-MM-YYYY)</i>			
<input type="checkbox"/>	I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.			
Conflict of Interest Declaration				
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
<i>Add company name</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<i>Add company name</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<i>Add or remove rows as required</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>