

CADTH REIMBURSEMENT REVIEW

Stakeholder Feedback on Draft Recommendation

berotralstat (Orladeyo) (BioCryst Pharmaceuticals Inc.)

Indication: hereditary angioedema (HAE)

February 3, 2023

Disclaimer: The views expressed in this submission are those of the submitting organization or individual. As such, they are independent of CADTH and do not necessarily represent or reflect the view of CADTH. No endorsement by CADTH is intended or should be inferred.

By filing with CADTH, the submitting organization or individual agrees to the full disclosure of the information. CADTH does not edit the content of the submissions.

CADTH does use reasonable care to prevent disclosure of personal information in posted material; however, it is ultimately the submitter's responsibility to ensure no identifying personal information or personal health information is included in the submission. The name of the submitting stakeholder group and all conflicts of interest information from individuals who contributed to the content are included in the posted submission.

CADTH

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	Canadian Hereditary Angioedema Network (CHAEN)		
Contact information ^a	Name: Peter Waite, Executive Director		
	Canadian Hereditary Angioedema Network		
Stakeholder agreement w	ith the draft recommendation		
1. Does the stakeholder ag	ree with the committee's recommendation.	Yes No	
	eholder agrees or disagrees with the draft recommendation. W specific text from the recommendation and rationale.	heneve	r
of the reduction in frequency	ised recommendation where CDEC determined that the clinica y of attacks from 2.35 attacks per month in the placebo group to oup was statistically significant and clinically relevant.		ice
from the APeX-2 trial did no	that upon reconsideration, CDEC carefully considered that HR t reflect the need for both a non-plasma derived and oral optior DEC respected patient and clinician group feedback with respe e of administration.	n for	
treatment of angioedema (e	Istat should not be used in combination with other long-term pro.g., C1-esterase inhibitors or lanadelumab), however, consider atients are transitioned to berotralstat.		tic
defined. Factors to consider	bach for switching a patient to oral berotralstat prophylaxis has include the timing of the transition, the half-life of the medication rugs, and patient-specific characteristics that may affect the tra	ons, the	
respect to starting LTP treat	AE Guideline (Betschel et al. Allergy Asthma Clin Immunol 201 ments states that decisions with respect to how a patient trans by the patient and an HAE specialist.		
necessary, to use C1 inhibit	st that patients on berotralstat should have the opportunity, whe or as short-term prophylaxis before known triggers such as sur nended by their HAE specialist.		
	rations for transition from subcutaneous to oral prophylaxis in the treatment o Immunol 17, 100 (2021). https://doi.org/10.1186/s13223-021-00603-9	of heredita	iry
Expert committee conside	eration of the stakeholder input		

2. Does the recommendation demonstrate that the committee has considered the	Yes	\boxtimes
stakeholder input that your organization provided to CADTH?	No	
If not, what aspects are missing from the draft recommendation?		
Clarity of the draft recommendation	1	
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.		
ICER		
On p. 4 in Table 1 (Reimbursement Conditions and Reasons). There is a pricing recomme	endatio	n:
The ICER for berotralstat is \$14,559,490 when compared with No LTP.		
A price reduction of 93% would be required for berotralstat to be able to achieve an \$50,000 per QALY compared to No LTP.	ICER	of
CHAEN represents expert clinicians with expert knowledge of the clinical factors related to treatment of HAE, and we typically do not delve into the economic aspects of a Health Tec Assessment.		У
However, we are concerned that CADTH's recent use of an ICER pegged at \$50,000 per (the willingness-to-pay (WTP) threshold for payers is not will aligned with the unique needs diseases, and favors treatments for more common diseases.		
We support the work of Canadian health technology assessment agencies and the pan Ca Pharmaceutical Alliance (pCPA) in assessing value and achieving value in prescription me for publicly funded drug programs. However, we are concerned that CADTH is arbitrarily establishing a new (and low) WTP threshold that could ultimately result in Canadian patien diseases being denied access to important new therapies.	dicatio	ns
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.	Ø	
CADTH may contact this person if comments require clarification.		

^a CADTH may contact this person if comments require clarification.

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	\boxtimes
	Yes	
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	No	\boxtimes
information used in this submission?	Yes	
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	No	
submitted at the outset of the CADTH review and have those declarations remained	0.977	
unchanged? If no, please complete section C below.	Yes	\boxtimes
If yes, please list the clinicians who contributed input and whose declarations have not changed:		
Clinician 1		
Clinician 2		
Add additional (as required)		

C. New or Updated Conflict of Interest Declarations

Name	Please state full name
Position	Please state currently held position
Date	Please add the date form was completed (DD-MM-YYYY)
	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.

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.

	Check Appropriate Dollar Range				
Company	\$0 to 5,000	\$5,001 to 10,000	\$10,001 to 50,000	In Excess of \$50,000	
Add company name					
Add company name					
Add or remove rows as required					

Name	Please state full name
Position	Please state currently held position
Date	Please add the date form was completed (DD-MM-YYYY)
	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.

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.

	Check Appropriate Dollar Range					
Company	\$0 to 5,000	\$5,001 to 10,000	\$10,001 to 50,000	In Excess of \$50,000		
Add company name						
Add company name						
Add or remove rows as required						

new or up	dated 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)					
	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.					
List any co	f Interest Declaration mpanies or organizations that ha who may have direct or indirect				er the past two	
List any co	mpanies or organizations that ha		ug under review	•		
List any co	mpanies or organizations that ha		ug under review			
List any co years AND	mpanies or organizations that ha who may have direct or indirect	interest in the dr	Check Approp \$5,001 to	oriate Dollar Rang \$10,001 to	ge In Excess o	
List any co years AND Company	mpanies or organizations that ha who may have direct or indirect	interest in the dr \$0 to 5,000	Ug under review Check Approp \$5,001 to 10,000	oriate Dollar Rang \$10,001 to 50,000	ge In Excess o \$50,000	

New or Up	dated Declaration for Clinician	4			
Name	Please state full name				
Position	Please state currently held position				
Date	Please add the date form was completed (DD-MM-YYYY)				
	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	f Interest Declaration				
	mpanies or organizations that have who may have direct or indirect i				r the past two
			Check Approp	riate Dollar Rang	je
Company		\$0 to 5,000	\$5,001 to 10,000	\$10,001 to 50,000	In Excess of \$50,000
Add compa	any name				
Add company name					
Add an use	nove rows as required	П		П	

new or Up	odated Declaration for Clinician	5				
Name	Please state full name					
Position	Please state currently held position					
Date	Please add the date form was completed (DD-MM-YYYY)					
	matter involving this clinician or	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 o	f Interest Declaration					
List any co	mpanies or organizations that have				er the past two	
List any co			rug under review.		62 - 1254 FC-404 0762107626-682886779-5	
List any co	ompanies or organizations that hav) who may have direct or indirect i		rug under review.		62 - 1254 FC-404 0762107626-682886779-5	
List any co years AND	ompanies or organizations that hav) who may have direct or indirect i	nterest in the dr	rug under review. Check Approp \$5,001 to	riate Dollar Rang \$10,001 to	ge In Excess of	
List any co years AND Company	ompanies or organizations that hav) who may have direct or indirect i any name	nterest in the dr \$0 to 5,000	rug under review. Check Approp \$5,001 to	riate Dollar Rang \$10,001 to	ge In Excess of	



CADTH Reimbursement Review

Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0723
Name of the drug and Indication(s)	Berotralstat (Orladeyo) for hereditary angioedema (HAE)
Organization Providing	FWG
Feedback	

1. Recommendation revisions Please indicate if the stakeholder requires the expert review committee to reconsider or clarify its recommendation.					
Request for	Major revisions: A change in recommendation category or patient population is requested				
Reconsideration	Minor revisions: A change in reimbursement conditions is requested				
No Request for	Editorial revisions: Clarifications in recommendation text are requested				
Reconsideration	No requested revisions	X			

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.

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.

CADTH

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				
Stakeholder agreement w	ith the draft recommendation			
1. Does the stakeholder agree with the committee's recommendation.				
possible, please identify the HAEC agrees with the revis the reduction in frequency o	The holder agrees or disagrees with the draft recommendation. We specific text from the recommendation and rationale. The recommendation that importantly recognizes the clinical relation of attacks demonstrated in the APeX-2 trial. HAEC also acknow gave to stakeholder feedback on the draft recommendation.	evance of		
Expert committee conside	ration of the stakeholder input			
	on demonstrate that the committee has considered the our organization provided to CADTH?	Yes ⊠ No □		
*				
Clarity of the draft recomm	nendation			
3. Are the reasons for the	recommendation clearly stated?	Yes ⊠ No □		
Re: Table 1. Reimbursemer	nt Conditions and Reasons			
Prescribing:				
	not be used in combination with other medications used for long nt of angioedema (e.g., C1-esterase inhibitors or lanadelumab)			
	DEC that berotralstat should not be used in combination with ot of angioedema, consideration needs to be given on how a pati	-		

"However, the optimal approach for switching a patient to oral berotralstat prophylaxis has not been defined. Factors to consider include the timing of the transition, the half-life of the medications, the dosing schedules for both drugs, and patient-specific characteristics that may affect the transition."

In concordance with The International/Canadian Hereditary Angioedema Guideline (Betschel et al. Allergy Asthma Clin Immunol 2019) with respect to starting LTP treatments, we believe decisions with respect to how a patient transitions to Berotralstat should be made by the patient and an HAE specialist.

We also suggest that patients on Berotralstat should have the opportunity, if necessary, to use C1 inhibitor as short-term prophylaxis before known triggers such as surgery, dental work, etc., as recommended by their HAE specialist.

4. Have the implementation issues been clearly articulated and adequately		
addressed in the recommendation?	No	
If not, please provide details regarding the information that requires clarification.		
5. If applicable, are the reimbursement conditions clearly stated and the rationale	Yes	\boxtimes
for the conditions provided in the recommendation?	No	
If not, please provide details regarding the information that requires clarification.		

^a CADTH may contact this person if comments require clarification.

¹ Gower, R.G., Wilber, M. Considerations for transition from subcutaneous to oral prophylaxis in the treatment of hereditary angioedema. *Allergy Asthma Clin Immunol* **17**, 100 (2021). https://doi.org/10.1186/s13223-021-00603-9

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.
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- CADTH may contact your group with further questions, as needed.
- Please see the <u>Procedures for CADTH Drug Reimbursement Reviews</u> for further details.

A D-414	One of the second second second					
Name	Group Information	HAEC Advos	any Committee			
Position	Jacquie Badiou, on behalf of the Chair of Advocacy Committee a					
Date	February 2, 2023	ING HAEC Pasi	President			
	I hereby certify that I have the a matter involving this patient gro patient group in a real, potential	up with a comp	any, organizatio	n, or entity that n		
B. Assista	nce with Providing Feedback					
4 811				(0	No	\boxtimes
1. Did yo	u receive help from outside you	r patient grou	p to complete y	our feedback?	Yes	П
2 Did vo	u receive help from outside you	r nationt grou	n to collect or a	nalvze anv	No	
inform	u receive help from outside you nation used in your feedback? se detail the help and who provide		p to collect or a	analyze any	No Yes	
inform If yes, plea	ation used in your feedback?	ed it.	p to collect or a	analyze any		
inform If yes, plea C. Previou	ation used in your feedback? se detail the help and who provide	ed it.				
inform If yes, plea C. Previou 1. Were o submi	ation used in your feedback? se detail the help and who provide sly Disclosed Conflict of Interes	ed it. st provided in pa review and ha	tient group inp ve those declar	ut that was	Yes	
inform If yes, plea C. Previou 1. Were o submi uncha	ation used in your feedback? se detail the help and who provide sly Disclosed Conflict of Interest conflict of interest declarations p tted at the outset of the CADTH	d it. provided in pa review and ha ction D below	tient group inp ve those declar	ut that was	Yes	
inform If yes, plea C. Previou 1. Were of submi uncha D. New or 3. List ar	action used in your feedback? se detail the help and who provide asly Disclosed Conflict of Interest conflict of interest declarations p tted at the outset of the CADTH nged? If no, please complete se	ed it. provided in pa review and ha ction D below claration hat have provi	tient group inp ve those declar ided your group	ut that was rations remained o with financial p	Yes d No Yes	
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inform If yes, plea C. Previou 1. Were of submi uncha D. New or 3. List ar past ty	ation used in your feedback? se detail the help and who provide sly Disclosed Conflict of Interest conflict of interest declarations p tted at the outset of the CADTH nged? If no, please complete se Updated Conflict of Interest Dec ny companies or organizations t	ed it. provided in pa review and ha ction D below claration hat have provi	tient group inp ve those declar ided your group interest in the	ut that was rations remained o with financial p drug under revi	Yes d No Yes payment ew.	over the
inform If yes, plea C. Previou 1. Were of submi uncha D. New or 3. List ar past ty Company	action used in your feedback? se detail the help and who provide asly Disclosed Conflict of Interest conflict of interest declarations p tted at the outset of the CADTH nged? If no, please complete se Updated Conflict of Interest Dec ny companies or organizations the wo years AND who may have dir	ed it. provided in pa review and ha ction D below claration hat have provi ect or indirect	tient group inp ve those declar ided your group interest in the <u>Check Appro</u> \$5,001 to	ut that was rations remained o with financial priate Dollar Ra \$10,001 to	Yes Yes d No Yes payment ew. nge In Exces \$50,000	over the
inform If yes, plea C. Previou 1. Were of submi uncha D. New or 3. List ar past ty	ation used in your feedback? se detail the help and who provide solve the provide of the provide solve the provide of the provide conflict of interest declarations provide the dat the outset of the CADTH nged? If no, please complete se Updated Conflict of Interest Decon the provide of the provide of the provide the provide of the provide of the provide of the provide the provide of the provide of the provide of the provide the provide of the provide of the provide of the provide the provide of the provide of the provide of the provide the provide of the provide of the provide of the provide of the provide the provide of the provide of	d it. provided in pa review and ha ction D below claration hat have provi ect or indirect \$0 to 5,000	tient group inp ve those declar ided your group interest in the <u>Check Appro</u> \$5,001 to 10,000	ut that was rations remained o with financial i drug under revi priate Dollar Ra \$10,001 to 50,000	d No Yes d Yes payment ew. nge In Exces \$50,000	over the

CADTH Reimbursement Review Feedback on Draft Recommendation

Stakeholder information			
CADTH project number	SR0723-000		
Brand name (generic)	Orladeyo® (berotralstat)		
Indication(s)	HAE		
Organization	BioCryst Pharmaceuticals Inc.		
Contact information ^a			
Stakeholder agreement wi	ith the draft recommendation		
1. Does the stakeholder ag	gree with the committee's recommendation.	Yes No	
hereditary angioedema (HA that can be used for the rou and older. As a Health Cana option, it meets an importan	perotralstat). This recommendation is an important step for pati- E). Orladeyo [®] is the first and only targeted orally administered tine prevention of HAE in adults and pediatric patients 12 years ada approved, efficacious, and well-tolerated oral long-term pro- t unmet need for patients with HAE in Canada.	treatm s of ag	ent e
		Yes	\boxtimes
2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?			
Not applicable.		No	
Clarity of the draft recomm	nendation		
		Yes	
3. Are the reasons for the recommendation clearly stated?			
Not applicable.		10000	
4. Have the implementation issues been clearly articulated and adequately			\square
addressed in the recommendation?			
Not applicable.			
and an and the second se			1.
	mbursement conditions clearly stated and the rationale	Yes	\boxtimes
	mbursement conditions clearly stated and the rationale ded in the recommendation?	Yes No	

^a CADTH may contact this person if comments require clarification.