CADTH

CADTH REIMBURSEMENT REVIEW

Stakeholder Feedback on Draft Recommendation

BELZUTIFAN (WELIREG)

(Merck Canada Inc.)

Indication: For the treatment of adult patients with von Hippel-Lindau (VHL) disease who require therapy for associated non-metastatic renal cell carcinoma (RCC), central nervous system (CNS) hemangioblastomas, or non-metastatic pancreatic neuroendocrine tumors (pNET), not requiring immediate surgery

August 18, 2023

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0309
Brand name (generic)	Welireg (belzutifan)
Indication(s)	For the treatment of patients with VHL disease-associated non-metastatic RCC, CNS hemangioblastomas or non-metastatic pNET, not requiring immediate surgery, consistent with the results of MK-6482-004 and in consideration of the high unmet need of these patients who have no options besides surgical resections.
Organization	Ontario Health (Cancer Care Ontario) CNS Cancer Drug Advisory Committee
Contact information[a]	Name: Dr. Sunit Das

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. The CNS DAC would like the recommendation to include the indication of patients with VHL associated endolymphatic sac tumors.		

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.		
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.

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		
1. Did you receive help from outside your clinician group to complete this submission?	No	☐
	Yes	☒
If yes, please detail the help and who provided it. OH-CCO has provided a secretariat function to the group.		
2. Did you receive help from outside your clinician group to collect or analyze any information used in this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
B. Previously Disclosed Conflict of Interest		
3. 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	☒
	Yes	☐
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

New or Updated Declaration for Clinician 1	
Name	*Dr. Sunit Das*
Position	*Lead, Ontario Health (Cancer Care Ontario) CNS Cancer Drug Advisory Committee*
Date	*15-08-2023*
☒	**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	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 2	
Name	*Dr. Warren Mason*
Position	*Member, Ontario Health (Cancer Care Ontario) CNS Cancer Drug Advisory Committee*
Date	*16-08-2023*
☒	**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
Merck	☒	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0309
Brand name (generic)	Welireg (belzutifan)
Indication(s)	For the treatment of patients with VHL disease-associated non-metastatic RCC, CNS hemangioblastomas or non-metastatic pNET, not requiring immediate surgery, consistent with the results of MK-6482-004 and in consideration of the high unmet need of these patients who have no options besides surgical resections.
Organization	Ontario Health (Cancer Care Ontario) Genitourinary Cancer Drug Advisory Committee ("GU DAC")
Contact information[a]	Name: Dr. Girish Kulkarni

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.		

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.		
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.

Appendix 2. Conflict of Interest Declarations for Clinician Groups

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  - 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		
1. Did you receive help from outside your clinician group to complete this submission?	No	☐
	Yes	☒
OH-CCO provided a secretariat function to the group.		
2. Did you receive help from outside your clinician group to collect or analyze any information used in this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
B. Previously Disclosed Conflict of Interest		
3. 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	☒
	Yes	☐
If yes, please list the clinicians who contributed input and whose declarations have not changed: • Clinician 1		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	*Dr. Girish Kulkarni*
Position	*Lead, Ontario Health (Cancer Care Ontario) Genitourinary Cancer Drug Advisory Committee*
Date	*16-08-2023*
☒	**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	☐	☐	☐	☐

New or Updated Declaration for Clinician 2	
Name	*Dr. Urban Emmenegger*
Position	*Member, Ontario Health (Cancer Care Ontario) Genitourinary Cancer Drug Advisory Committee*
Date	*16-08-2023*
☒	**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**
Merck	☒	☐	☐	☐
Add company name	☐	☐	☐	☐

New or Updated Declaration for Clinician 3	
Name	*Dr. Sebastien Hotte*
Position	*Member, Ontario Health (Cancer Care Ontario) Genitourinary Cancer Drug Advisory Committee*
Date	*16-08-2023*
☒	**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**
Merck	☒	☐	☐	☐
Add company name	☐	☐	☐	☐

New or Updated Declaration for Clinician 4	
Name	*Dr. Aly-Khan Lalani*
Position	*Member, Ontario Health (Cancer Care Ontario) Genitourinary Cancer Drug Advisory Committee*

Date	*16-08-2023*
☒	**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**
Merck	☒	☐	☐	☐

New or Updated Declaration for Clinician 5	
Name	*Dr. Chris Morash*
Position	*Member, Ontario Health (Cancer Care Ontario) Genitourinary Cancer Drug Advisory Committee*
Date	*16-08-2023*
☒	**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**
Merck	☒	☐	☐	☐

New or Updated Declaration for Clinician 6	
Name	*Dr. Akmal Ghafoor*
Position	*Member, Ontario Health (Cancer Care Ontario) Genitourinary Cancer Drug Advisory Committee*
Date	*16-08-2023*
☒	**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	☐	☐	☐	☐

CADTH

CADTH Reimbursement Review

Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0309
Name of the drug and Indication(s)	Belzutifan for patients with von Hippel-Lindau (VHL) disease who require therapy for associated non-metastatic renal cell carcinoma, central nervous system hemangioblastomas, or non-metastatic pancreatic neuroendocrine tumors.
Organization Providing Feedback	PAG

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
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. No algorithm is needed

Outstanding Implementation Issues

In the event of a positive draft recommendation, drug programs can request further implementation support from CADTH on topics that cannot be addressed in the reimbursement review (e.g., concerning other drugs, without sufficient evidence to support a recommendation, etc.). Note that outstanding implementation questions can also be posed to the expert committee in Feedback section 4c.

Algorithm and implementation questions
1. Please specify sequencing questions or issues that should be addressed by CADTH (oncology only)
1. 2.
2. Please specify other implementation questions or issues that should be addressed by CADTH
1. 2.
3. Please specify questions or issues that should be addressed by CAPCA. (oncology only)
1. 2.
Support strategy
4. Do you have any preferences or suggestions on how CADTH should address these issues?
May include implementation advice panel, evidence review, provisional algorithm (oncology), etc.

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0309 Welireg
Brand name (generic)	Belzutifan/Welireg
Indication(s)	For the treatment of adult patients with von Hippel-Lindau (VHL) disease who require therapy for associated non-metastatic renal cell carcinoma (RCC), central nervous system (CNS) hemangioblastomas, or non-metastatic pancreatic neuroendocrine tumors (pNET), not requiring immediate surgery
Organization	Merck
Contact information[a]	Name: Stephen Parrott

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.

On behalf of the ***Canadian VHL Alliance, Canadian Organization for Rare Disorders, Kidney Cancer Canada, Pancreatic Cancer Canada, and the Canadian Neuroendocrine Tumour Society,*** we agree with this recommendation as it generally aligns with the inclusion/exclusion criteria of the LITESPARK-004 study of Belzutifan.

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?

Economic Feedback

We applaud the pERC for taking the very positive step to evaluate belzutifan through the complex rare disease lens, including the significant unmet need for VHL patients. However, we are extremely concerned that this step forward could still result in significantly delaying or even denying access if the current economic cost utility (re)analysis stands. First, there is no justification for the "removal of belzutifan residual benefit after treatment discontinuation during the post-trial period; removal of caregiver disutility; and, removal of belzutifan trial RDI and generic costing assumptions." Second, the data used to calculate the ICER of $360,193 per QALY are not provided so there is no way of verifying this result. Third, and most important there is absolutely no justification for adherence to an decades-old and arbitrary threshold of $50,000 per QALY as the willingness-to-pay (WTP) for payers. All these results do is provide payers with the inappropriate ammunition to prolong negotiations, which jeopardizes patients' lives and well-being.

"The ICER for belzutifan is $360,193 per QALY gained for the VHL-RCC cohort when compared with active surveillance. A price reduction of 83% would be required for belzutifan to achieve an ICER of $50,000 per QALY gained compared to active surveillance."

Sharing Best Practices Guidelines
Regarding the "Stakeholder Perspectives, Clinician input, Input from clinical experts consulted by CADTH", on page 8, in the third paragraph, it is noted: "Thus, prescription may be limited to specialists (e.g., medical oncologist, neuro oncologists) working in these large centers."

To ensure fair, timely, and equitable access to belzutifan, we strongly urge CADTH to include in its recommendations that public drug plans, in addition to providing timely access, must put in place strategies to assure patients not adjacent to specialist centres, have access to this therapy. The recommendation should include a process for the development and dissemination of best practice guidelines for screening, genetic testing and diagnosis to identify patients that need this drug immediately and those who might need it in the future.

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.

The VHL community appreciates the clarity in the recommendation, but as detailed in our previous and following comments, we do not agree with all of the reasons, nor the recommendations.

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.

Again, the community supports pERC's efforts to find the difficult balance found for the rare disease therapy approval process and your conclusion regarding the significant value of this therapy.

Indeed, even as we were preparing our response to this recommendation, we have been contacted by patients that are suffering and desperately awaiting access to therapy. By way of illustration, we include here the story of [redacted], a VHL patient who lives in Edmonton. She currently has a 3 cm growth on her kidney that is getting larger. [redacted] has lost both eyes, undergone 5 brain surgeries and she has another growth in her brain that could demand another surgery. [redacted] notes that her tumours grow quickly. She clearly cannot wait another 6 to 12 months to have access to treatment.

On behalf of [redacted] and the other patients that are suffering today, we implore pERC to unequivocally state in its recommendation, the absolute urgency to make this new therapy available to Canadian patients as soon as possible. Please use this recommendation and your position as clinical leaders to recommend including a pathway for immediate access to those in critical need, even while the price is being negotiated. The recommendation should be clear: negotiations between the pan Canadian Pharmaceutical Alliance (pCPA) and public drug plans should be initiated and concluded as quickly as possible.
.

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.

In section 2 and 4 above, we ask you to reconsider the arbitrary willingness-to-pay threshold of $50,000 for reimbursement and please pass along the recommendation for urgency in the evaluation of this therapy.

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

Appendix 1. Conflict of Interest Declarations for Patient Groups

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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	*Stephen Parrott*
Position	*Chair Canadian VHL Alliance*
Date	*17-08-2023*
☒	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

1. 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	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐