CADTH

CADTH REIMBURSEMENT REVIEW

Stakeholder Feedback on Draft Recommendation

fidanacogene elaparvovec (Beqvez)

(**Pfizer Canada ULC**)

Indication: For the treatment of moderately severe to severe hemophilia B (congenital Factor IX deficiency) who are negative for neutralizing antibodies to variant AAV serotype Rh74

February 2, 2024

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SG0802-000
Brand name (generic)	Fidanacogene Elaparvovec
Indication(s)	For the treatment of adults (aged 18 years or older) with moderately severe to severe hemophilia B (congenital Factor IX deficiency) who are negative for neutralizing antibodies to variant AAV serotype Rh74r
Organization	Association of Hemophilia Clinic Directors of Canada (AHCDC)
Contact information[a]	Hannah Van Hofwegen, AHCDC Project Manager, [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.

We thank the committee for their important work and for taking into consideration input from patients and clinician groups in developing these draft recommendations. We appreciate the ethical and health equity considerations in including female patients in the reimbursement conditions. However, we are very concerned about the arbitrary use of a factor IX level ≤2% in the reimbursement decision-making (we have elaborated this in Q5 below with references). The main concern is well-recognized limitations in the accuracy and reproducibility of factor IX assays when measuring factor IX activity at lower levels, regardless of which specialized coagulation laboratories and which instruments/reagents are used. In the Ethical Considerations section, the inequities and injustice experienced by people with severe bleeding phenotype with a measured factor IX activity of ≤2% vs 3-5% were not acknowledged. Clinically, the definition of moderately severe hemophilia is ≤5%, not ≤2%. We would strongly recommend avoiding the use of an arbitrary (unreliable) laboratory threshold, and placing a greater emphasis on patients' clinical phenotype and clinician judgment from a small group of clinical experts in hemophilia care. We believe this would be in keeping with the core guiding principle of "Equity, Diversity, and Inclusion" of the CADTH 2022-2025 Strategic Plan.

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?
The report acknowledged input from clinical experts that "severity in clinical practice is defined by the patients' phenotype and not simply by their factor activity levels", and specifically "Using FIX:C ≤2% as the definition was acceptable from the perspective of conducting a clinical trial. However, from the perspective of daily clinical practice… using this FIX level as criteria for eligibility is not appropriate." Unfortunately, this critical input from clinical experts consulted by CADTH was not factored in the recommendation, and not clearly justified.

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 reason for the reimbursement condition requiring FIX:C ≤2% AND bleeding requiring ongoing prophylactic treatment is not justified. The document acknowledged on several occasions that the threshold of FIX:C ≤2% is an arbitrary threshold used for clinical trial criteria, but is inappropriate for clinical treatment decision-making. Furthermore, there is no plausible reason to consider Fidanacogene Elaparvovec to be less safe for symptomatic hemophilia B patients with baseline factor IX activity >2% than for those below this level. Under the "Reason" column justifying this reimbursement condition in Table 1, the listed reason (i.e. clinical experts indicate that disease severity should be based on multiple factors including FIX:C level, clinical phenotype and clinician judgement) appears to be contradictory to the recommendation.

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.

There are significant concerns from expert hemophilia clinicians and laboratory hematologists on the reimbursement conditions, around the stringency and arbitrary use of a factor IX activity of ≤2%, which may create inequities among Canadian persons with hemophilia. The historical classification based on clotting factor activities is outdated, resulting in the use of clinical bleeding phenotype in the updated World Federation of Haemophilia (WFH) guidelines. Some patients with a measured FIX activity of 3% may have more severe bleeding phenotype compared to others with a FIX activity of 1-2%, partly due to the inherent variability of factor assays, and partly due to numerous other modifiers of bleeding phenotype (e.g. levels of other procoagulant and anticoagulant proteins, joint status). More importantly, inter-laboratory variations in FIX activity have been well documented. Guidelines from the Clinical and Laboratory Standards Institute (CLSI) explicitly acknowledged limitations of the validity and reproducibility of measuring coagulation factor assays in patients with low factor activities. In section 4.3.2 Factor Assays in the Presence of Severe Deficiency, the guideline stated that "There may be particular difficulties in performing assays for factor activities below 3% (0.03 U/mL). Results at these low factor activities may not be accurate or reproducible." This is independent of which specialized coagulation laboratory is used for testing, as prior proficiency testing conducted by the North American Specialized Coagulation Laboratory Association (NASCOLA) showed comparable results across different laboratories (using different reagent/instrument combinations), but rather the coefficient of variation was worse with lower factor levels. type of clotting factor assays used

References:

1. Clinical and Laboratory Standards Institute. Determination of coagulation factor activities using the one-stage clotting assay; approved guideline, 2nd ed. CLSI document H48, March 2016.

2. COAG-1402-FA, tested low FVII: Zantek ND, Hsu P, Refaai MA, Ledford-Kraemer M, Meijer P, Van Cott EM. Factor VII assay performance: an analysis of the North American Specialized Coagulation Laboratory Association proficiency testing results. Int J Lab Hematol. 2013 Jun;35(3):314–21

[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	*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 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**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

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	☒
	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 information used in this submission?	No	☒
	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 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	*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 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	*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 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 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.

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 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 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 5	
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 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	☐	☐	☐	☐

Canada's Drug and Health Technology Agency

CADTH Reimbursement Review

Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SG0802
Name of the drug and Indication(s)	Fidanacogene Elaparvovec (Beqvez) for the treatment of adults (aged 18 years or older) with moderately severe to severe hemophilia B (congenital Factor IX deficiency) who are negative for neutralizing antibodies to variant AAV serotype Rh74
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
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

Version: 1.0
Publication Date: TBC
Report Length: 2 Pages

Single Technology

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.

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.
Support strategy
3. 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	SG0802-000-000
Brand name (generic)	fidanacogene elaparvovec
Indication(s)	Hemophilia B
Organization	Canadian Hemophilia Society
Contact information[a]	Name: David Page [redacted]

Stakeholder agreement with the draft recommendation		
1. Does the stakeholder agree with the committee's recommendation.	Yes	☒
	No	☐
Yes, the Canadian Hemophilia Society (CHS) agrees with the recommendation that fidanacogene elaparvovec be reimbursed for the treatment of adults (aged 18 years or older) with moderately severe to severe hemophilia B (congenital Factor IX deficiency), who are negative for neutralizing antibodies (nAbs) to variant adeno-associated virus (AAV) serotype Rh74 if certain conditions listed in Table 1 are met. Eligibility should be based not only on factor IX level but also on clinical bleeding phenotype.		
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	☒
Yes, the recommendation demonstrates consideration of CHS input. Paragraph 2 of the rationale states, *"Patients identified a need for treatments that will alter the underlying disease process, restore coagulation factors to clinically effective levels, reduce the need for venipunctures, prevent or reduce bleeds, and improve their quality of life. CDEC concluded that fidanacogene elaparvovec may meet <u>some</u> of these needs."* The CHS believes that, based on the clinical trial results, fidanacogene elaparvovec will meet <u>all</u> of these needs in the majority of patients. Discussion Point 5 states that *"Patients indicated that they hope gene therapy would lead to less stress, fewer restrictions on activities, and make it easier to travel but CDEC could not definitively conclude that fidanacogene elaparvovec would meet these needs based on the submitted evidence."* While CHS could not submit hard evidence of these benefits from Canadian patients before the therapy was even introduced, it is self-evident to patients, as demonstrated by the comments submitted, that a one-time therapy that provides constant factor IX expression in the upper range of mild to the lower range of normal (20-40%) for an indefinite period, obviating the need for weekly IV infusions, would inevitably lead to less worry about bleeding and greater ability to engage in activities of daily living, and therefore improved physical and mental fitness, without the risk of spontaneous bleeding. These expectations are borne out by the clinical trial results from the two hemophilia B gene therapies that have been approved by Health Canada.		
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	☒

The final Discussion Point states that, *"As a one-time therapy that cannot be terminated once infused, the committee highlighted the importance of robust informed consent and establishing reasonable expectations regarding long-term effectiveness."* The CHS is in full agreement with this point and has created a robust gene therapy education program (www.hemophilia.ca/gene-therapy) to promote shared decision-making.

It is also stated that, *"The committee discussed the importance of addressing potential geographic barriers to equitable access given the limited number of infusion centers in Canada."* The CHS would see like to see in the final report a recommendation that, with the goal of equity, provinces and territories provide financial support for individuals to travel to the infusion centres. This would reduce the geographic and financial barriers to treatment. Ideally, all provinces and territories will add fidanacogene elaparvovec to their formularies.

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

The Canadian Hemophilia Society is generally in agreement with Reimbursement Conditions 1, 2, 3, 4 and 7. Notably, we fully support the clinician view that that disease severity should be based on FIX:C level as well as the patient's clinical bleeding phenotype (Reimbursement Condition 1). Therefore, Reimbursement Condition 1.1 should be modified to read: *"Documented moderately severe to severe hemophilia B based on FIX:C ≤ 2%* ***and/or*** *clinical bleeding phenotype requiring prophylactic treatment."* The CHS agrees with the priorities as listed in Discussion Point 2. Moreover, where the demand for this therapy is higher than the supply, we suggest creation of a national group of clinicians to determine which candidates, regardless of province of residence, have the greatest unmet need and potential benefit, so as to be treated in priority.

With regard to conditions 5 and 6, we have these comments. Yes, the price must be reduced. Moreover, any comparison to the cost of factor IX prophylaxis must take into account the actual costs of factor IX concentrates as negotiated by Canadian Blood Services. Regarding the feasibility of adoption of fidanacogene elaparvovec, the CHS urges CADTH to recommend in its final report consideration by pCPA of alternate reimbursement mechanisms, such as annual payments spread over 5 to 7 years. This would reduce the budget impact in the initial years and allow more patients to access the therapy after introduction. At an appropriate negotiated price, CHS is convinced that fidanacogene elaparvovec gene therapy will result in long-term savings for the health system in addition to health and quality-of-life benefits.

[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	*Please state full name* David Page
Position	*Please state currently held position* Consultant, Safety and Supply of Coagulation Products, Canadian Hemophilia Society
Date	*Please add the date form was completed* (01-02-2024)

☒	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
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

Pfizer Canada
17300, autoroute Transcanadienne, Kirkland (Québec) H9J 2M5
17300 Trans-Canada Highway, Kirkland, QC H9J 2M5

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SG0802-000
Brand name (generic)	BEQVEZ (fidanacogene elaparvovec)
Indication(s)	For the treatment of adults (aged 18 years or older) with moderately severe to severe Hemophilia B (congenital Factor IX deficiency) who are negative for neutralizing antibodies to variant AAV serotype Rh74.
Organization	Pfizer Canada ULC
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.		

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	☐

Overall, the reimbursement conditions are clearly stated however, Pfizer respectfully requests that the following be taken into account:

Condition 1.1.
That the wording for initiation, *"and bleeding requiring ongoing prophylactic treatment"* be clarified to *"and bleeding requiring prophylactic treatment"*. This clarification may better align with the opinion of clinical experts that fidanacogene elaparvovec be given to patients who would benefit from FIX prophylaxis, rather than to those who have been on an ongoing FIX prophylaxis regimen. Further, this will aid in reflecting that FIX:C alone does not define clinical phenotype, as indicated by clinical experts, and ensure that access not be limited to those who may benefit but may not be receiving prophylaxis for a number of reasons (e.g., intravenous access limitations).

Condition 5. The reimbursement condition and the rationale are clearly stated. However, given limitations of conventional cost-effectiveness analysis as applied to rare diseases, the health technology assessment (HTA) for a treatment of a rare disease should entail a higher cost-effectiveness threshold than that used for standard HTA assessment. This underlines the need to have a HTA framework for drugs for rare diseases that offers important health benefits to the patients with rare conditions and high unmet need.

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