CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Instructions for Stakeholders

This template is for eligible stakeholders to provide feedback and comments on draft reimbursement recommendations. Draft recommendations are available for feedback for 10 business days.

CADTH will only consider feedback received from eligible stakeholders, including the sponsor, patient groups, clinician groups, and the participating drug programs. Individuals interested in providing feedback should contact the relevant patient and clinician organizations.

The sponsor may use this form to provide general feedback on the draft recommendation if they are not filing a request for reconsideration. If the sponsor is filing a request for reconsideration, they must complete the reconsideration template.

All submitted feedback must be disclosable and will be posted on the CADTH website.

If you have questions, please email requests@cadth.ca with the complete details of your question(s).

Before Completing the Template:

Please review the following documents to ensure an understanding of CADTH's procedures:

- Procedures for CADTH Reimbursement Reviews
- CADTH Pharmaceutical Review Updates for any applicable information.

Completing the Template:

Feedback should be presented clearly and succinctly in point form, whenever possible. The issue(s) should be clearly stated and specific reference must be made to the section of the recommendation document under discussion (i.e., page number, section title, and paragraph).

Comments should be restricted to the content of the draft recommendation and should not contain any language that could be considered disrespectful, inflammatory or could be found to violate applicable defamation law.

Feedback must be based on the information that was considered by the expert committee in making the draft recommendation. No new evidence will be considered at this part of the review process.

Feedback must not exceed 3 pages in length, using a minimum 11-point font on 8.5″ by 11″ paper. If comments exceed 3 pages, the feedback will not be accepted by CADTH. References may be provided separately; however, these cannot be related to new evidence.

Patient groups must complete Appendix 1 and clinician groups must complete Appendix 2.

Filing the Completed Template:

The feedback must be provided in Microsoft Word format by using the *Submit* link next to the drug on the Open Calls page. In order to ensure fairness in CADTH's procedures, all stakeholder feedback must be received by the deadline posted on the CADTH website.

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0710-000
Brand name (generic)	Trikafta (elexacaftor/tezacaftor/ivacaftor and ivacaftor)
Indication(s)	Cystic fibrosis, F508del CFTR mutation, 6 years and older
Organization	Cystic Fibrosis Canada
Contact information[a]	Name: Dr. John Wallenburg, Chief Scientific Officer

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

Cystic Fibrosis Canada (CF Canada) agrees that Canada's public drug programs should reimburse Trikafta (ETI) for this cohort. We are pleased that the draft recommendation for those 6+ comes without any upper lung function start criterion.

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	☐

We appreciate CDEC's thoughtful consideration of the evidence and stakeholder submissions. Our clinicians and our patient community are thankful that CADTH has recognized the importance of considering the many benefits and outcomes that patients may experience when taking ETI. We are pleased that CDEC has acknowledged the complexity of CF care and the initiation of ETI. We agree that this makes CF specialists uniquely positioned to prescribe and monitor treatment response. It follows that prescribing and monitoring of ETI should be limited to CF specialists.

CF Canada believes that the prescribing regimen of all CFTR modulators should be in alignment with the *Canadian Clinical Consensus Guideline for Initiation, Monitoring and Discontinuation of CFTR Modulator Therapies for Patients with Cystic Fibrosis* (the clinical consensus guideline), which was developed by CF clinicians specifically for Canadians living with the disease. The guideline is being updated to reflect the new 6–11-year-old Health Canada indication and the growing body of real world evidence (RWE) that demonstrates the impact of ETI on those currently indicated, as well as those who live with rarer mutations and who are post-transplant. There is also emerging evidence on use of ETI in pregnancy to treat mothers and/or fetuses with CF. CF Canada will provide CDEC with the revised guideline when available.

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

We appreciate that CDEC considered the RWE provided, which is important in paving the way for better access to high value drugs for rare diseases, including precision medicines. In reviewing the RWE, CDEC noted small sample size and lack of comparator group as limitations. For rare conditions, sample sizes will be small and there may be a lack a comparator group. We caution CADTH not to unfairly limit the value of RWE by applying unrealistic demands. These issues will become evident as CDEC considers future applications that may be made for patients aged 2 to 5 years, 18 months to 2 years, and 4 months to 18 months or when evaluating access for individuals who have undergone transplants and those with very rare mutations that can be treated with ETI.

	Yes	☐

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

Reduce the burden on clinics. Many CF clinics are already struggling to meet the initiation and reimbursement requirements of Canada's public and private payers. The addition of 6-11 year olds and individuals who are 12 years of age or older with lung functions of 90% or greater will increase this burden. CF clinicians are the experts in CF care. They use the clinical consensus guideline to inform their decision-making on access to therapy that includes a schedule for baseline evaluation and monitoring of patients aged 6 years of age and older.

Address the unintended use of CADTH recommendations. CADTH's reimbursement reviews are conducted for and with Canada's public drug programs in mind. However, increasingly private insurers are using CADTH recommendations to deny access to life-changing therapies for drugs for rare diseases. This became explicitly clear as clinically eligible patients were turned away for private coverage of ETI based on CDEC's recommended 90% price reduction for implementation of 12+ (which is also reflected in CDEC's 6+ recommendation). This is a significant barrier to access and needs addressing.

CF Canada would like to acknowledge Canada's public drug programs efforts to cover ETI quickly. Nevertheless, there are still people who are falling through the cracks in jurisdictions that charge high deductibles for public access or have convoluted coordination between public and private payers. This is an implementation issue that must be addressed to ensure needed access. CADTH can help by reinforcing that its recommendations serve and are designed for Canada's public drug programs.

Cystic Fibrosis Canada recommends that the following issues be addressed in CDEC's implementation guidance:

- Reduce the burden on clinics by reducing requirements where possible and streamlining processes and paperwork required to initiate, monitor and renew therapies. Where needed, jurisdictions should provide additional resources to CF clinics specifically to help them prioritize and thoroughly process patients in a timely manner.
- Address the unintended use of CADTH recommendations to limit access to treatment among private payers. In its recommendations, CADTH should explicitly state that its drug reviews are designed for the public payer market and are not intended to be used in whole or in part to deny access to patients who rely on private coverage.

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

Overall, CDEC's recommended initiation criteria align with the clinical consensus guideline. The guideline calls for treatment of CFTR modulators to be started at the youngest age approved by Health Canada with the goal of attenuating disease progression and improving clinical status.

One area for improvement relates to limiting access to patients with at least one copy of F508del. There is good laboratory evidence to support the use of ETI on other, very rare mutations.

Unfortunately, Canada is behind its international comparators when it comes to regulatory review and reimbursement of drugs for rare diseases. One driver of these access challenges is that Canada rejects certain forms of evidence especially useful for rare disease populations. Canada is without a framework to fairly consider laboratory based predictive tools for precision medicines. Yet, good in-vitro predictive tools exist in Canada (e.g. the Program for Individualized Cystic Fibrosis Therapy (CFIT) at SickKids) in Europe (HIT-CF Europe) and elsewhere that predict individual and mutation class responses of rare mutations to ETI.

In addition, clinicians can both empirically see and explicitly measure the response that such individuals have to a medication. Our regulatory, review and reimbursement bodies do not generally accept such evidence. Both the FDA in the United States and the NHS in the United Kingdom have

accepted in-vitro data to expand access (off-label in the UK) to ETI to an additional 177 mutations (or more). Cystic Fibrosis Canada recommends that CADTH follow the examples of the FDA and the NHS to recommend access for patients with rare mutations through use of laboratory based predictive tools.

CDEC is right to point out that patients who have had a solid organ transplant were excluded from the main studies of Trikafta. The clinical experts consulted by CDEC noted that treatment should be discontinued in patients who have received lung transplant given that lung transplants are a last resource for people with CF with end-stage lung disease. However, although CFTR modulators are not expected to improve the function of grafted lungs, they do have potential to alleviate extrapulmonary manifestations of CF such as chronic rhinosinusitis and gastrointestinal disease. Paranasal sinuses may act as a reservoir for pathogens following transplantation, so treatment of chronic rhinosinusitis with CFTR modulators may reduce respiratory infectious complications after lung transplantation. We propose that CADTH reconsider its blanket exclusion of patients post-transplant and recommend that a CF specialist have the ability to initiate and monitor ETI therapy in a post-transplant CF patient when there is a demonstrated medical need.

[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	Dr. John Wallenburg
Position	Chief Scientific Officer
Date	03-06-2022
☒	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	☐	☐	☐	☐