CADTH

CADTH REIMBURSEMENT REVIEW

Stakeholder Feedback on Draft Recommendation

PEMBROLIZUMAB (Keytruda)

(Merck Canada Inc.)

Indication: For the first line treatment of adult patients with unresectable or metastatic microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) colorectal cancer (CRC)

June 24, 2021

CADTH

CADTH Reimbursement Review Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0235-000
Brand name (generic)	pembrolizumab (Keytruda)/Merck
Indication(s)	**Indications:** For the first line treatment of adult patients with unresectable or metastatic microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) colorectal cancer (CRC) **Manufacturer Requested Reimbursement Criteria[1]:** For the first line treatment of adult patients with unresectable or metastatic microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) colorectal cancer (CRC)
Organization	Ontario Health (Cancer Care Ontario) Gastrointestinal Cancer Drug Advisory Committee
Contact information[a]	Name: Dr. Erin Kennedy [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. The GI DAC would like to comment that drug wastage should be taken into consideration related to the implementation of weigh-based dose of 2mg/kg /IV. Currently, Ontario does not reimburse cancer centres for drug wastage.		

dMMR staining through IHC should be standard of care.		
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. Contact information will not be included in any public posting of this document by CADTH.

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 provided secretariat support to the DAC in completing this input.		
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: • Dr. Erin Kennedy • Dr. Jim Biagi • Dr. Christine Brezden-Masley • Dr. Tim Asmis		

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

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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	☐	☐	☐	☐

CADTH

CADTH Reimbursement Review

Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0235-000
Name of the drug and Indication(s)	Pembrolizumab for the first line treatment of adult patients with unresectable or metastatic microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) colorectal cancer (CRC)
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	x
	No requested revisions	☐

2. Change in recommendation category or conditions Complete this section if major or minor revisions are requested
None

3. Clarity of the recommendation Complete this section if editorial revisions are requested for the following elements
a) Recommendation rationale
None
b) Reimbursement conditions and related reasons
None
c) Implementation guidance
- PAG is seeking clarity on whether retreatment is for an additional 17 doses (1 year) or until disease progression, whichever occurs first. - PAG is seeking clarity on the disease-free interval requirement for retreatment (i.e., 6 months) as other metastatic pembrolizumab policies do not have this restriction. - PAG noted in the implementation advice, the following question “Should patients with confirmed MSI-H/dMMR mCRC who received other systemic therapies for 1st line mCRC who experienced disease progression be eligible to receive pembrolizumab in later lines

of therapy?" was not answered and PAG would like to have this included in the implementation advice.

CADTH

CADTH Reimbursement Review Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0235-000
Brand name (generic)	**KEYTRUDA (PEMBROLIZUMAB)**
Indication(s)	**1st Line Treatment of Adult Patients with Unresectable or Metastatic Microsatellite Instability High (MSI-H) or Mismatch Repair Deficient (dMMR) Colorectal Cancer**
Organization	**Colorectal Cancer Resource & Action Network (CCRAN)** – Registered Charity
Contact information[a]	Name: Filomena Servidio-Italiano [redacted] [redacted]

Stakeholder agreement with the draft recommendation

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

CCRAN happily agrees with the draft recommendation but would like to respectfully point out the following regarding the first line reimbursement condition: (Pg.3, Table 1, Initiation, "Patient has not received…", 1,1). While the review was predicated on evidence provided from the KEYNOTE 177 study, which did not include patients who had previously received treatment for their MSI-H/dMMR metastatic colorectal cancer, a second study (KEYNOTE 164) focusing on second line treatment (or later), demonstrated a clinical benefit in patients who had previously received chemotherapy. Although this study was limited by a small sample size and did not include a comparator, the findings were nevertheless supported by the robust KEYNOTE 177 data. The study provided evidence that Pembrolizumab could be an additional treatment option for the 2nd line (or greater) MSI-H/dMMR patient population, helping to address a significant unmet need for patients.

The recently issued conditional, positive funding recommendation by INESSS in respect of Pembrolizumab took this unmet need of MSI-H/dMMR metastatic colorectal cancer (mCRC) patients who were previously treated with chemotherapy with or without biologic therapy into consideration and decided to include these additional patients to promote equity and ethical practice. CCRAN is respectfully requesting same to avoid any ethical or equity issues.

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, CCRAN is pleased with the Committee's review of our input. However, perhaps thoughtful consideration may be given to granting access to current 2nd line or higher MSI-H/dMMR confirmed mCRC patients who were previously treated with chemotherapy with or without a biologic therapy. Although Pembrolizumab is not indicated in the second- or third-line treatment of patients whose disease has progressed after FOLFOX or FOLFIRI (with or without a biologic therapy), from an ethical and equitable perspective, perhaps these patients who currently have confirmed MSI-H/dMMR disease should be afforded the opportunity to access and benefit from the therapy, rather than having to receive a less effective treatment. CCRAN provided compelling input from two patients who accessed Pembrolizumab in the second line setting. These patients derived significant benefit in the second line setting, supporting our request to consider incorporating the subset of the **current** patient population who have been previously treated such that they too may derive benefit from a new standard of care immunotherapy that targets their specific tumour biology.

Clarity of the draft recommendation

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

The reasons for the recommendation were clearly articulated in the draft recommendation and based on "*a review of **one** phase III RCT (KEYNOTE 177 study) as well as an indirect treatment comparison provided by the sponsor….*" (p.4, Sources of Information) which supports a first line treatment indication. As noted above, the KEYNOTE 177 study included the first line treatment of MSI-H/dMMR confirmed mCRC patients. Second or third line patients were not included in this study but were included in the KEYNOTE 164 study whose results indicate that Pembrolizumab bestows a clinical benefit in these previously treated patients. Improving patient outcomes for the MSI-H/dMMR mCRC patient population, whose disease has been deemed historically problematic to treat, is now within our reach and a reality.

Again, we kindly request that consideration be given to ensure current 2nd line or higher MSI-H/dMMR mCRC patients be permitted to access Pembrolizumab as early as possible in their treatment journey to help address a significant unmet need. This would align with the recommendation recently issued by **INESSS** and would certainly avoid any ethical and equity issues created by denying these patients access to a life prolonging therapy that promotes excellent Quality of Life. Regional disparities throughout Canada would also be avoided by helping to ensure **current** 2nd line and higher patients would be provided access.

In light of its first line indication and the requested accommodation for current 2nd line and higher patients, CCRAN believes the use of Pembrolizumab in subsequent lines of treatment would be limited and merely a temporary situation as Pembrolizumab undergoes the transition process following the provincial formulary listing. Hence, MSI-H/dMMR mCRC patients should be permitted to access Pembrolizumab to promote fairness, equity and best outcomes for a patient population who has historically experienced a poor prognosis and poor responses to standard of care therapies.

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

From a first line treatment perspective, yes, the implementation issues have been clearly articulated and nicely addressed in the draft recommendation. However, seeing that we are an ethical society, **distributive justice should prevail, allowing access to Pembrolizumab by currently diagnosed MSI-H/dMMR confirmed metastatic colorectal cancer patients regardless of line of therapy across Canada.** The funding of Pembrolizumab in subsequent lines of therapy would not be in perpetuity. Instead, it is anticipated that its use in subsequent lines of treatment would be limited in time considering its first line treatment indication.

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

Yes, the reimbursement conditions are clearly stated (p.3, Table, Reimbursement Conditions) for the MSI-H/dMMR mCRC patient population "*who have not received prior treatment*" for their disease. CCRAN respectfully requests, however, that thoughtful consideration be given to expanding access to Pembrolizumab for the time being to include current 2nd line or greater patients with confirmed MSI-H/dMMR disease as early as possible in their treatment sequence (lasting a limited period) because it would:

- Address a significant unmet clinical need in the MSI-H/dMMR patient population.
- Promote responsible, equitable, fair and ethical decision making across Canada, assuming the manufacturer were to contribute to the reduction in the economic burden.
- Improve patient outcomes.

CCRAN recognizes that Pembrolizumab is indicated for the first line treatment of MSI-H/dMMR mCRC, but its use in previously treated patients (chemotherapy with or without a biologic therapy) will be **short lived** as this immunotherapy now becomes the new standard of care in the **first line treatment of MSI-H/dMMR metastatic colorectal cancer**.

[a] CADTH may contact this person if comments require clarification. Contact information will not be included in any public posting of this document by CADTH.

Appendix 1. Conflict of Interest Declarations for Patient Groups

A. Patient Group Information	
Name	*Filomena Servidio-Italiano*
Position	*President & CEO, CCRAN*
Date	*(23-06-2021)*
☒	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**
AMGEN	☐	☐	☒	☐
BAYER	☐	☐	☒	☐
TAIHO	☐	☐	☒	☐
PFIZER	☐	☐	☒	☐
MERCK	☐	☐	☒	☐
ELI LILLY	☐	☐	☒	☐
IMV	☐	☒	☐	☐
OLYMPUS	☒	☐	☐	☐
MARSDEN CENTRE OF EXCELLENCE	☐	☐	☒	☐

CADTH

CADTH Reimbursement Review Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0235-000
Brand name (generic)	Pembrolizumab
Indication(s)	For the first line treatment, as monotherapy, of adult patients with metastatic microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) colorectal cancer (CRC)
Organization	Merck Canada Inc.
Contact information[a]	Name: David Germélus [redacted]

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

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	☒

In the clinical review report, clinical experts consulted by CADTH and clinicians who provided input as part of a group advocated that "*patients who experience disease progression after being treated with chemotherapy could receive pembrolizumab next*" and that it "*would be used alone for any line of therapy*". Additionally, the Patient Group Input included testimonies of patients who received pembrolizumab for the treatment of mCRC in the 1st line setting, but also in the 2nd, 3rd and 4th lines. Furthermore, during its review, CADTH requested that Merck provide the clinical study report for the KEYNOTE-164 (KN-164) trial, which evaluated the antitumor activity of pembrolizumab in previously treated metastatic MSI-H/dMMR colorectal cancer. Given these trends, it may suggest that the current recommendation does not necessarily reflect stakeholder input.

Merck kindly requests CADTH to consider that, at the time of implementing a funding recommendation for pembrolizumab, jurisdictions may consider addressing the time-limited need for pembrolizumab in patients who have experienced disease progression after being treated with chemotherapy, as advocated by stakeholders.

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	☒

Retreatment

In the 1st and 2nd implementation guidance points on page 3, it is stated that "*The Keynote 177 study did not have specific guidelines regarding retreatment with pembrolizumab*". Merck strongly disagrees with this statement as it is erroneous. The KEYNOTE-177 trial protocol (available online as supplementary material to the *Andre et al. 2020, Pembrolizumab in Microsatellite-Instability–High Advanced Colorectal Cancer* publication) clearly states the following:

"*Subjects who stop pembrolizumab (MK-3475) with SD or better may be eligible for up to 17 additional trial treatments (approximately 1 year) if they progress after stopping study treatments. Retreatment with pembrolizumab (MK-3475) is termed the Second Course Phase and is only available if the subject meets the following conditions*:

· ***Either***

- *Stopped initial/crossover treatment with pembrolizumab (MK-3475) after attaining an investigator-determined confirmed CR according to RECIST 1.1*
- *Was treated with at least 8 study medications (approximately 6 months) with pembrolizumab (MK-3475) before discontinuing therapy*
- *Received at least 2 treatments with pembrolizumab (MK-3475) beyond the date when the initial CR was declared*

OR

- *Had SD, PR or CR and stopped pembrolizumab (MK-3475) after 35 study medications (approximately 2 years) for reasons other than disease progression or intolerability*

· ***AND***

- *Experienced an investigator-determined radiographic disease progression (which must also be verified centrally) after stopping their initial/crossover treatment with pembrolizumab (MK-3475). If a subject is unstable as a result of a new or progressing brain metastasis, the subject will not be eligible for the Second Course Treatment Phase, unless stability per exclusion criterion # 6 is satisfied after the management of the new/progressing brain metastasis*
- *Did not receive any anticancer treatment since the last dose of pembrolizumab (MK-3475)*
- *Has a performance status of 0 or 1 on the ECOG Performance Scale*
- *Demonstrates adequate organ function as detailed in Table 4.*
- *Female subject of childbearing potential should have a negative serum test within 72 hours prior to receiving retreatment with pembrolizumab (MK-3475).*
- *Female subject of childbearing potential should be willing to use 2 methods of birth control or be surgically sterile, or abstain from heterosexual activity for the course of the study through 120 days after the last dose of pembrolizumab (MK-3475) (Reference Section 5.7.2). Subjects of child bearing potential are those who have not been surgically sterilized or have been free from menses for > 1 year.*
- *Male subject should agree to use an adequate method of contraception starting with the first dose through 120 days after the last dose of pembrolizumab (MK-3475).*
- *Does not have a history or current evidence of any condition, therapy, or laboratory abnormality that might interfere with the subject's participation for the full duration of the study or is not in the best interest of the subject to participate, in the opinion of the treating investigator.*

Subjects who enter the Second Course Phase will be retreated at the same dose frequency as when they last received pembrolizumab (MK-3475). Pembrolizumab (MK-3475) may be administered for up to an additional 17 study medications (approximately 1 year). "

These retreatment guidelines have been used consistently across pembrolizumab clinical trial protocols. In previous submissions for pembrolizumab reviewed by the pERC, retreatment has been recommended as per trial protocols, without a suggested 6-month progression free period prior to eligibility.

Considering the previous information, Merck kindly requests CADTH to correct the implementation guidance with a statement containing the following: "Retreatment would be reasonable as per conditions mentioned in the KN-177 protocol."

400 mg Q6W dosing regimen

It can be noted that the draft recommendation only mentions the approved 200 mg Q3W pembrolizumab dosing regimen on page 3, 3rd implementation guidance point. Merck would like to highlight that a new pembrolizumab dosing regimen has been approved by Health Canada on April 29th, 2021. This alternate dosing regimen is 400 mg IV every six weeks (Q6W).

As the draft recommendation is based on the May 13th, 2021 pERC meeting, Merck kindly requests CADTH to acknowledge this new dosing regimen in its final recommendation.

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

In the first paragraph of the Economic Evidence section (page 7), it is mentioned that "*Pembrolizumab is available as a 100 mg/4 mL vial, priced at $4,400 per vial. The recommended dosage is 200 mg every three weeks, at a cost of $11,733 per cycle*." The cited cost per cycle is erroneous and should be corrected. It should either mention a cost per cycle of $8,800 or a cost per 28-days of $11,733.

[a] CADTH may contact this person if comments require clarification. Contact information will not be included in any public posting of this document by CADTH.

Appendix 1. Conflict of Interest Declarations for Patient Groups

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- 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

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  - 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	☐	☐	☐	☐