CADTH

CADTH REIMBURSEMENT REVIEW

Stakeholder Feedback on Draft Recommendation

tebentafusp (Kimmtrack)

(Medison Canada)

Indication: unresectable or metastatic uveal melanoma.

December 15, 2022

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0290-000
Brand name (generic)	Kimmtrak (tebentafusp)
Indication(s)	For the treatment of human leukocyte antigen (HLA)-A*02:01-positive adult patients with unresectable or metastatic uveal melanoma.
Organization	Ontario Health (Cancer Care Ontario) Skin Cancer Drug Advisory Committee ("Skin DAC")
Contact information[a]	Name: Dr. Frances Wright

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. Please comments in Question 5 below re: reimbursement conditions.		

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.		

1. System and economic issues

Tebentafusp requires specialized clinicians for administration/preparation/monitoring, thus treatment is likely to be limited to larger centres. This introduces potential need for travel, additional impact to daily life, and potential for increased expenses for eligible patients. Drug wastage is quite significant as the standard dose is considerably less than the vial size (68 mcg vs 100 mcg) and single vial use is recommended. In some jurisdictions, wastage is not reimbursed by the drug plan and so hospitals may not be able to absorb the wastage cost.	*Comment from the drug programs to inform pERC deliberations.*

Re: Ontario currently does not reimburse drug wastage. The Skin DAC comments that vial size and treatment dose would lead to drug wastage and that the reimbursement should be for the vial (one vial = one treatment, regardless of the dose, as the drug volume will make it not possible for sharing). Additionally, vials cannot be shared as blood bank will not allow sharing of albumin, which is used as part of drug preparation.

The Skin DAC also wants to flag that the use of albumin for drug preparation has been challenging. For example, coordination of getting albumin ready for the day of infusion has been challenging. Blood bank regulation makes this very onerous on the pharmacies to get albumin. One Ontario centre's experience is that albumin is obtained from transfusion medicine and involves consent. Canadian Blood Services dispenses on a per patient basis due to current regulations. Some centres find the preparation and administration of tebendefusp too challenging and this may limit the ability to treat some patients closer to home.

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.

1. Reimbursement Conditions:

Table 1. Reimbursement Conditions and Reasons

Reimbursement condition	Reason	Implementation guidance
Initiation		
1. Treatment with tebentafusp should be reimbursed when initiated in adult patients who have HLA-A*02:01-positive unresectable or metastatic uveal melanoma in the first line setting	Evidence from Study 202 demonstrated that treatment with tebentafusp resulted in statistically significant and clinically meaningful improvement in OS, compared with investigator's choice of ipilimumab, pembrolizumab, or dacarbazine, in HLA-A*02:01-positive adult patients with unresectable or metastatic uveal melanoma in the first-line setting.	It would be reasonable for jurisdictions to consider reimbursement of tebentafusp in a second- or later- line setting on a time-limited basis.

Re: Second- or later-line setting: The Skin DAC recommends removal of "time-limited basis" and that reimbursement should also be available for patients beyond 1L setting (2L and later-line settings) on a routine basis based on significant unmet need and clinical benefit to previously treated patients is maintained despite prior therapy, as demonstrated by recent data from Study 102 (emerging biological correlation with ctDNA reduction, improved overall survival compared to historical controls) as noted on Page 16 of the draft recommendation report. There is significant unmet need – there is no standard treatment option available for patients with uveal melanoma.

The Skin DAC also raises concerns around equitable access to tebendafusp for patients, especially because tebendafusp treatment requires weekly infusion, and may limit certain patients geographically. As a result, some patients may preferentially be treated with 1L immunotherapy (e.g., pembrolizumab every 6 weeks). For patients who received immunotherapy 1L due to geographical limitations, they **should be eligible** to receive tebentafusp in later lines as there is data (as noted above, Study 102) to support 2L line and beyond use.

The Skin DAC underlines the CADTH clinical expert's statement that "outcomes of tebentafusp in Study 102 were clinically meaningful and demonstrated the activity of the drug were compatible to the Phase III Study 202." While

the DAC acknowledges that tebentafusp in 1L is best supported by the available data, there is no data to support denying tebentafusp in 2L if 1L administration is not preferred for the reasons outlined above.

2. Re: Discontinuation criteria

Discontinuation		
3. Tebentafusp should be discontinued in patients who no longer derive clinical benefit or have intolerable toxicity: 3.1. assessment for clinical benefits should be assessed for treatment response every 3 to 4 months or as per physician discretion	In Study 202, patients receiving tebentafusp or immunotherapy were allowed to continue treatment beyond initial radiographic progression if there was evidence of clinical benefit, or in the absence of intolerable toxicity. The clinical expert noted there is generally a poor correlation between tumour response and survival in patients with metastatic uveal melanoma receiving systemic treatments and in clinical practice, patients would continue tebentafusp beyond initial radiographic progression unless there is clear evidence of significant progression. The clinical expert also noted that in a post-hoc exploratory analysis of Study 202 among patients who had disease progression as their best overall response, patients who received tebentafusp had longer OS than patients in the investigator's choice arm.	pERC agreed with the clinical experts that the decision to discontinue treatment should be left to the discretion of the treating clinician.

The Skin DAC agrees that "the decision to discontinue treatment should be left to the discretion of the treating clinician" as RECIST radiographic progression does not correlate with clinical benefit of tebendafusp. Some patients may continue to benefit from treatment even with RECIST progression. The assessment should be based on investigator/treating physician's discretion.

[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 provided secretariat support to complete this submission.		
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. Frances Wright*
Position	*Lead, OH-CCO Skin DAC*
Date	*07-12-2022*
☒	**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**
No COI to declare	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 2	
Name	*Dr. Marcus Butler*
Position	*Member, OH-CCO Skin DAC*
Date	*07-12-2022*
☒	**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**
Medison Canada	☒	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 3	
Name	*Dr. Xinni Song*
Position	*Member, OH-CCO Skin DAC*
Date	*07-12-2022*
☒	**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**
Medison Canada	☒	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 4	
Name	*Dr. Elaine McWhirter*
Position	*Member, OH-CCO Skin DAC*
Date	*07-12-2022*
☒	**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**
Medison Canada	☒	☐	☐	☐
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 Reimbursement Review

Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0290
Name of the drug and Indication(s)	Tebentafusp for human leukocyte antigen (HLA)-A*02:01-positive adult patients with unresectable or metastatic uveal melanoma
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
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
None.

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CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0290-000
Brand name (generic)	tebentafusp
Indication(s)	unresectable or metastatic uveal melanoma
Organization	Melanoma Canada
Contact information[a]	Name: Annette Cyr

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. Melanoma Canada agrees with the recommendation that the drug should be funded and reimbursed. As was stated in the submission, there are few treatments for this rare form of melanoma and the prognosis for the majority of patient is grim. This treatment provides meaningful improvement in treatment and survival. It provides hope and improved quality of life for many patients and their families. We are concerned if the following statement in the draft relegates the drug therapy to second line, as it should be made available as a first line therapy, depending on patient and clinician determination, and also be available as a second line therapy should it not be used as first line. "It would be reasonable for jurisdictions to consider reimbursement of tebentafusp in a second- or later- line setting on a timelimited basis."		
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 1. Conflict of Interest Declarations for Patient Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
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A. Patient Group Information	
Name	*Annette Cyr*
Position	*Chair of the Board*
Date	*09-12-2022*
☒	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	☐	☐	☐	☐

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0290-000
Brand name (generic)	KIMMTRAK (tebentafusp)
Indication(s)	For the treatment of human leukocyte antigen (HLA)-A*02:01-positive adult patients with unresectable or metastatic uveal melanoma.
Organization	Medison Pharma Canada Inc.
Contact information[a]	[redacted]

Stakeholder agreement with the draft recommendation		
1. Does the stakeholder agree with the committee's recommendation.	Yes	☒
	No	☐
2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☒
	No	☐

Clarity of the draft recommendation		
3. Are the reasons for the recommendation clearly stated?	Yes	☒
	No	☐
4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☒
	No	☐
5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☒
	No	☐

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