

CADTH REIMBURSEMENT REVIEW

Stakeholder Feedback on Draft Recommendation

tebentafusp (Kimmtrack)

(Medison Canada)

Indication: unresectable or metastatic uveal melanoma.

December 15, 2022

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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 antige	en (HLA)-A*02	2:01-
	positive adult patients with unresectable or n	netastatic uve	eal
	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	e committee's recommendation.	Yes No	
Please explain why the stakeholder agree	ees or disagrees with the draft recommendation	n. Whenever	ſ
possible, please identify the specific text	from the recommendation and rationale.		
Disease comments in Question 5 holews			
Please comments in Question 5 below r	e: reimbursement conditions.		
Expert committee consideration of th	e stakeholder input		
	trate that the committee has considered	Yes	\boxtimes
the stakeholder input that your orga		No	
If not, what aspects are missing from the	e draft recommendation?		
Clarity of the draft recommendation			
		Yes	\boxtimes
3. Are the reasons for the recommend	lation clearly stated?	No	
If not, please provide details regarding the	ne information that requires clarification.		
4. Have the implementation issues be	en clearly articulated and adequately	Yes	
addressed in the recommendation?		No	\boxtimes
If not, please provide details regarding the	ne information that requires clarification.		
1. System and economic issues Tebentafusp requires specialized clinicians for	Comment from the drug programs to inform	n nERC delibera	tions
administration/preparation/monitoring, thus tre	atment is likely		.10/13.
to be limited to larger centres. This introduces for travel, additional impact to daily life, and po			
increased expenses for eligible patients.			
Drug wastage is quite significant as the standa	ard dose is		
considerably less than the vial size (68 mcg vs single vial use is recommended. In some juriso			
wastage is not reimbursed by the drug plan an			
may not be able to absorb the wastage cost.			

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	Yes		
rationale for the conditions provided in the recommendation?	No	\boxtimes	

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	
 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 <u>Procedures for CADTH Drug Reimbursement Reviews</u> 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 submissi	on? No	
	Yes	\boxtimes
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	No	\ge
information used in this submission?	Yes	
	165	
If yes, please detail the help and who provided it.		
If yes, please detail the help and who provided it. B. Previously Disclosed Conflict of Interest	No	
If yes, please detail the help and who provided it. B. Previously Disclosed Conflict of Interest	No	
 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 remain unchanged? If no, please complete section C below. 	ed 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 remain unchanged? If no, please complete section C below. 	ed 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 remain unchanged? If no, please complete section C below. If yes, please list the clinicians who contributed input and whose declarations have not chan	ed No Yes	

C. New or Updated Conflict of Interest Declarations

New or Up	dated 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.

	Check Appropriate Dollar Range				
Company	\$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 Up	dated Declaration for Clinician 2
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.

		Check Approp	riate Dollar Ranç	je
Company	\$0 to 5,000	\$5,001 to 10,000	\$10,001 to 50,000	In Excess of \$50,000
Medison Canada	\boxtimes			
Add company name				
Add or remove rows as required				

New or Up	dated Declaration for Clinician	3			
Name	Dr. Xinni Song				
Position	Member, OH-CCO Skin DAC				
Date	07-12-2022				
\boxtimes	I hereby certify that I have the matter involving this clinician or place this clinician or clinician g	clinician group	with a company,	organization, or e	entity that may
List any co	Interest Declaration				er the past two
List any co					er the past two
List any co	mpanies or organizations that have		ug under review		
List any co	mpanies or organizations that have		ug under review		
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List any cor years AND Company	mpanies or organizations that hav who may have direct or indirect i anada	nterest in the dr \$0 to 5,000	Check Approp \$5,001 to 10,000	riate Dollar Rang \$10,001 to	ge In Excess of \$50,000

New or Up	dated 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 matter involving this clinician or place this clinician or clinician g	clinician group	with a company,	organization, or e	entity that may
Conflict of	Interest Declaration				
List any co	f Interest Declaration mpanies or organizations that hav who may have direct or indirect i				er the past two
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New or Up	dated Declaration for Clinician	5			
Name	Please state full name				
Position	Please state currently held posi	ition			
Date	Please add the date form was o	completed (DD-	MM-YYYY)		
	I hereby certify that I have the matter involving this clinician or place this clinician or clinician g	clinician group	with a company,	organization, or e	entity that may
Conflict of	Interest Declaration				
	mpanies or organizations that hav who may have direct or indirect i				r the past two
			rug under review.		-
			rug under review.		-
years AND	who may have direct or indirect i	nterest in the d	rug under review. Check Approp \$5,001 to	riate Dollar Rang \$10,001 to	ge In Excess of
years AND Company	who may have direct or indirect i	nterest in the d	rug under review. Check Approp \$5,001 to	riate Dollar Rang \$10,001 to	ge In Excess of

CADTH Reimbursement Review

Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0290
Name of the drug and	Tebentafusp for human leukocyte antigen (HLA)-A*02:01-positive
Indication(s)	adult patients with unresectable or metastatic uveal melanoma
Organization Providing	PAG
Feedback	

1. Recommendat Please indicate if the recommendation.	ion revisions ne stakeholder requires the expert review committee to reconsider or clari	fy its
Request for	Major revisions: A change in recommendation category or patient population is requested	
Reconsideration	Minor revisions: A change in reimbursement conditions is requested	
No Request for Reconsideration	Editorial revisions: Clarifications in recommendation text are requested	
	No requested revisions	х

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.



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 wi	th the draft recommendation		
1. Does the stakeholder ag	gree with the committee's recommendation.	Yes No	
Melanoma Canada agrees we As was stated in the submiss prognosis for the majority of treatment and survival. It pr families. We are concerned second line, as it should be determination, and also be a	specific text from the recommendation and rationale. with the recommendation that the drug should be funded and re- ssion, there are few treatments for this rare form of melanoma a patient is grim. This treatment provides meaningful improvem rovides hope and improved quality of life for many patients and if the following statement in the draft relegates the drug therap made available as a first line therapy, depending on patient an available as a second line therapy should it not be used as first jurisdictions to consider reimbursement of tebentafusp in a seco- imited basis."	and the ent in their y to d clinic line.	;
Expert committee conside	eration of the stakeholder input		
	on demonstrate that the committee has considered the	Yes	\boxtimes
	our organization provided to CADTH?	No	
If not, what aspects are miss	sing from the draft recommendation?		
Clerity of the dualt recover	nondetion		
Clarity of the draft recomm	nendation	Vee	
3. Are the reasons for the	recommendation clearly stated?	Yes	
If not place provide details	regarding the information that requires clarification.	No	
In not, please provide details			
4. Have the implementation	n issues been clearly articulated and adequately	Yes	\boxtimes
addressed in the recom		No	
If not, please provide details	s regarding the information that requires clarification.		
	mbursement conditions clearly stated and the rationale ded in the recommendation?	Yes No	
	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.
- 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 <u>Procedures for CADTH Drug Reimbursement Reviews</u> for further details.

A. Patient	Group Information					
Name	Annette Cyr					
Position	Chair of the Board					
Date	09-12-2022					
	I hereby certify that I have the a matter involving this patient gro patient group in a real, potential	up with a comp	any, organizatio	on, or entity that m		
B. Assista	nce with Providing Feedback					
				No	\boxtimes	
1. Did yo	u receive help from outside you	r patient grou	p to complete y	our feedback?	Yes	
inform	u receive help from outside you ation used in your feedback? se detail the help and who provide		p to collect or a	analyze any	No Yes	
inform If yes, plea	ation used in your feedback? se detail the help and who provide	d it.	p to collect or a	analyze any		
inform If yes, plea C. Previou	ation used in your feedback? se detail the help and who provide sly Disclosed Conflict of Interes	ed it.				
inform If yes, plea C. Previou 1. Were o submi	ation used in your feedback? se detail the help and who provide	ed it. St provided in pa review and ha	tient group inp	ut that was	Yes	
inform If yes, plea C. Previou 1. Were o submi uncha	ation used in your feedback? se detail the help and who provide sly Disclosed Conflict of Interest conflict of interest declarations p tted at the outset of the CADTH	d it. provided in pa review and ha ction D below	tient group inp	ut that was	Yes	
inform If yes, plea C. Previou 1. Were o submi uncha D. New or 3. List ar	ation used in your feedback? se detail the help and who provide sly Disclosed Conflict of Interest conflict of interest declarations p tted at the outset of the CADTH nged? If no, please complete se	ed it. provided in pa review and ha ction D below claration hat have provi	tient group inp ve those decla ided your grou	ut that was rations remained o with financial p	Yes No Yes bayment	
inform If yes, plea C. Previou 1. Were o submi uncha D. New or 3. List ar	ation used in your feedback? se detail the help and who provide sly Disclosed Conflict of Interest conflict of interest declarations p tted at the outset of the CADTH nged? If no, please complete se Updated Conflict of Interest Dec by companies or organizations t	ed it. provided in pa review and ha ction D below claration hat have provi	tient group inp ve those decla ided your grou t interest in the	ut that was rations remained o with financial p	Yes No Yes Yes bayment ew.	
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inform If yes, plea C. Previou 1. Were of submi uncha D. New or 3. List ar past ty Company	ation used in your feedback? se detail the help and who provide sly Disclosed Conflict of Interest conflict of interest declarations p tted at the outset of the CADTH nged? If no, please complete se Updated Conflict of Interest Dec by companies or organizations t vo years AND who may have dir	ed it. provided in pa review and ha ction D below claration hat have provi ect or indirect	itient group inp ive those decla ided your grou interest in the <u>Check Appro</u> \$5,001 to	ut that was rations remained o with financial p drug under revie priate Dollar Rar \$10,001 to	Yes No Yes Yes ayment ew. nge In Exces \$50,000	over the
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CADTH Reimbursement Review Feedback on Draft Recommendation

CADTH project number	PC0290-000				
Brand name (generic)	KIMMTRAK (tebentafusp)				
Indication(s)	For the treatment of human leukocyte antigen (HLA)-A*02:07	1-positiv	'e		
	adult patients with unresectable or metastatic uveal melanoma.				
Organization	Medison Pharma Canada Inc.				
Contact information ^a					
Stakeholder agreement w	ith the draft recommendation				
Dese the state halden as			\geq		
. Does the stakeholder a	gree with the committee's recommendation.	No			
. Does the recommendat	ion demonstrate that the committee has considered the	Yes	\geq		
stakeholder input that y	our organization provided to CADTH?	No	Γ		
Clarity of the draft recomi	mendation				
		Yes	D		
a. Are the reasons for the	recommendation clearly stated?	No	Γ		
4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?		Yes	\geq		
		No	C		
		No			

^a CADTH may contact this person if comments require clarification.