CADTH

CADTH REIMBURSEMENT REVIEW

Stakeholder Feedback on Draft Recommendation

SETMELANOTIDE (Imcivree)

(Rhythm Pharmaceuticals, Inc.)

Indication: IMCIVREE (setmelanotide solution for subcutaneous injection) is indicated for weight management in adult and pediatric patients 6 years of age and older with obesity due to: Bardet-Biedl syndrome (BBS) Genetically confirmed biallelic pro-opiomelanocortin (POMC), proprotein convertase subtilisin/kexin type 1 (PCSK1), or leptin receptor (LEPR) deficiency due to variants interpreted as pathogenic, likely pathogenic, or of uncertain significance

September 28, 2023

CADTH

CADTH Reimbursement Review

Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0769
Name of the drug and Indication(s)	Setmelanotide (Imcivree) for weight management
Organization Providing Feedback	FWG

1. Recommendation revisions Please indicate if the stakeholder requires the expert review committee to reconsider or clarify its recommendation.		
Request for Reconsideration	**Major revisions:** A change in recommendation **category** or patient **population** is requested	☐
	Minor revisions: A change in reimbursement **conditions** is requested	☐
No Request for Reconsideration	**Editorial revisions:** Clarifications in recommendation **text** are requested	X☐
	No requested revisions	☐

2. Change in recommendation category or conditions Complete this section if major or minor revisions are requested
Deletion of Initiation reimbursement condition 2 (2.1 - 2.3). Rationale is that these types of assessments are generally conducted for numerous drugs by the prescriber. This is not in alignment with other CADTH recommendations and not typical initiation criteria. This is typically included in product monographs and often included in clinical trial exclusion criteria as these populations are not studied i.e. renal and liver impairment.

3. Clarity of the recommendation Complete this section if editorial revisions are requested for the following elements
a) Recommendation rationale
Please provide details regarding the information that requires clarification.
b) Reimbursement conditions and related reasons
Please provide details regarding the information that requires clarification.
c) Implementation guidance
Please provide high-level details regarding the information that requires clarification. You can provide specific comments in the draft recommendation found in the next section. Additional implementation questions can be raised here. Implementation guidance would be helpful to

determine what might be considered a clinically meaningful decrease in BMI Z-score in patients aged 6–11 years.

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0769
Brand name (generic)	IMCIVREE® (setmelanotide)
Indication(s)	For weight management in adult and pediatric patients 6 years of age and older with obesity due to Bardet-Biedl syndrome (BBS)
Organization	Rhythm Pharmaceuticals, Inc. (Rhythm)
Contact information[a]	Name: [redacted] [redacted] Rhythm Pharmaceuticals, Inc.

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

Rhythm agrees with and welcomes the draft recommendation. As stated in the recommendation, "CDEC considered the rarity and severity of the condition, patient population, and the lack of therapeutic options available, all of which represent a significant unmet need for this population. Early-onset obesity and hunger or hyperphagia (and related behaviours and HRQoL impacts) have been identified by patient and clinician input as two of the most distressing features of BBS" (p. 6). Rhythm agrees with CDEC that setmelanotide was associated with clinically meaningful reductions in total body weight or BMI and has the potential to address important unmet needs identified in patient and clinician input.

Rhythm respectfully disagrees with some of the key limitations identified by CADTH in the pharmacoeconomic analysis, including the most appropriate utility value for severe hyperphagia and comorbidity prevalence rates.

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	☐

Not applicable

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

Yes, the reasons for the recommendation were clearly stated.

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

Yes, CDEC clearly articulated and adequately addressed the potential implementation issues in the recommendation.

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

The reimbursement conditions were clearly stated and the rationale for the conditions was provided in the recommendation.

Rhythm notes that there is misalignment between reimbursement condition 2.2 and the Health Canada-approved product monograph, which allows pediatric and adult patients 12 years of age and older with severe renal dysfunction (estimated glomerular filtration rate [eGFR] 15-29 mL/min) to be treated with IMCIVREE at a modified dosage. Allowing reimbursement for this patient group would ensure alignment with the product monograph and improve access for patients.

Additionally, Rhythm would like to clarify that the IMCIVREE product monograph and clinical guidelines define moderate renal impairment as an eGFR of 30-59 mL/min. Therefore, renal impairment <30 mL/min should be referred to as severe to align with the product monograph.

Rhythm would also like to comment with regard to reimbursement condition 4 that BMI Z-score, rather than BMI or total body weight, is the most appropriate measure to use for children under the age of 18 who are continuing to grow and experience normal weight gain. Growth chart data from the CDC confirm that BMI continues to increase between the ages of 12-18.[1] Normal weight gain accompanies height increases during childhood growth and development, which, in turn, can confound weight loss analyses in children.[2] The BMI Z-score evaluates how pediatric patients' BMI deviates from the mean value for age- and sex-matched peers.

Finally, Rhythm would like to clarify, with regard to reimbursement condition 6, that additional specialists may be involved and/or responsible for the care of patients with BBS, including nephrologists and geneticists, in line with clinical experts' comments: "The clinical experts indicated to CDEC that ideally, an interdisciplinary team of specialist medical doctors, mental health supports, and registered dieticians should be overseeing the care of BBS patients" (p. 5, 12).

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

References

1. Centers for Disease Control and Prevention. CDC Extended BMI-for-age Growth Charts. Updated December 15, 2022. Accessed September 25, 2023, https://www.cdc.gov/growthcharts/Extended-BMI-Charts.html
2. Kelly AS, Fox CK, Rudser KD, Gross AC, Ryder JR. Pediatric obesity pharmacotherapy: current state of the field, review of the literature and clinical trial considerations. *International Journal of Obesity*. 2016;40(7):1043-1050. doi:10.1038/ijo.2016.69