

### **CADTH REIMBURSEMENT REVIEW**

# Stakeholder Feedback on Draft Recommendation

cannabidiol (Epidiolex)

(Jazz Pharmaceuticals Canada, Inc.)

Indication: Epidiolex (cannabidiol) is indicated for use as adjunctive therapy for the treatment of seizures associated with Lennox-Gastaut Syndrome (LGS) or Dravet Syndrome (DS) or Tuberous Sclerosis Complex (TSC) in patients one year of age and older.

April 8, 2024

**Disclaimer:** The views expressed in this submission are those of the submitting organization or individual. As such, they are independent of CADTH and do not necessarily represent or reflect the view of CADTH. No endorsement by CADTH is intended or should be inferred.

By filing with CADTH, the submitting organization or individual agrees to the full disclosure of the information. CADTH does not edit the content of the submissions.

CADTH does use reasonable care to prevent disclosure of personal information in posted material; however, it is ultimately the submitter's responsibility to ensure no identifying personal information or personal health information is included in the submission. The name of the submitting stakeholder group and all conflicts of interest information from individuals who contributed to the content are included in the posted submission.

# CADTH Reimbursement Review Feedback on Draft Recommendation

reedback on Dra	att Recommendation			
Stakeholder information				
CADTH project number	SR0799			
Brand name (generic)	Cannabidiol			
Indication(s)	Dravet Syndrome			
Organization	Canadian League Against Epilepsy (CLAE)			
Contact information <sup>a</sup>	Juan Pablo Appendino (in representation of CLAE)			
Stakeholder agreement wi	th the draft recommendation			
1. Does the stakeholder ac	ree with the committee's recommendation.	Yes	$\boxtimes$	
	,	No		
Francis consists a consiste	untion of the state halden in mot			
	eration of the stakeholder input	\ <u> </u>	57	
	on demonstrate that the committee has considered the	Yes	$\boxtimes$	
Stakeholder input that y	our organization provided to CADTH?	No		
Clarity of the draft recomm	nendation			
Clarity of the draft recomm	nendation	Yes		
3. Are the reasons for the recommendation clearly stated?		No	$\boxtimes$	
The CLAE would like CADT	H to reconsider the following condition/s:	140		
<ul> <li>#5: Cannabidiol should not be reimbursed in patients concurrently using cannabis or other cannabinoid-based medications.</li> <li>CLAE supports the concept of remaining on other cannabinoids/CBD products prior to starting cannabidiol and during their transition from a less purified medical cannabis product to Epidiolex as we believe that the recommendation #5 is prohibitive for patients who are currently on other CBD products and would like to switch to cannabidiol. A "wash out" period could be very dangerous in some cases (responders to CBD) as it can bring seizure increase with higher chances of injuries or even SUDEP. A gradual transition could/should be considered without the need of a "wash out"</li> </ul>				
<ul> <li>#6: A price reduction of 44% would be required for adjunctive cannabidiol to achieve an ICER of \$50,000 per QALY compared to usual care alone.</li> <li>CLAE would strongly recommend retaining the recommendation #6 of implementing "A reduction in price". As you well stated, a price reduction of at least 40-45% is required. A price comparison of a similar product may help to guide the pharmaceutical company on what we are looking for (i.e. RHO Phyto is \$0.027/mg [https://mymedi.ca/products/rho-phyto-micro-drop-100-cbd-cannabis-oil/]; Tilray 2:100 is \$0.1/mg [https://www.tilraymedical.ca/products/105]). Bravo for your recommendation!</li> </ul>				
4. Have the implementation addressed in the recommendation	n issues been clearly articulated and adequately mendation?	Yes No		
Yes, these are clearly stated		140		
. 22, misso are clourly stated	<del></del>	Yes		

5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?		$\boxtimes$
See Rationale in Question 3.		

<sup>&</sup>lt;sup>a</sup> 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		
2. Did you receive help from outside your clinician group to complete this submission?	No	$\boxtimes$
	Yes	
3. Did you receive help from outside your clinician group to collect or analyze any	No	$\boxtimes$
information used in this submission?		
B. Previously Disclosed Conflict of Interest		
4. Were conflict of interest declarations provided in clinician group input that was	No	$\boxtimes$
	No Yes	
4. Were conflict of interest declarations provided in clinician group input that was		
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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.  If yes, please list the clinicians who contributed input and whose declarations have not changed:		
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.  If yes, please list the clinicians who contributed input and whose declarations have not changed:  Clinician 1		

### C. New or Updated Conflict of Interest Declarations

New or Up	dated Declaration for Clinician 1
Name	Dr. Juan Pablo Appendino
Position	Pediatric Neurologist, Alberta Children's Hospital. Leader of the Medical and Therapeutics Committee CLAE.
Date	28-03-2024
	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

	mpanies or organizations that hav who may have direct or indirect i				er the past two		
			Check Approp	riate Dollar Ran	ge		
Company		\$0 to 5,000	\$5,001 to 10,000	\$10,001 to 50,000	In Excess of \$50,000		
Jazz Pharn	naceuticals						
UCB Pharn	naceuticals						
Takeda Ph	Pharmaceutical						
New or Up	dated Declaration for Clinician	2					
Name	Please state full name						
Position	Please state currently held posi	tion					
Date	Please add the date form was d	completed (DD-	-MM-YYYY)				
	I hereby certify that I have the	authority to dis	close all relevant	information with r	espect to any		
	matter involving this clinician or	clinician group	with a company,	organization, or e	entity that may		
	place this clinician or clinician g	roup in a real, ¡	potential, or perce	eived conflict of inf	terest situation.		
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years AND	who may have direct or indirect i	nterest in the d	rug under review.				
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Add or remove rows as required

Add company name

## **CADTH Reimbursement Review**

## **Feedback on Draft Recommendation**

Stakeholder information	
CADTH project number	SR0799
Name of the drug and Indication(s)	Cannabidiol (Epidiolex) as adjunctive therapy for the treatment of seizures associated with Dravet Syndrome (DS) in patients 2 years of age and older.
Organization Providing Feedback	FWG

1. Recommendat Please indicate if the recommendation.	ion revisions ne stakeholder requires the expert review committee to reconsider or clari	fy its
Request for Reconsideration	<b>Major revisions:</b> A change in recommendation <b>category</b> or patient <b>population</b> 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	

## 2. Change in recommendation category or conditions Complete this section if major or minor revisions are requested

Please identify the specific text from the recommendation and provide a rationale for requesting a change in recommendation.

### 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.



# **CADTH Reimbursement Review Feedback on Draft Recommendation**

Stakeholder information			
CADTH project number	SR0799-000		
Brand name (generic)	EPIDIOLEX (cannabidiol)		
Indication(s)	As adjunctive therapy for seizures associated with DS in patie	nts two	0
years of age and older.			
Organization	Jazz Pharmaceuticals Canada		
Contact information <sup>a</sup>			
Stakeholder agreement wi	th the draft recommendation		
1. Does the stakeholder ag	ree with the committee's recommendation.	Yes	$\boxtimes$
No comment.		No	
NO COMMENT.			
Expert committee conside	ration of the stakeholder input		
2. Does the recommendati	on demonstrate that the committee has considered the	Yes	$\boxtimes$
stakeholder input that y	our organization provided to CADTH?	No	
No comment.			
Clarity of the draft recomm	nendation		
	nendation recommendation clearly stated?	Yes	
3. Are the reasons for the	recommendation clearly stated?	No	$\boxtimes$
3. Are the reasons for the Page 21, Budget Impact, p	recommendation clearly stated?  paragraph 2: "CADTH reanalyses adopted a higher maintena	No	$\boxtimes$
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Jazz disagrees with restricting access to EPIDIOLEX to only patients who have at least four convulsive seizures per month prior to initiation.

- Although it is necessary in a clinical trial setting to establish minimum number of seizures
  during the baseline period, in clinical practice the decision to start patients on EPIDOLEX
  would be based on their lack of seizure control, not a specific number of seizures.
- Additionally, it is often difficult for patients with Dravet syndrome (DS), who experience a
  variety of developmental and cognitive delays, and/or caregivers to accurately track the
  number of seizures that a patient is experiencing.

It is Jazz's position that the initiation criteria for EPIDIOLEX should be based only on a patient having inadequately controlled seizures, and not a minimum number of seizures during a specific time period.

**Page 4, reimbursement condition 4:** "4. Cannabidiol for DS should be prescribed by neurologists or pediatric neurologists with experience in the treatment of patients with DS."

Jazz disagrees with restricting access to EPIDOLEX to only patients who are under the care of a neurologist. DS is a complex epilepsy which requires comprehensive management strategies. In practice, while neurologists play a pivotal role in overseeing the treatment of DS, the nature of this syndrome often necessitates coordinated care involving multiple healthcare professionals. Given the multidisciplinary approach required for effective management of DS, restricting prescription authority would be challenging as other specialists may be the primary point of care for the patient.

- Many patients DS are pediatrics and have their disease managed by pediatricians, as well as neurologists. For other patients who live far away from epilepsy centers, care may be coordinated between their community physician who is experienced in managing epilepsy and their neurologist at the epilepsy center. Therefore, for many patients, pediatricians and family physicians prescribe anti-seizure medications (ASMs) for seizure control.
- Other ASMs that are indicated and funded for DS and similar developmental and epileptic
  encephalopathies do not require patients to be under the care of a neurologist. For stiripentol,
  which is indicated for patients with DS, the Ontario Exceptional Access Program (EAP)
  criteria requires that the request is submitted by a neurologist or pediatrician.<sup>3</sup>
  - Similarly, for rufinamide, which is indicated for patients with Lennox-Gastaut syndrome (LGS), CADTH recommended patients be under the care of a physician experienced in treating LGS,<sup>4</sup> and the Ontario EAP criteria only requires that the patient is in the care of a physician experienced in managing seizures, not specifically a neurologist.<sup>3</sup>

It is Jazz's position that EPIDIOLEX should be prescribed by a physician with experience in the diagnosis and management of patients with DS, not restricted specifically to neurologists.

<sup>&</sup>lt;sup>a</sup> CADTH may contact this person if comments require clarification.

<sup>&</sup>lt;sup>1</sup>GW Research Ltd (2023) (Product Monograph for EPIDIOLEX (cannabidiol)). November 15, 2023.

<sup>&</sup>lt;sup>2</sup>Jazz Pharmaceuticals (2022) VV-MED-29432 - Epidyolex Daily Dose in LGS and DS - Patient INSIGHTS (INSIGHT Health) Germany. In.

<sup>&</sup>lt;sup>3</sup>Ontario Ministry of Health (2023). Exceptional Access Program Reimbursement Criteria for Frequently Requested Drugs. Available online at: <a href="https://files.ontario.ca/moh-frequently-requested-drugs-en-2023-12-21.pdf">https://files.ontario.ca/moh-frequently-requested-drugs-en-2023-12-21.pdf</a>. Accessed: April 2024.

<sup>&</sup>lt;sup>4</sup>Canadian Agency for Drugs and Technologies in Health (2012). *CDEC Final Recommendation: Rufinamide*. Available online at: https://www.cadth.ca/rufinamide. Accessed: April 2024.