CADTH

CADTH REIMBURSEMENT REVIEW

Stakeholder Feedback on Draft Recommendation

atogepant (Qulipta)

(AbbVie Corporation)

Indication: The prevention of migraine in adults who have at least 4 migraine days per month.

June 27, 2024

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder		
CADTH project number	SR0817-000 Stakeholder Feedback on Draft Recommendation	
Brand name (generic)	Atogepant	
Indication(s)	Prevention of Migraine in adults who have at least 4 migraine days per month	
Organization	Canadian Migraine Society	
Contact information[a]	Name: Maya Carvalho	
Stakeholder agreement with the draft recommendation		
1. Does the stakeholder agree with the committee's recommendation.	Yes	X
	No	☐
Yes, we agree with the draft recommendation to reimburse Atogepant for adults who have at least 4 migraine days per month however, we disagree with some of the implementation and reimbursement criteria which I have outlined below.		
Expert committee consideration of the stakeholder input		
2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization	Yes	X
	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	X
	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	X

TABLE 2: Responses to Questions from the Drug Programs

Page 7, Considerations for continuation or renewal of therapy: "The Committee acknowledged the need to align atogepant with other CGRP inhibitors for the continuation or renewal of therapy for the indication"

- the current renewal for other CGRP inhibitors is a 6 month renewal process. We believe that this is both administratively cumbersome for physicians and patients and that it also impedes the continuity of the prescribed migraine treatment plan.
- In a short poll we conducted this week in Canadian Migraine Society's support group, out of 31 respondents, 100% indicated that a 6 month renewal process negatively affects their quality of life and ability to function. No one responded that a 6 month renewal process would be manageable for them.
- Patients told us that this process causes breaks in their treatment plans while the renewals are being assessed and approved. Sometimes these renewals can take months, leaving the patient without a clear and concrete direction for their treatment plan. For people living with chronic migraine, as soon as treatment stops, the pain returns, therefore these types of breaks are not tolerable.
- Patients also told us that it was incredibly difficult to access their physicians and to have their physicians make the time to fill out this paperwork.There is a dearth of neurologists who treat headache in Canada. A 6 month renewal can be almost impossible for patients in small communities who live several hours away from their neurologists — this leads to health inequities.
- Even more importantly, it puts extra strain on an already strained healthcare system when doctors have to do even more paperwork for their patients.
- One patient stated "It took 3 months to get ajovy approved for the provincial drug plan in Saskatchewan. Having to do this process twice a year with the delays for approval would be more than a little problematic for my health. Not to mention additional appointments with doctors that are hard to get into with additional costs to get the paperwork completed"
- We ask that CADTH reconsider the renewal period not just for Atogepant but for the entire class of CGRP inhibitors. We would like this to be changed to a two year renewal period or longer, to be assessed by the physician and patient.

Page 7: Considerations for prescribing of therapy: "The Committee would prefer avoiding these combinations….In the clinical expert's experience, using Botox with monoclonal antibodies is common in practice. If there are no specific contraindications or drug interactions the combination is allowed"

- We would just like to reiterate that the combination of Botox and Gepants, or Botox and CGRP monoclonal antibodies is incredibly important to this community. Many patients are being denied access to both, even if they have private insurance for Botox and can access the provincial drug plans for CGRP inhibitors.
- In a short poll conducted this week to investigate the use of Botox with CGRP inhibitors (MABS or Gepants), out of 86 responding patients with chronic migraine, 66% (57 patients) responded that they "required a combination of Botox and a CGRP inhibitor in order to function in my life" vs.using a CGRP inhibitor alone or Botox alone. These patients are in pain at least 50% of their days and should be given the combinations of medications that their physicians deem appropriate for them in order to function.
- One patient stated: "Having both together drastically improved my quality of life. My sick time usage at work went way down, I could play with my kids, I had energy to clean my house. Then my insurance said I couldn't have both covered, pick one."
- Another patient stated: "Having both together has really improved my life. My migraine days have dropped from 20+ to 10-12. I very rarely miss work now or If I do, I work from home instead. Whereas before, I was probably missing at least 1 if not 2 days of work a week when just on botox. I enjoy going out with friends now."
- Another patient stated that "Botox helps with my pain levels but not the frequency. I need a CGRP to help with the frequency as well or else I have too much suffering to have any quality of life. Botox plus a CGRP is the best treatment I have found for chronic migraine — it helps me limit the amount of pain meds I have to take and gives me a better chance at a normal life."

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

TABLE 1: Reimbursement Conditions and Reasons

Page 3: 1. “Eligibility of reimbursement of Atogepant should be based on the criteria….of other CGRP inhibitors” It is hard to determine the specifics of this criteria since they are not included in this document. If this is based on the recommendations for previous CGRP inhibitors we would like to address these two points:

Reimbursement Condition #5 (from Vyepti recommendations):

“The physician must provide proof of beneficial clinical effect when requesting continuation of reimbursement, defined as a reduction of at least 50% in the average number of migraine days per month…”

- it is widely accepted that success with a migraine preventive medication is determined by assessing BOTH the frequency and/or the intensity of each migraine attack. For many people taking anti-CGRP medications, their frequency (MMDS) may remain consistent but the intensity of their attacks may be greatly diminished. A reduction in intensity can make a huge difference in the quality of life of the patient, and in their ability to work, take care of their families etc. These variable must also be considered.

“Some jurisdictions may want to include a reduction of at least 30% in the number of headache days per month and an improvement of at least five points in the HIT-6 score, compared with baseline, as an alternative criterion for renewal of reimbursement.”

- While some jurisdictions CAN implement this more nuanced approach to determining success of a migraine preventive, in practice, only one province, Ontario, agreed to this criteria with other anti-CGRPs. We feel that this criteria should simply state that a reduction of 30-50% reduction in frequency OR a 5 point reduction in the HIT-6 score will be accepted. This recognizes that vast array of patient responses in this very complicated disease.

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

Appendix 1. Conflict of Interest Declarations for Patient Groups

A. Patient Group Information	
Name	*Maya Carvalho*
Position	*Founder, Canadian Migraine Society*
Date	*21-06-2024*
X	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	X
	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	X
	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	X

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0817-000 Stakeholder Feedback on Draft Recommendation
Brand name (generic)	Qulipta (atogepant)
Indication(s)	Migraine, prevention
Organization	Migraine Canada
Contact information[a]	Name: Wendy Gerhart

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.		
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.		

It is evident that the committee recommends reimbursing Atogepant with conditions, which we greatly appreciate.

In response to the reimbursement conditions and rationale, we have the following comments:

Table 1: Reimbursement Conditions & Reasons

1. No comment.
2. We believe clinicians should have the flexibility to manage their patients with combination therapy based on patient assessments and medical histories. There is a small percentage of

patients who have recognized the benefit of the combination therapy in helping to manage their migraine attacks and if deemed appropriate by the provider should be allowed.
3. No Comment.

Table 2: Responses to questions from the Drug Programs

Considerations for initiating therapy

Relevant Comparators

1. No Comment.
2. No Comment.

Considerations for Initiation of Therapy

1. Requiring two trials of oral preventives, instead of three, is positive. We advocate for all provinces to adopt these recommendations to ensure equitable access to medications across Canada. Patients also find newer medications like CGRP antibodies to be better tolerated and more effective than the older medications. As per AHS position statement issued in spring 2024, these medications should actually be used first line.
2. See above.
3. No comment.
4. No comment.

Consideration for continuation or renewal of therapy.

1. An initial six-month authorization is reasonable, with renewals at minimum every 12 to 18 months. Requiring physicians to complete paperwork every six months is inefficient. The administrative burden on physicians also impacts the overall healthcare system. This also causes patient distress from having to visit their provider every 6 months and the stress of possibly not getting renewed. Having to visit healthcare providers given the shortage of healthcare providers and wait times isn't optimal. For some patients travel and time off work is burdensome. In some patients 6 months may not be enough time on a new medication due to the unpredictability of the disease. Continuous therapy is vital for patients who respond well, as interruptions can lead to the return of migraines or response rate. And lastly, assessing every six months from a drug plan perspective isn't reasonable; patients will not stay on medication if it isn't working.

Consideration for discontinuation of therapy

1. There is little evidence to suggest when a patient should be discontinued and should be the discretion of the healthcare provider. A reduction of at least 50% in the frequency of migraine headache days per month compared with baseline; **OR a** reduction of at least 30% in the frequency of migraine headache days per month compared with baseline AND an improvement of greater than or same as 5 points in the HIT-6 score compared with baseline. Modest improvements are vital for severely affected patients who have tried multiple treatments.

Considerations for prescribing of therapy

1. No comment.
2. We would like to acknowledge the change in the language to include “prescriber with clinical experience” and the removal of physician. It’s essential to also recognize that while an accurate migraine diagnosis is crucial, the shortage of headache specialists and neurologists means that primary care providers (GP’s and NP) must be able to prescribe these medications. Many migraine patients are treated by primary care clinicians due to the condition's prevalence. Making specialist consultation mandatory is not an efficient or responsible use of healthcare resources.
3. We agree that in certain patients combining a CGRP with Botox should be allowed.

Generalizability

1. No comment.
2. No comment.

[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 *Procedures for CADTH Drug Reimbursement Reviews* for further details.

A. Patient Group Information	
Name	*Wendy Gerhart*
Position	*Executive Director*
Date	*26-06-2024)*
☒	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 Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0817-000 Stakeholder Feedback on Draft Recommendation
Brand name (generic)	Qulipta
Indication(s)	Migraine, prevention
Organization	Canadian Headache Society
Contact information	Name: Delaney Wilcox

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.

The Canadian Headache Society (CHS) prefers no set renewal criteria, but, if necessary, we are advocating for renewal criteria to be extended to 12 months. Ideally, renewal criteria should always be at the discretion of the physician.

Concerns about patients remaining on medications unnecessarily without a forced renewal process are unfounded. A number of studies assessing patient adherence to migraine preventives longitudinally supports the idea that the vast majority of patients (studies ranging from approximately 70-80%) will not persist in their use of a preventive at one year, and are therefore unlikely to remain on a medication that is providing insufficient benefit or intolerable effects (1,2,3,4,5). A retrospective claims analysis by Ojo, A. T. et al. looked at how frequently patients in Canada are adherent to migraine preventative therapy, how frequently they switch between preventatives, and the costs involved. The authors reported that only 24.9% of patients continued their initial medication for two years. Approximately 27% switched to a different preventative, while 50% ceased preventative use altogether. Despite lower discontinuation rates and higher efficacy, angiotensin receptor blockers and CGRP antagonists were not prescribed as often as antidepressants and anticonvulsants, although the latter two drug classes had much higher discontinuation rates. The study also found that higher preventative adherence led to fewer acute treatment use including opioids. The conclusion being that migraine-specific and tolerable preventive medications from the outset could improve treatment adherence and reduce overall healthcare utilization costs. The study findings suggest that the current status quo where treatment algorithms are based on "step-therapy" requirements may prioritize cost savings over patient needs (1).

We would like to note that health care providers have no impetus to keep patients on medications that are not helping chronic conditions. Similarly, patients do not wish to remain on medications that are not helpful for them. For this reason, we believe that renewal should be at the discretion of the physician.

Requiring frequent renewal forms be completed not only adds administrative burden and raises government costs, it puts extra strain on an already overburdened healthcare system. Similarly, needless or baseless rejections of renewal requests also generate more patient visits and increase overall health care costs.

References:

1. Ojo, A. T., Zhang, S., Zimskind, D., Bleibdrey, N., Keshvani, N., & Chalmers, R. (2022). Persistence and switching patterns of migraine prophylactic medications in Canada: A retrospective claims analysis comparing adherence and evaluating the economic burden of illness. *Journal of Pharmacy & Pharmaceutical Sciences, 25*(1), 402-417.
2. Rimmele F, Müller B, Becker-Hingst N, Wegener S, Rimmele S, Kropp P, Jürgens TP. Medication adherence in patients with cluster headache and migraine: an online survey. Sci Rep. 2023 Mar 20;13(1):4546.
3. Orlando V, Mucherino S, Monetti VM, Trama U, Menditto E. Treatment patterns and medication adherence among newly diagnosed patients with migraine: a drug utilisation study. BMJ Open. 2020 Nov 4;10(11):e038972.
4. Woolley JM, Bonafede MM, Maiese BA, et al. Migraine prophylaxis and acute treatment patterns among commercially insured patients in the United States. Headache 2017;57:1399–408.
5. Hepp Z, Dodick DW, Varon SF, et al. Adherence to oral migraine-preventive medications among patients with chronic migraine. Cephalalgia. 2015;35:478-488.

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 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	☒
	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	*William Kingston, MD, FRCPC, FAHS*
Position	*Headache Neurologist, Board member – Canadian Headache Society*
Date	*21-06-2024*
☒	**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	

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**
Teva	☐	☐	☒	☐
Novartis	☐	☐	☒	☐
AbbVie/Allergan	☐	☐	☒	☐
Eli Lilly	☐	☐	☒	☐
Miravo	☐	☒	☐	☐
Lundbeck	☐	☒	☐	☐

New or Updated Declaration for Clinician 2	
Name	*Alexander N. Melinyshyn, BSc, MD, FRCPC (Neurology)*
Position	*Headache Neurologist*
Date	*21-06-2024*
☒	**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

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**
Teva (Honoraria)	☐	☐	☒	☐
Lundbeck (Honoraria)	☐	☐	☒	☐
Eli Lilly (Honoraria)	☐	☐	☒	☐
Novartis (Honoraria)	☐	☒	☐	☐
Miravo (Honoraria)	☐	☒	☐	☐
AbbVie (Honoraria)	☐	☐	☒	☐
Pfizer (Honoraria)	☐	☒	☐	☐

New or Updated Declaration for Clinician 3	
Name	*Danny Adel Monsour, MD, FRCPC*
Position	*Headache Neurologist*
Date	*26-06-2024*
☒	**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				
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**
Miravo (Honoraria)	☐	☒	☐	☐
AbbVie (Honoraria)	☐	☒	☐	☐
Lundbeck (Honoraria)	☒	☐	☐	☐
Teva (Honoraria)	☒	☐	☐	☐
Eli Lilly (Honoraria)	☐	☒	☐	☐
Pfizer (Honoraria)	☐	☒	☐	☐
Novartis (Honoraria)	☒	☐	☐	☐

CADTH Reimbursement Review

Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0817
Name of the drug and Indication(s)	Atogepant (Qulipta) for the prevention of migraine in adults who have at least 4 migraine days per month
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	☐
	No requested revisions	X

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.