Canada's Drug Agency
L'Agence des médicaments du Canada

CDA-AMC REIMBURSEMENT REVIEW

Stakeholder Feedback on Draft Recommendation

ravulizumab (Ultomiris)

(Alexion Pharma Canada Inc.)

Indication: Ultomiris (ravulizumab for injection) is indicated for the treatment of adult patients with anti-acetylcholine receptor (AChR) antibody-positive generalized Myasthenia Gravis (gMG). Ultomiris was studied in adult gMG patients with a Myasthenia Gravis Foundation of America (MGFA) clinical classification Class II to IV and a Myasthenia Gravis Activities of Daily Living (MG-ADL) total score ≥ 6.

December 5, 2024

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0765-000
Brand name (generic)	Ravulizumab
Indication(s)	Myasthenia Gravis
Organization	Muscular Dystrophy Canada
Contact information[a]	Homira Osman, PhD

Stakeholder agreement with the draft recommendation

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

Muscular Dystrophy Canada (MDC) supports and appreciates CDA's draft recommendation that Ravulizumab be reimbursed for the treatment of AChR antibody-positive myasthenia gravis. This is an important step towards addressing the unmet treatment needs for those affected by myasthenia gravis in Canada.

We are in agreement on the majority of the reimbursement conditions outlined in the review, as these reflect and are relevant to Canadian patients.

However, we would like to raise significant concerns regarding the recommendation for reassessment every six months (page 5, point 6). This frequency imposes unnecessary challenges for patients and their family members, many of whom already face substantial logistical, emotional, and financial burdens associated with managing a complex, chronic condition like myasthenia gravis.

Frequent reassessment requires patients to take additional time off work or school, arrange transportation, and potentially travel long distances to attend clinic visits—disruptions that are particularly challenging for those in rural or underserved areas. This interval also adds strain on caregivers, who often need to adjust their own schedules to accommodate these demands.

A six-month reassessment is inconsistent with established practices for other biological therapies, such as Efgartigimod, which are assessed annually. It also diverges from current clinical practice in MG, where non-steroidal immunomodulatory therapies like Rituximab and oral treatments are routinely renewed on an annual basis. These therapies have demonstrated the feasibility and effectiveness of a longer reassessment interval, providing stability and predictability for patients without compromising clinical oversight.

Aligning Ravulizumab's renewal reassessment with the annual standard would significantly reduce the administrative and logistical burden on patients and caregivers. It would also allow clinicians to focus their time and resources on providing high-quality care, rather than navigating overly frequent bureaucratic processes.

Adopting a 12-month interval for both initial authorization and renewal reassessment would not only align reimbursement policies with clinical realities but also ensure that patients experience a more manageable and supportive treatment journey. Such a change would reflect a patient-centered approach to healthcare, prioritizing equitable access and improving overall quality of life for those living with MG.

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	☐
Yes, the recommendation reflects that the committee has considered the stakeholder input we provided to CADTH, particularly regarding the unmet treatment needs for AChR antibody-positive myasthenia gravis patients in Canada. This population requires effective therapeutic options to address their complex medical challenges, and the inclusion of Ravulizumab as a treatment option is a positive step toward meeting these needs. We appreciate the acknowledgment of this gap and the effort to expand access to innovative therapies like Ravulizumab.		
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.
- 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	*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 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	SR0765-000
Brand name (generic)	Ravulizumab
Indication(s)	Myasthenia Gravis
Organization	NMD4C Neuromuscular Clinician Group
Contact information[a]	Name: Dr. Hans Katzberg Co-Authors: Dr. Michael Nicolle; Dr. Michelle Mezei; Dr. Amer Ghavanini; Dr. Hanns Lochmuller; Dr. Zaeem Siddiqi; Dr. Vera Bril; Dr. Angela Genge; Dr. Kristine Chapman; Elizabeth Pringle; Dr. Carolina Barnett Tapia

Stakeholder agreement with the draft recommendation

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

The NMD4C Neuromuscular Clinician Group agrees with the recommendation that Ravulizumab be reimbursed for treatment of AChR antibody positive myasthenia gravis.

The NMD4C Neuromuscular Clinician Group agrees with the majority of the reimbursement conditions provided in the review, which closely match the CHAMPION clinical trial population and are applicable to a Canadian population.

The NMD4C Neuromuscular Clinician group does not agree with the committee's recommendation regarding reimbursement on page 4, point 4, which states that maximum duration of initial authorization is 6 months. Data from extension studies past 26 weeks have shown that some patients (~10%) may respond past this time frame, and as such a 12-month maximum duration of initial authorization would be in the best interest of patients undergoing an initial treatment trial.

The NMD4C Neuromuscular Clinician Group does not agree with the committee's recommendation on page 5, point 6, which states that reassessment for renewal should occur every 6 months. This renewal interval is not consistent with other new biological therapies including Efgartigimod, which have a renewal reassessment time frame of 12 months. Also, the recommendation is not in line with current clinical practice in MG, where all non-steroidal immunomodulatory therapies including Rituximab and oral therapies are renewed on annual basis by the payer, whether ther private or provincial. The frequent renewal requirements place undue strain on both clinicians and patients and are not in line with the expected clinical reassessment intervals for MG patients once they have demonstrated stability and clinical response to Ravulizumab. As such, the NMD4C Neuromuscular Clinician Group recommends a 12 month renewal reassessment interval for Ravulizumab.

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, please provide details regarding the information that requires clarification.

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.

CADTH Reimbursement Review

Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0855
Name of the drug and Indication(s)	Ultomiris
Organization Providing Feedback	The Pharmaceutical Advisory Committee Formulary Working Group

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	☐

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.

Outstanding Implementation Issues

In the event of a positive draft recommendation, drug programs can request further implementation support from CADTH on topics that cannot be addressed in the reimbursement review (e.g., concerning other drugs, without sufficient evidence to support a recommendation, etc.). Note that outstanding implementation questions can also be posed to the expert committee in Feedback section 4c.

Algorithm and implementation questions
1. Please specify sequencing questions or issues that should be addressed by CADTH (oncology only)
1. 2.
2. Please specify other implementation questions or issues that should be addressed by CADTH
1. 2.
Support strategy
3. Do you have any preferences or suggestions on how CADTH should address these issues?
May include implementation advice panel, evidence review, provisional algorithm (oncology), etc.

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0855
Brand name (generic)	ULTOMIRIS® (ravulizumab)
Indication(s)	Generalized myasthenia gravis (gMG)
Organization	Alexion Pharma GmbH
Contact information[a]	[redacted]

Stakeholder agreement with the draft recommendation		
1. Does the stakeholder agree with the committee's recommendation.	Yes	☒
	No	☐
Alexion Pharma GmbH (Alexion) agrees with the committee's recommendation to reimburse ULTOMIRIS for the treatment of adult patients with anti-acetylcholine receptor (AChR) antibody-positive generalized Myasthenia Gravis (gMG).		
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	☐
The committee has fully considered the clinical evidence provided by Alexion to address the evidence gaps identified by CDA-AMC during the initial review. In addition, the committee considered the strong clinician input supporting reimbursement of ULTOMIRIS for patients with gMG who are symptomatic despite a stable dose of standard of care with AChEIs, CSs, and/or NSISTs.		
Clarity of the draft recommendation		
3. Are the reasons for the recommendation clearly stated?	Yes	☒
	No	☐
The rationale for the recommendation is clearly stated, which outlined that the submitted clinical population was reflective of Canadian patients with gMG who have unmet needs and the clinical data demonstrated the robustness of the pivotal CHAMPION-MG trial through cohort analyses and results from the end-of-study long-term extension data.		
4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☒
	No	☐
In general, the implementation issues were outlined in detail and adequately addressed by CDEC. Alexion would like to highlight that the Formulary Working Group (FWG) had provided input to encourage alignment of reimbursement criteria for ULTOMIRIS with that of efgartigimod alfa in the treatment of gMG: *Drug Program Response, Ultomiris Draft Recommendation, Table 2, page 12*[1] "FWG noted that **consistency with initiation criteria associated with other drugs in the same therapeutic space, specifically efgartigimod alfa, should be considered**. This drug has been reviewed by CDA-AMC in the same population, and a positive CDEC recommendation was issued in December 2023." However, CDEC recommended more frequent reassessments for continuation of Ultomiris treatment (every 6 months) compared to efgartigimod alfa (every 12 months).		

Ultomiris Draft Recommendation, Table 1, page 4-5[1]

> *"Renewal Criteria*
> 6. For subsequent renewal, the treating clinician must provide proof that the initial response achieved after the first 6 months of therapy with ravulizumab for the MG-ADL score has been maintained.
> **Reassessment for renewal should occur every 6 months**."

Efgartigimod alfa Final Recommendation, Table 1, page 5[2]

> *"Renewal Criteria*
> Reimbursement of treatment with efgartigimod alfa should be continued if, after the initial 3 cycles of treatment, there is documented improvement in MG-ADL score of 2 points or greater. **Reassessment should occur every 12 months thereafter**."

To address potential operational challenges, Alexion proposes that drug programs consider reassessments for renewal of ULTOMIRIS every 12 months. Overly frequent reassessments for reimbursement renewal would represent an unnecessary administrative burden on clinicians and public drug plan administrators and may increase the risk of lapses in ULTOMIRIS treatment if required documentation are not submitted on time to meet every 6-month reassessment requirements. For ease of administration for the jurisdictions and clinicians and to avoid any unwanted confusion, a consistent renewal criterion within the class would best support patients, healthcare providers and drug plan administrators.

This is especially important in the context of chronic illnesses such as gMG where ravulizumab treatment may be required for multiple years, as stated by the clinical expert when informing the reimbursement conditions.

Ultomiris Draft Recommendation, Table 1, page 5[1]

> *"Implementation guidance*
> Based on clinical expert opinion, there is the possibility of ravulizumab being used for one year or more years."

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

Overall, the reimbursement conditions are clearly stated. However, as noted, Alexion would like to emphasize that the reimbursement criteria should align with those recommended for efgartigimod alfa in line with the FWG's note within the *Ultomiris Draft Recommendation*. In particular, Alexion proposes that reassessments for renewal of ULTOMIRIS take place every 12 months, in alignment with the recommendation for efgartigimod alfa.

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

REFERENCES

1. CDA-AMC. CDA-AMC Reimbursement Recommendation: Ravulizumab (Ultomiris) (Draft). https://www.cda-amc.ca/ravulizumab-4
2. CADTH. *CADTH Reimbursement Recommendation: Efgartigimod Alfa (Vyvgart)*. 2024. https://www.cadth.ca/efgartigimod-alfa