CADTH

CADTH REIMBURSEMENT REVIEW

Stakeholder Feedback on Draft Recommendation

Efgartigimod alfa (Vyvgart)

(argenx Canada inc.)

Indication: Vyvgart (efgartigimod alfa for injection) is indicated for the treatment of adult patients with generalized myasthenia gravis (gMG) who are antiacetylcholine receptor (AChR) antibody positive. .

November 30, 2023

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0782-000
Brand name (generic)	efgartigimod alfa
Indication(s)	Acetylcholine receptor antibody positive generalized myasthenia gravis
Organization	Neuromuscular Disease Network for Canada
Contact information[a]	Name: Dr. Vera Bril

Stakeholder agreement with the draft recommendation

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

The stakeholder disagrees with the comparison of efgartigimod to rituximab for the following reasons:

1. Rituximab is not available in all provinces of Canada as a treatment for gMG and so its' use as a comparator is discriminatory to MG patients in those provinces.
2. Rituximab is not effective in the majority of patients with gMG; controlled trials have shown negative results. Therefore, its' use is inappropriate based on efficacy. Perhaps 25% of gMG may have a positive response with this drug.
3. Efgartigimod acts rapidly within 2 weeks to improve status in MG patients whereas rituximab takes at least 3 months to take effect; these differences make rituximab inappropriate as a comparator.
4. The potential side-effects of rituximab include but are not limited to: Fatal Infusion Reactions, Severe Mucocutaneous Reactions, Hepatitis B Virus Reactivation, and Progressive Multifocal Leukoencephalopathy. These should be compared to the safety of efgartigimod which has not demonstrated any of these events and therefore, rituximab is an inappropriate comparator.
5. Efgartigimod will be used in place of IVIG/SCIG which are the more appropriate cost comparators. The onset of action is similar (i.e.: rapid in 1-2 weeks when that is needed, not 3 months like rituximab) and the benefits are similar. The safety is also similar to efgartigimod and much better than rituximab.
6. It is clear that the choice of comparator was made by people who do not have experience in treating patients with MG and the current conditions will disadvantage those patients with MG who would benefit from this treatment if available.

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	☒

No. We had made clear in the submission that those needing intervention most are those getting worse quickly and therefore need a therapy that works quickly such as efgartigimod (within 1-2 weeks in most patients). Of particular concern are those who may develop MG crisis rapidly. In consideration of the trial evidence, efgartigimod is an excellent treatment option for patients who are candidates for or are intolerant to IVIg or SCIg therapy. We think that FcR inhibitors, such as efgartigimod, are likely to replace Ig therapies.

Clarity of the draft recommendation

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

The recommendation overlooks the delay in onset of rituximab action, the lack of efficacy in 75% of patients with AChR + gMG, and the long list of safety concerns.		
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	☒
See above for comments on reimbursement. Saving money is important but not at the potential costs of lack of efficacy and death in our patients.		

[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		
1. 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. Homira Osman, VP Research & Public Policy at Muscular Dystrophy Canada		
2. 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		
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 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	*Vera Bril*
Position	***Professor of Medicine (Neurology), University of Toronto***
Date	*24-11-2023*
☒	**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**
ArgenX	☐	☒	☐	☐
UCB	☐	☒	☐	☐

New or Updated Declaration for Clinician 2	
Name	***Catherine Elizabeth Pringle***
Position	*Associate Professor (Neurology), University of Ottawa*
Date	*29-11-2023*
☒	**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**
ArgenX	☒	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 3	
Name	***Hans Katzberg***
Position	*Associate Professor of Medicine (Neurology), University of Toronto*
Date	*28-11-2023*

☒	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
ArgenX	☐	☒	☐	☐
UCB	☐	☐	☒	☐

New or Updated Declaration for Clinician 4	
Name	***Dubravka Dodig, MD, FRCP C***
Position	*Neuromuscular Neurologist*
Date	*30-11-2023*
☒	**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
ArgenX	☐	☒	☐	☐
Alnylam	☒	☐	☐	☐
Akcea	☒	☐	☐	☐
Sanofi			☒	
AZ-Alexion			☒	

New or Updated Declaration for Clinician 5	
Name	*Angela Genge*
Position	*Neurologist*
Date	*Same as previous*

☒	**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
Quralis	☐	☐	☐	☒
AL-S Pharma	☐	☐	☐	☒
AZ Alexion	☐	☒	☐	☐
Amyylx	☐	☐	☒	☐
MTPA	☐	☒	☐	☐
Sanofi	☒	☐	☐	☐
UCB	☒	☐	☐	☐

CADTH

CADTH Reimbursement Review

Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0782
Name of the drug and Indication(s)	Efgartigimod alfa (Vyvgart) For the treatment of adult patients with generalized myasthenia gravis (gMG) who are anti-acetylcholine receptor (AChR) antibody positive.
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
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.

Service Line: CADTH Drug Reimbursement Recommendation
Version: 1.0
Publication Date: Oct. 25, 2023
Report Length: 3 Pages

Single Technology

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. • For reimbursement condition 1, implementation guidance states, “Stable dose may be defined as adequate trial of at least one of AChEIs, CSs, and/or NSISTs in the previous 12 months.” Specific drugs/dosages/durations from the classes listed would help determine what an "adequate trial" is for adjudication purposes. • For reimbursement condition 5, implementation guidance states, “…if a patient has responded, treatment would be given as long as the patient continues to have a clinically meaningful response.” Does this mean a patient would receive continuous cycles (where a cycle = weekly infusions x 4, followed by 4 weeks off) without any defined duration? • For reimbursement condition 6, implementation guidance states, “If a patient had responded to efgartigimod alfa after the 3 initial cycles and was stable for a year, but worsens afterwards, the patient can reinitiate therapy, as long as, they met initiation criteria.” Is this referring to patients who continued to receive treatment cycles after the initial 3 cycles, or patients who received nothing after the initial 3 cycles? And when it says, "they met initiation criteria", does that mean a patient would be expected to try standard care (AChEIs, CSs, and/or NSISTs) again? • In Table 2, under “Dosing, schedule/frequency, dose intensity”, it is noted that, “Both experts agreed that waiting at least 4 weeks before initiating a re-treatment cycle seems rational.” Can any further guidance/information be provided to help drug plans understand what is considered an appropriate duration between treatment cycles? For example, what factors would a prescriber look at and how would they determine whether to give another cycle right away or wait (and wait how long)?

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	SR0782-000
Brand name (generic)	Vyvgart - efgartigimod alfa
Indication(s)	generalized myasthenia gravis (gMG) who are antiacetylcholine receptor (AChR) antibody positive
Organization	Muscular Dystrophy Canada
Contact information[a]	Homira Osman, Vice-President Research & Public Policy

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

We agree with CDEC's recommendation and endorse the reimbursement of efgartigimod alfa for treating adult patients with generalized myasthenia gravis (gMG) who test positive for anti-acetylcholine receptor (AChR) antibodies. However, we find it surprising that comparisons were drawn with Rituximab. It's important to note that the accessibility of rituximab is not a practical option for the majority of patients in Canada. In fact, access to rituximab continues to pose a significant obstacle for most patients, with British Columbia being the sole exception with a comparatively less restrictive approach – contributing to inequities in access. Our particular concern lies in CDEC's observation that, at the proposed price point, the anticipated incremental budget impact of efgartigimod alfa exceeds $40 million annually. We suggest a reassessment of this calculation, considering that efgartigimod will substitute IVIG/SCIG, which are more suitable cost comparators in this context.

From the patients' lens, it is crucial we to respond to the observation raised by CDEC regarding the potential for higher treatment burden initially with efgartigimod alfa as an add-on therapy compared to conventional approaches. Although there may appear to be an initial impact on treatment burden, it's essential to highlight the meaningful clinical benefits and the rapid onset of action with efgartigimod (within 2 weeks) is appreciated. This stands in stark contrast to the current reality, where patients often need to remain on treatments for years before demonstrating 'failure' in order to receive access to other treatments. This was discussed originally in our patient input submission:

"My doctor told me it could take 6 maybe even 9 months for the treatment to take effect."

"Imagine living half the year waiting for a drug to show benefit and then to find out you need to be switched to something else.

"I was told it would take a while for the benefits to kick in."

"My whole life revolves around MG. I feel the effects of lack of IVIG close to the end of the month. Then I am knocked for a day or two after IVIG. It takes effect but loses its effect by the third week."

In the feedback provided by patients on the draft recommendation, there's an expressed apprehension regarding the requirement for "proof of no worsening of MG-ADL." There is a raised question about whether this metric adequately captures the experiences of poor responders and is sensitive to lack of response. The suggestion is to consider allowing neuromuscular clinicians to exercise their expert judgment in assessing improvement, reaching a plateau, or observing no effects instead.

It's important to emphasize, from the patients' standpoint, that statement "approximately 90% of patients respond to current treatments, and that response is often partial, leading to persistent symptoms affecting quality of life and function" serves as a compelling rationale for the reimbursement of efgartigimod alfa. There

are unmet treatment needs and lack of effective therapies for patients with all types of MG, but certainly for those with gMG who are AChR) antibody positive

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, it was clear that the perspectives and real-life experiences were reviewed and included in the recommendation. Thank you.		

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	☐
Not well-discussed as the recommendation was negative.		
5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☒
	No	☐
Not applicable as reimbursement was not recommended.		

[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.
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- 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	*Homira Osman*
Position	*Vice-President, Research and Public Policy*
Date	*30-11-2023*
☒	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

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0782-000
Brand name (generic)	VYVGART® (efgartigimod alfa)
Indication(s)	For the treatment of adult patients with generalized myasthenia gravis (gMG) who are anti-acetylcholine receptor (AChR) antibody positive.
Organization	argenx Canada Inc.
Contact information[a]	[redacted]

Stakeholder agreement with the draft recommendation		
1. Does the stakeholder agree with the committee's recommendation.	Yes	☒
	No	☐
The stakeholder (argenx Canada Inc.) agrees with the draft recommendation.		
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	☐
N/A		
Clarity of the draft recommendation		
3. Are the reasons for the recommendation clearly stated?	Yes	☒
	No	☐
N/A		
4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☒
	No	☐
N/A		
5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☒
	No	☐
N/A		

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