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Reimbursement Recommendation

Rozanolixizumab (Rystiggo)

Indication: For the treatment of adult patients with generalized myasthenia gravis who are anti-acetylcholine receptor or anti-muscle-specific tyrosine kinase antibody positive

Sponsor: UCB Canada Inc.

Final recommendation: Reimburse with conditions

Summary

What Is the Reimbursement Recommendation for Rystiggo?

Canada's Drug Agency (CDA-AMC) recommends that public drug plans reimburse Rystiggo as an add-on therapy for the treatment of adult patients with generalized myasthenia gravis (gMG) who are anti-acetylcholine receptor (AChR) or anti-muscle-specific kinase (MuSK) antibody positive and for whom symptoms persist despite conventional therapy with acetylcholinesterase inhibitors (AChEIs), corticosteroids, and/or nonsteroidal immunosuppressive therapies (NSISTs) if certain conditions are met.

Which Patients Are Eligible for Coverage?

Rystiggo should only be covered to treat patients who have a diagnosis of class II to IV gMG based on the Myasthenia Gravis Foundation of America (MGFA) system, have tested positive for AChR or MuSK antibodies, and have a Myasthenia Gravis Activities of Daily Living (MG-ADL) scale score of at least 3 with at least 3 points for symptoms not related to their eyes. Rystiggo should only be covered to treat patients if their symptoms persist despite a stable dose of conventional therapy with AChEIs, corticosteroids, and/or NSISTs.

What Are the Conditions for Reimbursement?

Rystiggo should not be reimbursed when given during a gMG exacerbation (i.e., a moment when the patient experiences weakness in some or all muscles, without needing assistance to breath) or crisis (i.e., a moment when respiratory muscles are too weak, limiting air flow in and out of the lungs and, as a result, the patient is unable to breathe), or within 6 months of thymectomy (i.e., surgical removal of the thymus gland). Rystiggo should only be reimbursed if prescribed by or in consultation with a neurologist with expertise in managing patients with gMG, and the total cost of Rystiggo should not exceed the total drug cost with the least costly advanced treatments for gMG. Rystiggo should not be used concomitantly with rituximab, efgartigimod alfa, and/or complement inhibitors such as eculizumab.

Why Did CDA-AMC Make This Recommendation?

- Evidence from 1 clinical trial showed that after 43 days of treatment, Rystiggo resulted in a statistically significantly higher treatment response and clinically significantly better reduction in symptom severity compared with placebo. The results also indicated that Rystiggo is likely

Summary

better than a placebo in improving patients' quality of life related to myasthenia gravis.

- The Canadian Drug Expert Committee (CDEC) concluded that Rystiggo meets some of the unmet treatment needs identified by patients, including offering another mode of administration with the potential for at-home administration, which may meet a need for improved independence and improving patients' quality of life related to myasthenia gravis with minimal side effects.
- Based on the CDA-AMC assessment of the health economic evidence, Rystiggo does not represent good value to the health care system at the public list price. The committee determined that there is not enough evidence to justify a greater cost for Rystiggo compared with the other advanced add-on therapies used for the treatment of AChR or MuSK antibody-positive gMG.
- Based on public list prices, Rystiggo is estimated to cost the public drug plans approximately $132 million over the next 3 years.

Additional Information

What Is gMG?

gMG is an uncommon and long-lasting illness that happens when the body's own defence system (autoimmune) attacks the connection point between nerves and muscles, causing muscles in certain parts of the body, or all over the body, to become weak. Some common signs of gMG are feeling very tired (fatigue); eyelids that hang low (droopy eyelids); seeing double (diplopia); difficulty breathing, swallowing, or chewing; and weakness in arms or legs. Most patients with gMG (85%) have blood that tests positive for AChR antibody, while 8% are MuSk antibody positive. Overall, about 26 out of every 100,000 people in Canada are living with gMG and about 23 new people out of every million are diagnosed each year.

Unmet Needs in gMG

Patients identified a decrease in the number of exacerbations (significant flareups), a reduction in medication side effects, the maintenance of independence, reducing the number of serious hospital admissions, and improved health-related quality of life (HRQoL) as key important outcomes.

How Much Does Rystiggo Cost?

Treatment with Rystiggo is expected to cost approximately $218,478 to $655,434 per patient per year, depending on the patient’s weight.

Recommendation

CDEC recommends that rozanolixizumab be reimbursed as an add-on therapy for the treatment of adult patients with gMG who are either AChR or MuSK antibody positive and for whom symptoms persist despite conventional therapy with AChEIs, corticosteroids, and/or NSISTs only if the conditions listed in Table 1 are met.

Rationale for the Recommendation

One phase III, double-blind, randomized placebo-controlled trial (MyCarinG; N = 200 patients) demonstrated that treatment with rozanolixizumab results in added clinical benefit for adult patients with AChR-positive or MuSK antibody-positive gMG compared with placebo. The primary outcome indicated that after 43 days of treatment, reduction in symptom severity was clinically significantly better with rozanolixizumab than with placebo, as measured by changes from baseline in MG-ADL scores (least squares [LS] mean difference between groups of −2.586; 95% confidence interval [CI], −4.091 to −1.249; P < 0.001). The between-group difference in patients achieving at least a 2-point improvement in this outcome (i.e., MG-ADL responders) was 39.8% (95% CI, 24.2 to 55.4) in favour of rozanolixizumab. Treatment response was also statistically significantly better with rozanolixizumab than placebo, as indicated by an LS mean difference between groups of −3.483 (95% CI, −5.614 to −1.584; P < 0.001) in Quantitative Myasthenia Gravis (QMG) scores. Assessment of patients' HRQoL using the disease-specific Revised Myasthenia Gravis Quality of Life 15-Item (MG-QoL15r) scale showed that rozanolixizumab would likely improve patients' quality of life related to myasthenia gravis better than placebo, with a between-group LS mean difference of −2.245 (95% CI, −4.096 to −0.394).

Patients identified a decrease in the number of exacerbations, reduction in medication side effects, the maintenance of independence, reducing the number of serious hospital admissions and HRQoL as key important outcomes. CDEC concluded that rozanolixizumab may meet some of the patients' needs, including offering another mode of administration with the potential of at-home administration, which may meet a need for improved independence and improving patients' quality of life related to myasthenia gravis with minimal side effects.

At the sponsor-submitted price for rozanolixizumab, publicly listed price for rituximab, eculizumab, or efgartigimod alfa, and prices based on published literature for plasma exchange (PLEX) and IV immunoglobulin (IVIg) or subcutaneous immunoglobulin (SCIg), rozanolixizumab plus conventional therapy may be more or less costly than other advanced treatments. Given the uncertainty with the comparative clinical evidence, the total drug cost of rozanolixizumab should not exceed the total drug cost with the least costly advanced treatments for gMG.

Table 1: Reimbursement Conditions and Reasons

Reimbursement condition	Reason	Implementation guidance
Initiation		
1. Treatment with rozanolixizumab should be reimbursed for adult patients with gMG who have all of the following: 1.1. positive serologic test for either AChR or MuSK antibody 1.2. an MG-ADL score at baseline of ≥ 3 (with at least 3 points coming from nonocular symptoms) 1.3. MGFA class II to IV disease 1.4. symptoms persisting despite stable doses of conventional therapy with AChEIs, corticosteroids, and/or NSISTs.	The results from 1 phase III, multicentre, double-blind, randomized, placebo-controlled trial (MyCarinG) demonstrated that, compared with placebo, treatment with rozanolixizumab results in a statistically significantly reduction of 2 in the primary outcome of MG-ADL score in adult patients (aged ≥ 18 years) with gMG who are either AChR or MuSK antibody positive. The enrolled patients in MyCarinG had an MG-ADL score ≥ 3, an MGFA class of II to IV, and persistent symptoms despite a stable dose of conventional therapy with AChEIs, corticosteroids, and/or NSISTs at baseline.	*Stable dose* may be defined as an adequate trial (as determined by the treating physician) of at least 1 AChEI, corticosteroid, and/or NSIST in the previous 12 months. CDEC noted that rituximab may be available in some jurisdictions; however, CDEC heard from the clinical expert that access to rituximab remains a barrier for some patients. The clinical expert noted to CDEC that an MG-ADL score of 3 or greater with at least 3 points coming from nonocular symptoms will easily get to an MG-ADL score of 5 or 6 when adding double and/or blurred vision.
2. Rozanolixizumab should not be initiated in either of the following cases: 2.1. during a gMG exacerbation or crisis 2.2. for those who have had a thymectomy within 6 months.	Patients were excluded from the MyCarinG trial if they had had a thymectomy within 6 months before screening. The efficacy and harms of rozanolixizumab in such patients are unknown.	Regarding initiating rozanolixizumab with respect to thymectomy, CDEC noted that the drug plans may use the within 3 months timing applied in the recommendation of efgartigimod alfa for gMG as applicable in the jurisdictions.
3. An MG-ADL score must be measured and provided by the physician at baseline.	This condition is in line with other targeted treatments for gMG, and aligns with the MyCarinG trial, in which baseline MG-ADL score was measured and used to determine response to treatment.	—
4. The response to rozanolixizumab should be assessed after an initial 6-week treatment period.	In the MyCarinG trial, rozanolixizumab was administered as a subcutaneous infusion once weekly for 6 weeks. In addition, the recommended dosage by Health Canada is administered as a subcutaneous infusion once weekly for 6 weeks.	—
Renewal		
5. Reimbursement of treatment with rozanolixizumab should be continued if, after the initial 6 weeks of treatment, there is documented improvement in disease symptoms, indicated by a reduction in MG-ADL score of 2 points or greater.	Although no MID has been estimated, an improvement of approximately 2 points in the total MG-ADL score is a recommended response threshold that indicates clinical improvement at the level of individual patients with MG. In the MyCarinG trial, after the 6-week treatment period, patients entered an 8-week observation period. Patients who	If the patient has a clinically meaningful response after the initial 6-week treatment with rozanolixizumab, subsequent treatment cycles may be given based on the attending clinician's evaluation. Regarding the maximum duration of therapy, rozanolixizumab could be continued as long as it demonstrates a clinically beneficial

Reimbursement condition	Reason	Implementation guidance
Reassessment should occur every 12 months thereafter.	completed the 6-week treatment period and 8-week observation period had the opportunity to roll over into MG0004, an open-label extension study that assessed the long-term safety and efficacy of the rozanolixizumab weekly dosing regimen for 52 weeks.	response or until the disease remits spontaneously. Subsequent treatment with rozanolixizumab should align with the 6-week treatment cycle followed by an observation period of up to 8 weeks as observed in the MyCarinG trial and stated in the product monograph. The safety of initiating subsequent cycles sooner than 4 weeks from the last infusion of the previous treatment cycle has not been established.
6. For subsequent renewal, the physician must provide proof of no worsening of MG-ADL score.	This is to ensure that a patient's disease is maintaining its response to treatment with rozanolixizumab.	There is the possibility of rozanolixizumab being used for 1 or more years if a patient's disease responds to rozanolixizumab after the initial weekly injections for 6 weeks and is stable for a year but worsens afterward. A patient who continues to receive treatment after the initial weekly injections for 6 weeks but is no longer receiving rozanolixizumab (i.e., their disease initially showed response but they are no longer receiving treatment) can reinitiate therapy if they meet the initiation criteria. The patient would not be expected to try standard care (AChEIs, corticosteroids, and/or NSISTs) again.
Prescribing		
7. Rozanolixizumab should be prescribed by or in consultation with a neurologist with expertise in managing patients with gMG.	Accurate diagnosis and follow-up of patients with gMG are important to ensure that rozanolixizumab is prescribed to appropriate patients.	—
8. Rozanolixizumab should not be used concomitantly with rituximab, efgartigimod alfa, and/or complement inhibitors such as eculizumab.	The MyCarinG trial did not assess such combinations, and the efficacy and safety of rozanolixizumab in combination with rituximab, efgartigimod alfa, eculizumab, or ravulizumab are unknown.	—
Pricing		
9. Rozanolixizumab should be negotiated so that it does not exceed the drug program cost of treatment with the least costly advanced treatment reimbursed for the treatment of gMG.	Given the uncertainty associated with the comparative clinical evidence, there is insufficient evidence to justify a cost premium for rozanolixizumab over the least expensive advanced treatment reimbursed for gMG.	—

Reimbursement condition	Reason	Implementation guidance
Feasibility of adoption		
10. The economic feasibility of adoption of rozanolixizumab must be addressed.	At the submitted price, the incremental budget impact of rozanolixizumab is expected to be greater than $40 million in years 2 and 3.	—

AChEI = acetylcholinesterase inhibitor; CDEC = Canadian Drug Expert Committee; gMG = generalized myasthenia gravis; MG = myasthenia gravis; MG-ADL = Myasthenia Gravis Activities of Daily Living; MGFA = Myasthenia Gravis Foundation of America; MID = minimal important difference; NSIST = nonsteroidal immunosuppressive therapy.

Discussion Points

- **Limited evidence in the MuSK antibody-positive population:** CDEC noted that while the MyCarinG trial included patients with gMG who were either AChR or MuSK antibody positive and were being considered by the investigator for additional treatment, such as IVIg or PLEX., less than 10% of those enrolled were MuSK antibody positive. CDEC observed that the clinical expert projected that the proportion of patients with MuSK antibody-positive gMG in his practice was about 5%, which would suggest that the small size of the MuSK antibody-positive subgroup in the MyCarinG trial aligns with what is seen in clinical practice. However, the small sample limits any conclusions that can be drawn about the efficacy or safety of rozanolixizumab in the MuSK antibody-positive subpopulation.
- **Prior treatments:** CDEC noted that although most patients (96%) included in the MyCarinG trial had received at least 1 prior therapy, many of the patients had only been treated with 1 class of conventional therapy (AChEIs only = 15.5%, steroid only = 27.5%, and NSIST only = 13.5%). CDEC observed that the post hoc subgroup analysis evaluating response in patients who had 2 or more prior therapies had limitations, including a small sample size and lack of information about the adequacy of the trial with alternative therapies, limiting the conclusions that could be drawn from it.
- **Lack of direct comparative evidence:** In the absence of trials directly comparing rozanolixizumab to other drugs used for treating gMG, CDEC considered the evidence from the sponsor-submitted indirect treatment comparisons assessing the efficacy and harms of rozanolixizumab versus comparators. The committee noted that the submitted network meta-analysis (NMA) was limited by imprecision and heterogeneity in the included studies, and the results from the matching-adjusted indirect comparison (MAIC) were uncertain due to potential for residual confounding, small sample size, imprecision, and generalizability of evaluating treatment response. Therefore, a definitive conclusion could not be drawn from the indirect treatment comparisons regarding the comparative efficacy of rozanolixizumab versus eculizumab or efgartigimod alfa. Comparative data on harms were not reported.
- **Efficacy:** CDEC noted that the effect estimates for the efficacy outcomes (MG-ADL, QMG, and MG-QoL15r) exceeded the suggested thresholds identified by the clinical expert as clinically meaningful, and assessments using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach concluded a moderate certainty in evidence. CDEC noted that overall, treatment

with rozanolixizumab resulted in consistently greater decreases from baseline in MG-ADL score at day 43 across all subgroups compared with placebo (not rated with GRADE); however, the wide CI associated with outcomes for patients who were MuSK antibody positive indicated imprecision that may be due to the small sample size of the subgroup.

- **Long-term outcomes:** CDEC noted that the treatment duration of the pivotal MyCarinG trial was 6 weeks, with responses assessed at day 43, and the long-term extensions phase did not involve any comparators. Therefore, CDEC could not draw any conclusions on the comparative long-term efficacy and harms of rozanolixizumab.
- **Cost-effectiveness of rozanolixizumab:** CDEC discussed that if other recently recommended treatments for refractory gMG are reimbursed by CDA-AMC–participating drug plans, there is no robust comparative clinical evidence for rozanolixizumab to be priced higher than the lowest cost advanced treatment reimbursed for AChR or MuSK antibody-positive refractory gMG.

Background

Myasthenia gravis is a rare, chronic, autoimmune neuromuscular disease in which antibodies against the neuromuscular junction disrupt neuromuscular transmission, resulting in localized or generalized skeletal muscle weakness. Patients experience a variety of symptoms, including fatigue, droopy eyelids, diplopia, neck weakness, difficulty swallowing or chewing, speech disturbances, difficulty breathing, and upper and/or lower limb weakness. Based on serology, 85% of patients with gMG are AChR antibody positive, 8% are MuSk antibody positive, 1% are LRP4 antibody positive, and the remaining 6% of cases are seronegative with no detectable antibodies. Globally, the incidence of myasthenia gravis varies from 4 to 30 cases per million person-years and the prevalence ranges from 150 to 200 cases per million. In Canada, the incidence and prevalence of gMG are estimated at 23 per 1 million person-years and 26.3 per 100,000, respectively. The mortality rate of myasthenia gravis has been reported to be between 0.06 to 0.89 per million person-years. The symptoms of gMG occur unpredictably and fluctuate in nature, intensity, and severity on a day-to-day basis throughout a patient's life, requiring intervention or treatment change. The unpredictable exacerbation and myasthenic crisis, in combination with a variety of symptoms, result in a chronic disease with significant burden negatively impacting a patient's quality of life.

There are currently no Canadian guidelines for the treatment of gMG. The MGFA international consensus guidelines for the management of myasthenia gravis were updated in 2020 and are now the most recent guidelines for the management of myasthenia gravis. According to these guidelines and clinical experts from Canada, the goal of treatment for patients with gMG is to reduce disease symptoms as well as adverse effects of myasthenia gravis therapy and to allow the patient to function and work normally with good HRQoL. Other treatment goals include avoiding myasthenia gravis exacerbations and myasthenic crises, minimizing hospitalizations and intensive care unit admissions, and reducing the numbers and doses of therapies (especially corticosteroid use) required for symptom control.

Conventional therapy for all patients with gMG generally begins with AChEIs, though an AChEI can worsen MuSK antibody-positive myasthenia gravis symptoms and so may not be used in all MuSK antibody-positive gMG. If AChEI therapy alone provides insufficient symptom relief, immunosuppressive therapy with a corticosteroid such as prednisone is administered. In patients whose disease does not respond to corticosteroids, or for those who have significant comorbidities such that long-term corticosteroid treatment is contraindicated, or in whom doses of corticosteroids cannot be tapered, treatment with NSISTs such as azathioprine, mycophenolate mofetil, cyclophosphamide, cyclosporine, tacrolimus, or methotrexate may be initiated either alone or in combination with corticosteroids. It can take several months to years, depending on the NSIST, for the drug to produce a clinically relevant effect and reduce a patient's gMG symptoms. While patients wait for NSIST treatment to take effect, they may experience myasthenia gravis exacerbations and/or myasthenic crises, which require acute use of IV or subcutaneous immunoglobulin or PLEX. If patients continue to experience gMG symptoms, the dose may be increased or the drug switched to an alternative NSIST.

It is estimated that 15% to 40% of patients will continue to experience symptoms despite conventional therapy with AChEIs, corticosteroids, and/or NSISTs. Patients with AChR antibody-positive gMG whose symptoms persist despite conventional therapy would be eligible for treatment with rituximab, chronic IV or subcutaneous immunoglobulin, and/or chronic PLEX. Currently, rozanolixizumab is the only targeted therapy approved by Health Canada for the treatment of MuSK antibody-positive gMG. Patients with MuSK antibody-positive gMG have disease that is less responsive to AChEIs and are frequently intolerant to pyridostigmine at conventional doses. Patients with MuSK antibodies have disease that typically responds well to corticosteroids and NSISTs but they tend to remain dependent on corticosteroids despite concomitant therapy with NSISTs. For patients with MuSK antibody-positive gMG whose symptoms persist despite treatment with corticosteroids and NSISTs, options include rituximab and PLEX, while IV immunoglobulin is usually less effective. Rituximab is recommended by international consensus guidance for MuSK antibody-positive gMG whose disease has an unsatisfactory response to initial immunotherapy. That is in contrast to patients with AChR antibody-positive gMG, for whom rituximab is only considered if the patient's disease does not respond to other immunotherapies, or if they cannot tolerate other immunotherapies.

Rozanolixizumab has a Health Canada–approved indication for the treatment of adult patients with gMG who are AChR or MuSK antibody positive. Rozanolixizumab is a humanized immunoglobulin (Ig) G4 monoclonal antibody that decreases serum immunoglobulin (IgG) concentration by inhibiting the binding of IgG to FcRn, a receptor that normally protects IgG from intracellular degradation and recycles IgG back to the cell surface. It is available as one 280 mg/2 mL (i.e., 140 mg/mL) single-dose vial. The recommended dosage (based on body weight) is administered as a solution for subcutaneous infusion using an infusion pump at a rate of 20 mL/hour once weekly for 6 weeks.

Sources of Information Used by the Committee

To make its recommendation, the committee considered the following information:

- a review of 1 phase III, randomized, double-blind and placebo-controlled study (MyCarinG) in adults with gMG; with 2 long-term extension studies (MG0004 and MG0007)
- 4 indirect treatment comparisons
- patients' perspectives gathered by 1 patient group: Muscular Dystrophy Canada
- input from 1 clinician group: the Neuromuscular Disease Network for Canada
- input from public drug plans that participate in the reimbursement review process
- 1 clinical specialist with expertise diagnosing and treating patients with gMG
- a review of the pharmacoeconomic model and report submitted by the sponsor.

Perspectives of Patients, Clinicians, and Drug Programs

Patient Input

- There was 1 patient group submission, from Muscular Dystrophy Canada, which collected input via a survey and semistructured virtual interview, for a total sample of 194 patients.
- Patients reported issues with productivity, fatigue, low energy levels and quality of life, mental health, respiratory health, mobility and strength, independence, relationships and social participation, eyes and/or vision, speech, and swallowing. Respondents stated that the impact of gMG extended beyond physical symptoms, impacting the quality of life and the well-being of their families.
- Outcomes of importance to patients include a decrease in the number of exacerbations, a reduction in medication side effects, maintenance of independence, and reducing the number of serious hospital admissions.
- With respect to their experience with currently available therapies, the main themes that emerged included their negative experiences with steroids, that conventional treatments take a long time to take effect, and the treatment pathway involved a lot of trial and error.

Clinician Input

Input From Clinical Expert Consulted for This Review

- The clinical expert consulted on this review noted numerous needs that are not being met by current therapies, including that 10% of patients have disease that is refractory to all currently available treatments, that there is a delayed effect to immunosuppressants, and there are harms associated with the conventional therapies, notably the corticosteroids. The clinical expert noted that it is these patients with refractory disease who are most likely to require hospitalization or costly and more involved rescue therapies, such as IVIg and PLEX, on a more chronic basis.

- The clinical expert sees rozanolixizumab as add-on therapy, for use in a similar manner to IVIg and efgartigimod, specifically in patients who have tried glucocorticoids and/or a steroid-sparing drug and had an inadequate disease response, or in whom steroids could not be tapered or side effects were intolerable. The clinical expert also noted the potential for rozanolixizumab to act as bridging therapy while waiting for the typically delayed effects of immunosuppressants several months after initiation.
- The clinical expert believed that the patients most likely to respond to rozanolixizumab would be the type included in the pivotal trial, namely those who are MuSK antibody positive or AChR antibody positive and continue to be symptomatic (based on their MG-ADL score) despite trials of a first-line therapy.
- According to the clinical expert, response to treatment would be assessed using patient's subjective response (symptoms) and whether there has been improved functional capacity according to the treating clinician. Treatment would be discontinued for lack of response (although how long a trial would last is currently unclear) and side effects. The clinical expert estimated that they would suggest a trial of 3 to 6 months before discontinuing for lack of efficacy. Also, treatment discontinuation may be considered if the patient determines their treatment goals have been achieved based on the response.

Clinician Group Input

- Input was received from 1 clinician group, the Neuromuscular Disease Network for Canada, which included responses from 5 of the clinicians in the group.
- The clinician group was generally in agreement with the views of the clinical expert consulted with respect to unmet needs, patients most likely to have disease that responds to treatment, and that key outcomes are the MG-ADL and QMG scores.
- The clinician group did not indicate whether they had experience using rozanolixizumab; however. they did note that it is likely to replace standard immunoglobulin therapies.

Drug Program Input

Input was obtained from the drug programs that participate in the reimbursement review process. The following were identified as key factors that could potentially impact the implementation of a recommendation for rozanolixizumab:

- considerations for initiation of therapy
- considerations for continuation or renewal of therapy
- considerations for discontinuation of therapy
- considerations for prescribing of therapy
- generalizability of trial populations to the broader populations in the jurisdictions
- care provision issues
- system and economic issues.

The clinical expert consulted for the review provided advice on the potential implementation issues raised by the drug programs.

Table 2: Responses to Questions From the Drug Programs

Drug program implementation questions	Clinical expert response
Relevant comparators	
Clinical expert: If both efgartigimod alfa and rozanolixizumab were available through public reimbursement, which drug would be preferred, and why, for patients with AChR antibody-positive gMG?	The clinical expert noted that the choice between efgartigimod alfa and rozanolixizumab would largely come down to patient preference, as they did not see a clear advantage of 1 over the other. *CDEC agreed with the clinical expert.*
Clinical expert: If both rituximab and rozanolixizumab were available through public reimbursement, which drug would be preferred, and why, for patients with MuSK antibody-positive gMG?	The clinical expert noted that although efficacy-wise there are no data to necessarily prefer 1 over the other, rituximab has some significant safety issues that might make it the less favourable of these 2 options. Rituximab also does not have approval for the treatment of MuSK gMG. *CDEC noted the clinical expert's comment.*
Clinical expert: If you had access to rituximab through public reimbursement, would it be used as a first-line treatment in patients with AChR or MuSK antibody-positive disease? If so, in what clinical situations?	The clinical expert noted that rituximab would not be first-line therapy for AChR-positive disease. The clinical expert noted that for patients who are MuSK antibody positive, rituximab might be first-line treatment in those who are more severely impacted by their disease (i.e., an MG-ADL of 5 or higher), such as patients with swallowing difficulties, or at least might be used early if there is limited benefit from glucocorticoids, IVIg, or PLEX. *CDEC noted the clinical expert's comment.*
Clinical expert: What is the prevalence of patients with MuSK antibody-positive gMG in your practice?	The clinical expert estimated that patients who are MuSK antibody positive make up about 5% of patients with gMG in their practice. *CDEC noted the clinical expert's comment.*
Clinical expert: Does rozanolixizumab meet an unmet need for adult patients with AChR or MuSK antibody positive gMG symptoms despite conventional treatment?	The clinical expert noted that rozanolixizumab meets an unmet need for patients whose disease is refractory to, or who are intolerant of, other therapies. *CDEC noted the clinical expert's comment.*
Considerations for initiation of therapy	
Patients enrolled in the MycarinG (MG0007) trial must have met the following criteria: • documented diagnosis of gMG • positive record of autoantibodies against AChR or MuSK • MGFA class II to IVa • MG-ADL score of at least 3 (with ≥ 3 points from a nonocular symptom) and a QMG score of at least 11 • considered for additional treatment such as IVIg or PLEX by the investigator. The primary end point was change from baseline to day 43 in MG-ADL score.	The clinical expert noted that the inclusion criteria for the MyCarinG trial are consistent with the patients they would encounter in their practice. The clinical expert noted that it would be reasonable for the initiation criteria to align closely with the trial's inclusion criteria, except when a patient for whom IVIg or PLEX may not be appropriate is being considered for additional treatment. Such patients may benefit from rozanolixizumab. *CDEC agreed with the clinical expert.*

Drug program implementation questions	Clinical expert response
Clinical expert: Do the scores in the previously outlined criteria align with what you would see in practice of initiating treatment? **CDA-AMC:** Should the initiation criteria align with the inclusion criteria?	
Clinical expert: • If patients with AChR antibody-positive gMG experience treatment failure with efgartigimod alfa or rituximab, would they be eligible for treatment with rozanolixizumab? • If patients with MuSK antibody-positive gMG experience treatment failure with rituximab, would they be eligible for treatment with rozanolixizumab?	The clinical expert believed that patients with AChR antibody-positive gMG who experience treatment failure with efgartigimod or rituximab should be eligible for treatment with rozanolixizumab. The clinical expert believed that patients with MuSK antibody-positive gMG who experience treatment failure on rituximab should be eligible for treatment with rozanolixizumab. *CDEC agreed with the clinical expert.*
Clinical expert: Under what conditions can a patient restart treatment with rozanolixizumab?	The clinical expert noted that they would look at the patient response, then treat when needed. The clinical expert added that you do not want to re-treat for minor symptoms, but you also do not want the patient to deteriorate too much before intervening. *CDEC agreed with the clinical expert.*
Considerations for prescribing of therapy	
Rozanolixizumab is administered via a short (< 18 minute) subcutaneous injection using an infusion pump and a single-dose vial of rozanolixizumab vial once weekly for 6 weeks. **Clinical expert:** Efgartigimod alfa is administered as IV over 1 hour once weekly for 4 doses. Does the shorter infusion time and subcutaneous administration influence your choice of therapies?	The clinical expert believed that they would prefer a shorter infusion time and a subcutaneous route of administration because these routes use less resources and are preferred by patients. *CDEC agreed with the clinical expert.*
Drug administration: • The draft product monograph states that rozanolixizumab should only be prepared and infused by a health care professional. • UCB Canada will offer an optional patient support program providing patient education and health care professional support for administration of rozanolixizumab at program infusion clinics or in the patient's home. • Following the first treatment cycle, subsequent cycles are administered according to clinical evaluation. • The frequency of treatment cycles may vary by patient. Pooled data from the phase III and extension studies suggest a mean annualized rate of 17.8 infusions (2.97 completed cycles) and 3.4 initiated cycles. **Clinical expert:** Are there any scenarios in which administration at a clinic would be preferred over at-home treatments?	The clinical expert noted that generally speaking, administration at a clinic would not be preferred over home administration, with the lone exception of the first dose, for which you may wish to observe the patient in case they have a reaction. *CDEC agreed with the clinical expert.*
Consistency with prescribing criteria associated with other drugs reviewed by CDA-AMC in the same therapeutic space: **CDA-AMC:** Should the prescribing criteria align with efgartigimod alfa?	The clinical expert believed that it would be reasonable for the criteria to align. *CDEC agreed with the clinical expert.*

Drug program implementation questions	Clinical expert response
System and economic issues	
Concerns regarding the anticipated budget impact and sustainability: • The price of each single-dose vial is $12,260.2760. • The sponsor assumed the average annual cost of rozanolixizumab is $436,956 per patient. • Quality-adjusted life-years would result in a similar cost to efgartigimod alfa.	*This is a comment from the drug programs to inform CDEC deliberations.*
Additional costs to be considered (other than related to care provision as previously detailed): The sponsor indicated that they would offer an optional patient support program to provide patient education and health care professional support for the administration of rozanolixizumab at program infusion clinics or in the patient's home.	*This is a comment from the drug programs to inform CDEC deliberations.*
Presence of confidential negotiated prices for comparators: • Efgartigimod alfa is currently under negotiation with pCPA.	• *This is a comment from the drug programs to inform CDEC deliberations.*

CDEC = Canadian Drug Expert Committee; gMG = generalized myasthenia gravis; IVIg = IV immunoglobulin; MG-ADL = Myasthenia Gravis Activities of Daily Living; MGFA = Myasthenia Gravis Foundation of America; pCPA = pan-Canadian Pharmaceutical Alliance; PLEX = plasma exchange; QMG = Quantitative Myasthenia Gravis.

Clinical Evidence

Systematic Review

Description of Studies

MycarinG was a phase III, sponsor-funded, double-blind randomized controlled study. Eligible patients were adults aged older than 18 years with AChR antibody-positive or MuSK antibody-positive gMG (MGFA disease class II to IVa), an MG-ADL score of 3 or greater (with at least a score of 3 from nonocular symptoms), a QMG score of 11 or greater, and who were being considered by the investigator for additional treatment such as IVIg or PLEX. The study began enrolling patients in June 2019 and concluded in October 2021, with a final data cut-off date of September 17, 2021. A total of 200 patients were enrolled and randomized in a 1:1:1 ratio to receive 6 weekly subcutaneous infusions of rozanolixizumab 10 mg/kg, 7 mg/kg, or matching placebo. The recommended dose under review by Health Canada is 7 mg/kg, which will be the focus of this review. The study spanned 81 sites across 17 countries with 4 sites in Canada. The total duration of study participation for all patients was up to approximately 18 weeks, including a screening period of up to 4 weeks, a 6-week treatment period, and an 8-week observation period. Patients who completed the 6-week treatment period and 8-week observation period had the opportunity to roll over into MG0004, an open-label extension study in which the long-term safety, tolerability, and efficacy of rozanolixizumab was measured in patients with gMG over 52 weeks of weekly chronic treatment. The MG0004 trial was terminated in 2021 and replaced by the MG0007 trial, an ongoing open-label extension study that consists of

6-week treatment cycles based on myasthenia gravis worsening. Patients could roll over from the MycarinG or MG0004 trials directly into the MG0007 trial.

Patients in the pivotal study were 52 years of age (standard deviation [SD] = 16 years) on average, and the majority (61%) were female. Most patients were MGFA class IIa or IIb (39%) or class IIIa or IIIb (57%) at baseline. The majority (83%) of patients were AChR antibody positive and 9% were MuSK antibody positive at baseline.

Efficacy Results

The outcomes determined to be of importance based on consultation with a clinical expert and input received from patient and clinician groups and public drug plans are discussed herein.

Myasthenia Gravis Activities of Daily Living

The primary end point was change from baseline to day 43 in MG-ADL score (range = 0 to 24, with higher scores indicating more severe symptoms). From a baseline mean MG-ADL score of 8.4 (SD = 3.8) in the rozanolixizumab group and 8.4 (SD = 3.4) in the placebo group, the LS mean change from baseline was −3.22 (SD = 0.480) and −0.65 (SD = 0.363). The LS mean difference in change from baseline was −2.586 (95% CI, −4.091 to −1.249; P < 0.001), favouring rozanolixizumab. The results from the sensitivity analysis were consistent with those from the main analysis. Overall, compared with placebo, treatment with rozanolixizumab resulted in consistently greater decreases from baseline in MG-ADL score at day 43 across all subgroups, except for the subgroups with a low number of patients. Forty-five patients (68.2%) in the rozanolixizumab group had an MG-ADL response with at least a 2-point improvement at day 43 versus 19 patients (28.4%) in the placebo group, with a between-group difference of 39.8% (95% CI, 24.2 to 55.4).

The sponsor also reported data from a post hoc subgroup analysis for the [redacted] patients in the rozanolixizumab group and [redacted] patients in the placebo group who had 2 or more prior myasthenia gravis–specific therapies. From a mean baseline score of [redacted] in the rozanolixizumab group and [redacted] in the placebo group, the LS mean change from baseline to day 43 in MG-ADL scores was [redacted] for rozanolixizumab and [redacted] for placebo, with a LS mean difference between groups of [redacted]. In this subgroup, the number of responders with at least a 2-point improvement in MG-ADL score at day 43 was [redacted] and [redacted] in the rozanolixizumab and placebo groups, respectively.

QMG Score

The QMG score ranges from 0 to 39, with higher scores indicating more severe impairment. From a mean baseline of 15.4 (SD = 3.7) in the rozanolixizumab group and 15.8 (SD = 3.5) in placebo, the LS mean change from baseline was –5.598 (standard error [SE] = 0.679) with rozanolixizumab and –1.915 (SE = 0.685) with placebo. The LS mean between-group difference in change from baseline was –3.483 (95% CI, 5.614 to –1.584; P < 0.001), favouring rozanolixizumab. Results for various sensitivity analyses were consistent with the overall analysis of change from baseline to day 43 in QMG score.

The sponsor also reported subgroup analyses of QMG scores by baseline antibody status for the 59 patients in the rozanolixizumab group and 51 patients in the placebo group who were AChR antibody positive and

the 4 patients in the rozanolixizumab group and 7 patients in the placebo group who were MuSK antibody positive. In the AChR antibody-positive subgroup, the LS mean change from baseline to day 43 was –4.660 (SE = 1.605) with rozanolixizumab and –1.189 (SE = 1.575) for an LS mean difference between groups of –3.471 (97.5% CI; –5.433 to –1.510). In the MuSK antibody-positive subgroup, the LS mean change from baseline to day 43 was –10.276 (SE = 3.490) with rozanolixizumab and –2.662 (SE = 2.710) with placebo, for an LS mean difference between groups of –7.614 (97.5% CI, –16.291 to 1.062).

The sponsor also reported data from a post hoc subgroup analysis of the [redacted] patients in the rozanolixizumab group and [redacted] patients in the placebo group who had 2 or more prior myasthenia gravis–specific therapies. From a mean baseline score of [redacted] in the rozanolixizumab group and [redacted] in the placebo group, the mean change from baseline to day 43 in QMG scores with rozanolixizumab was [redacted] and for placebo [redacted] for an LS mean difference between groups of [redacted].

Revised 15-Item Myasthenia Gravis Quality of Life Questionnaire

The MG-QoL15r ranges from 0 to 30, with higher scores indicating a more severe impact of disease on HRQoL. From a mean baseline of 15.7 (SD = 7.7) in the rozanolixizumab group and 15.0 (SD = 6.4) with placebo, the LS mean change from baseline was –4.0 (SE = 6.1) with rozanolixizumab compared to –1.3 (SE = 4.3) with placebo. The LS mean between-group difference in change from baseline was –2.245 (95% CI, –4.096 to –0.394), favouring rozanolixizumab.

Myasthenia Gravis Composite Score

The *Myasthenia Gravis Composite* (MG-C) score ranges from 0 to 50, with higher scores indicating more severe impairment. The LS mean change from baseline was –5.23 (SE = 0.828) with rozanolixizumab and –1.47 (SE = 0.722) with placebo. The LS mean between-group difference in change from baseline was –3.901 (95% CI, –6.634 to –1.245; P < 0.001), favouring rozanolixizumab. The results of the sensitivity analyses were consistent with the overall analysis.

Harms Results

Adverse Events

Overall, the number of patients who experienced adverse events (AEs) in the study was 52 (81.3%) with rozanolixizumab and 45 (67.2%) with placebo. The most common AEs (10% or more in either group) for rozanolixizumab versus placebo, respectively, were diarrhea (25.0 versus 13.4%), pyrexia (12.5 versus 1.5%), and headache (45.3 versus 19.4%).

Serious Adverse Events

A comparable number of study patients in the rozanolixizumab and placebo groups reported serious AEs (5; 7.8%) and placebo (6; 9.0%). The only serious AEs reported in more than 1 study patient per treatment group was myasthenia gravis crisis, which occurred in no patients in the rozanolixizumab group and 2 (3.0%) in the placebo group.

Withdrawals Due to Adverse Events

The incidence of AEs leading to permanent discontinuation of the study drug was similar in the rozanolixizumab 7mg/kg group (2; 3.1%) and the placebo group (2; 3.0%).

Mortality

There were no deaths reported in the study.

Notable Harms

Infection was identified as a notable harm for this review, and “infections and infestations” occurred in 10 patients (15.6%) in the rozanolixizumab group and 13 patients (19.4%) in the placebo group.

Critical Appraisal

- The MyCarinG trial was relatively well-conducted with adequate allocation concealment and steps taken to maintain blinding. With the exception of the MG-ADL responders and MG-QoL15r outcomes, all efficacy outcomes were multiplicity controlled, reducing the risk of type I error. Although there were some imbalances in baseline characteristics between groups, the clinical expert did not believe these were of clinical relevance.
- With respect to external validity, the clinical expert believed that the population in the MyCarinG trial was generalizable to the population of patients for whom they would expect to use the drug in Canada. Although the sponsor is seeking reimbursement for patients whose symptoms persist despite treatment with AChEIs, corticosteroids, and/or NSISTs, the pivotal trial did not restrict enrolment based on prior treatment. However, most patients (96%) had received at least 1 prior gMG-specific therapy before the trial. The sponsor provided data from a post hoc subgroup analysis of patients who had received 2 prior therapies; however, limited conclusions can be drawn from these data because of the inherent limitations in post hoc analyses.

GRADE Summary of Findings and Certainty of the Evidence

For pivotal studies and randomized controlled trials identified in the sponsor’s systematic review, GRADE was used to assess the certainty of the evidence for outcomes considered most relevant to inform CDA-AMC expert committee deliberations, and a final certainty rating was determined as outlined by the GRADE Working Group.

Following the GRADE approach, evidence from randomized controlled trials started as high-certainty evidence and could be rated down for concerns related to study limitations (which refers to internal validity or risk of bias), inconsistency across studies, indirectness, imprecision of effects, and publication bias.

When possible, certainty was rated in the context of the presence of an important (nontrivial) treatment effect; if this was not possible, certainty was rated in the context of the presence of any treatment effect (i.e., the clinical importance is unclear). In all cases, the target of the certainty of evidence assessment was based on the point estimate and where it was located relative to the threshold for a clinically important effect (when a threshold was available) or to the null. The target of the certainty of evidence assessment was the presence or absence of an important effect based on thresholds identified in the literature and supported by the clinical expert for the change from baseline to day 43 in MG-ADL and QMG scores; presence or absence

of an important effect based on thresholds informed by the clinical expert consulted for this review for MG-ADL responders; and the presence or absence of any [non-null] effect for the change from baseline to day 43 in MG-QoL15r scores and for notable harms (infections and infestations).

The selection of outcomes for GRADE assessment was based on the sponsor's Summary of Clinical Evidence, consultation with a clinical expert, and the input received from patient and clinician groups and public drug plans. The following list of outcomes was finalized in consultation with expert committee members:

- MG-ADL score (change from baseline to day 43; responders [patients with at least a 2-point improvement from baseline in MG-ADL score])
- QMG score (change from baseline to day 43)
- MG-QoL15r score (change from baseline to day 43)
- notable harms: infections and infestations.

Table 3: Summary of Findings for Rozanolixizumab Versus Placebo for Patients With gMG

Outcome and follow-up	Patients (studies), N	Relative effect (95% CI)	Absolute effects			Certainty	What happens
			Placebo	Rozanolixizumab (SE)	Difference (95% CI)		
MG-ADL							
Change from baseline (scale from 0 to 24, higher scores indicate more severe symptoms) Follow-up: day 43	127 (1 RCT)	NA	−0.65	−3.22 (0.480)	−2.586 (−4.091 to −1.249)	Moderate[a]	Rozanolixizumab likely results in a clinically important improvement in MG-ADL scores compared to placebo.
Patients achieving response, n (%) (response defined as at least a 2-point improvement in MG-ADL) Follow-up: day 43	133 (1 RCT)	OR = 5.765 (2.100 to 14.882)	28 per 100	68 per 100	39.8 more per 100 (24.2 to 55.4 per 100 more)	Moderate[b]	Rozanolixizumab likely results in a clinically important increase in the number of MG-ADL responders compared to placebo.
MG-QoL15r							
LS mean change from baseline to day 43 in MG-QoL15r score	133 (1 RCT)	NA	−2.1	−4.4 (0.9)	−2.245 (−4.365 to −0.125)	Moderate[c]	Rozanolixizumab likely results in an improvement in MG-QoL15r scores compared to

Outcome and follow-up	Patients (studies), N	Relative effect (95% CI)	Absolute effects			Certainty	What happens
			Placebo	Rozanolixizumab (SE)	Difference (95% CI)		
(scale from 0 to 30, with higher scores indicating more severe impact of disease on HRQoL)							placebo. The clinical significance of this improvement is not known.
QMG							
Mean change from baseline to day 43 in QMG score (scale from 0 to 39 with higher scores indicating more severe impairment)	127 (1 RCT)	NA	−0.89	−4.22 (0.574)	−3.483 (−5.614 to −1.584)	Moderate[d]	Rozanolixizumab likely results in a clinically important improvement in QMG scores compared to placebo.
Harms							
Infections and infestations Follow-up: to 8 weeks after the final dose	133 (1 RCT)	NA	19 per 100	16 per 100 (NR)	4 fewer per 100 (17 fewer to 9 more per 100)	Low[e]	Rozanolixizumab may result in little to no difference in the risk of infection compared to placebo.

CI = confidence interval; gMG = generalized myasthenia gravis; HRQoL = health-related quality of life; LS = least squares; MG-ADL = Myasthenia Gravis Activities of Daily Living; MG-QoL15r = Revised Myasthenia Gravis Quality of Life 15 Item; MID = minimal important difference; NA = not applicable; NR = not reported; OR = odds ratio; QMG = Quantitative Myasthenia Gravis; RCT = randomized controlled trial; SE = standard error.

Notes: Study limitations (which refer to internal validity or risk of bias), inconsistency across studies, indirectness, imprecision of effects, and publication bias were considered when assessing the certainty of the evidence. All serious concerns in these domains that led to the rating down of the level of certainty are documented in the table footnotes.

Results for the MG-ADL response and change from baseline in MG-QoL15r were not adjusted for multiplicity and should be considered as supportive evidence.

[a]Rated down 1 level for serious imprecision; the point estimate suggests a clinically important benefit, while the upper bound of the 95% CI crosses the MID found in the literature. The literature-based MID was estimated for within-group effects; input from the clinical expert consulted by the review team considered that a between-group difference smaller than 2 points was not likely to be clinically important.

[b]Rated down 1 level for serious imprecision; there is a small sample size and number of events, raising concern for prognostic imbalance and the potential that the effect may be overestimated.

[c]Rated down 1 level for serious imprecision; the null was used as the threshold and the point estimate suggests benefit, but the upper bound of the 95% CI includes a value that most would agree is unimportant.

[d]Rated down 1 level for serious imprecision; the point estimate suggests a clinically important benefit, while the upper bound of the 95% CI crossed the MID found in the literature.

[e]Rated down 2 levels for very serious imprecision; the points estimate suggests little to no difference, but the 95% CI includes a potential for both benefit and harm.

Sources: Details included in the table are from the sponsor's Summary of Clinical Evidence and from the sponsor's response to a request for information.

Long-Term Extension Studies

Description of Studies

Results from 2 open-label extension studies, MG0004 (NCT04124965; data cut-off date of September 1, 2021) and MG0007 (NCT04650854; data cut-off date of July 8, 2022) were reviewed. MG0007 was

approximately ongoing for 1.5 years at the date of data cut-off for interim analysis. Results for the 7mg/kg group are only summarized to align with the reimbursement request.

The MG0004 Study

MG0004 was a phase III, multicentre, randomized, open-label extension study of MyCarinG (MG0003) to investigate the long-term safety, tolerability, and efficacy of rozanolixizumab (weekly dosing regimen for 52 weeks) in adults with gMG who were experiencing moderate to severe symptoms and under consideration for IVIg or PLEX therapy, indicating they needed additional therapeutic intervention. Patients were randomized to 2 different treatment arms in a 1:1 ratio to receive subcutaneous rozanolixizumab either at 7 mg/kg or 10 mg/kg. The primary safety end points were the occurrence of treatment-emergent adverse event (TEAE) and those leading to permanent withdrawal of the study medication. Other safety end points included occurrence of AEs of special monitoring (potential Hy's law, defined as AST or ALT > 3x upper limit normal and TBL > 2x upper limit normal and ALP < 2x upper limit normal, with no other explanation for the biochemical abnormality), vital signs, electrocardiogram assessments, and clinical laboratory findings. Patients who experienced disease worsening (e.g., an increase of 2 points on the MG-ADL scale or 3 points on the QMG scale between 2 consecutive visits) were considered for rescue therapy, and if the patient received IVIg or PLEX during the study, treatment with rozanolixizumab was discontinued or paused for a minimum of 2 weeks but continued with visits per the schedule of assessments, after which the patient continued to receive rozanolixizumab at the discretion of the investigator. Following the temporary discontinuation of the study medication, patients restarted at the same dose of rozanolixizumab as they had received previously. Patients at a dose level of 7 mg/kg rozanolixizumab could have been restarted at 10 mg/kg rozanolixizumab at the discretion of the investigator.

Of the 71 patients enrolled, 35 patients were randomized to the 7 mg/kg rozanolixizumab group. The mean age was 50.6 (SD = 14.2) years. More than half of all patients were female (54.3%). Most patients permanently discontinued the study during the COVID-19 pandemic (29; 82.9%). One patient (2.9%) before the COVID-19 pandemic and 2 patients (5.7%) during the COVID-19 pandemic permanently discontinued the study due to a TEAE. Most of the patients permanently discontinued the study to transition to the MG0007 study (25 [71.4%] in the 7 mg/kg group).

The mean duration of the study medication by first dose received was 22.93 weeks. There was no treatment nonadherence or incorrect treatment or dosing. Beyond 18 weeks, the numbers of patients steadily decreased; this decrease was mainly due to the 53 patients (74.6%) who discontinued the study to transition to the MG0007 study.

The MG0007 Study

MG0007 was a phase III, two-arm, randomized, open-label extension study of the MycarinG study and replaced the MG0004 study to evaluate the long-term safety, tolerability, and efficacy of repeated 6-week treatment cycles of rozanolixizumab based on myasthenia gravis worsening in adults with gMG. Worsening of disease was defined as the worsening of gMG symptoms (e.g., an increase of 2 points on the MG-ADL scale or 3 points on the QMG scale) between 2 consecutive visits. Patients were randomized to receive an initial fixed 6-week treatment cycle of rozanolixizumab either at 7 mg/kg or 10 mg/kg once weekly, followed

by an observation period that began after the last dose of that treatment cycle. Eligible patients from the MG0004 study who completed at least 6 scheduled visits in the treatment period could move directly into the observation period in the MG0007 study. In the case of worsening myasthenia gravis symptoms, patients underwent another 6 weeks of treatment followed by an observation period. Rescue therapy was given per conventional therapy and at the discretion of the investigator. Patients who continued to experience moderate to severe symptoms despite treatment with rozanolixizumab may have been treated with the following as rescue therapy: IVIg, SCIg, PLEX or plasmapheresis, or IV corticosteroids (at a higher dose than previous oral dose). Patients who were treated with rescue therapy were withdrawn from the study.

Of the 157 patients enrolled, 79 received 7 mg/kg rozanolixizumab. The mean age was 52.7 years (SD = 15.7). More than half were female (55.7%). A total of 16 patients (20.3%) treated with rozanolixizumab permanently discontinued the study during the COVID-19 pandemic; the most common reason for study discontinuation was a TEAE (8; 10.1%), followed by “withdrawal by patient” (5; 6.3%).

Of the 79 patients who received 7 mg/kg rozanolixizumab in cycle 1, 18 patients (22.8%) only had 1 treatment cycle, and 43 patients (54.4%) continued to receive rozanolixizumab 7 mg/kg in subsequent cycles. Sixteen patients (20.5%) switched to rozanolixizumab 7 mg/kg in subsequent cycles (5 switched at cycle 2, 3 at cycle 4, 2 at cycle 5, 2 at cycle 7, 3 switched at cycle 2 and switched back at cycle 3, and 1 switched at cycle 3 and switched back at cycle 4). Five patients (6.3%) in the rozanolixizumab 7 mg/kg group received rescue medication (4 received immunoglobulins [1 of whom continued treatment with efgartigimod alfa] and 1 received methylprednisolone sodium succinate); 2 patients (2.5%) required a rescue procedure (i.e., PLEX).

Efficacy Results

Change in MG-ADL

The MG0004 Study

Changes from baseline in MG-ADL score showed a stable trend up to week 33; study participant numbers steadily declined over time. The maximum mean reduction from baseline up to week 33 was −3.1 (week 13; n = 30). When assessed by autoantibodies subgroup, a consistent reduction in MG-ADL scores was observed from baseline in patients with MuSK antibody-positive disease up to week 25. The greatest reduction (improvement) from baseline was −2.4 points, which was observed at week 5 (n = 5). The lowest reductions (improvement) from baseline were −1.6 points, observed at week 9 (n = 5) and sustained at week 13 (n = 5), and −1.3 points at week 21 (n = 3). For AChR antibody-positive disease, the greatest reduction (improvement) from baseline up to week 29 was −3.4 points (n = 25; week 13). Between weeks 29 and 52, there was a consistent improvement in MG-ADL scores from baseline ranging from −4.2 points (week 37; n = 5) to −2.0 points (week 49; n = 3).

The MG0007 Study

Baseline MG-ADL scores and changes from baseline to day 43 in MG-ADL scores for the 6 treatment cycles were summarized. Baseline values were defined as the last available value before or on the same date of first administration of the medication at each cycle (i.e., baseline [day 1]) value for that cycle. The number of

participants declined across cycles from 79 at cycle 1 to 11 at cycle 6. Within each cycle, the mean change from baseline ranged from −3.0 to −4.3 points, depending on the cycle. When assessed by antibodies subgroup, a consistent reduction (improvement) in MG-ADL scores was observed from baseline at day 43, with repeated cyclic treatments for both patients who are MuSK antibody positive (n = 8; cycles 1 to 4) and AChR antibody positive (n = 62; cycles 1 to 6); however, sample sizes steadily declined within each cycle. For patients who had MuSK antibody-positive disease, the mean change from baseline ranged from −6.5 points (cycle 1; n = 8) to −3.8 points (cycle 3; n = 3). For patients who had AChR antibody-positive disease, the mean change from baseline ranged from −4.0 points (cycle 6; n = 6) to −2.8 points (cycle 2; n = 41).

Change in QMG

The MG0004 Study

Changes from baseline showed a stable trend over time to week 52; study participant numbers steadily declined over time. The maximum mean reduction from baseline up to week 29 for the AChR antibody-positive subgroup was −5.4 points (week 29; n = 11) and −6.0 points for the MuSK antibody-positive subgroup (week 25; n = 3). The sample sizes in both groups steadily declined over time (n ≤ 10).

The MG0007 Study

Baseline QMG scores and changes from baseline at day 43 in QMG scores for the 6 treatment cycles were summarized. The sample size declined from 79 at cycle 1 to 11 at cycle 6. The mean change from baseline ranged from −4.1 to −6.4 across cycles. A consistent improvement in QMG scores was observed with repeated cyclic treatment from baseline at day 43 by participants who were MuSK antibody positive (from cycles 1 to 4) and AChR antibody positive (from cycles 1 to 5). However, sample sizes declined over time with 10 or fewer patients in any subgroup.

Change in MG-C

The MG0004 Study

Changes from baseline showed a consistent trend to week 52; study participant numbers declined steadily over time. A consistent change from baseline up to week 25 and 29 was observed when assessed by MuSK antibody-positive and AChR antibody-positive disease, respectively. The maximum mean reduction was −7.0 points (week 25; n = 15) from baseline up to week 29 for the AChR antibody-positive subgroup (week 25; n = 15) and −3.6 points (week 5; n = 5) from baseline up to week 25 for the MuSK antibody-positive subgroup. The sample sizes declined over time across the subgroups.

The MG0007 Study

Baseline MG-C scores and changes from baseline to day 43 in MG-C scores for the 6 treatment cycles were summarized. The sample size declined over time, from 79 at cycle 1 to 11 at cycle 4. The mean change from baseline ranged from −6.1 to −9.6 across cycles. A consistent improvement in MG-C scores was observed from baseline at day 43, with repeated cyclic treatment when assessed by antibody subgroup.

Change in MG-QoL15r

The MG0004 Study

Baseline QMG scores and changes from baseline to day 43 in QMG scores for the 6 treatment cycles were summarized. The mean MG-QoL15r score at baseline was 14.4 points. An improvement in HRQoL was observed. The maximum mean reduction from baseline up to week 33 was –5.1 points (week 21; n = 20).

The MG0007 Study

Quality of life for patients with myasthenia gravis was an exploratory outcome. The sample size declined over time, from 79 at cycle 1 to 11 at cycle 4. The mean change from baseline ranged from −2.2 to −6.1 across cycles.

Harms Results

Adverse Events

The MG0004 Study

Seventy-six percent of the patients in the 7mg/kg group experienced any TEAE. The most common AEs (20% of patients or more) were nervous system disorders (36.0%), gastrointestinal disorders (26.0%), infections and infestations (26.0%), investigations (22.0%), and musculoskeletal and connective tissue disorders (20.0%).

The MG0007 Study

Sixty-eight patients (69.4%) in the 7mg/kg group experienced any TEAE. Nervous system disorders (36.7%), infections and infestations (34.7%), gastrointestinal (24.5%), and general site administration issues (27.6%) were the most reported.

Serious Adverse Events

The MG0004 Study

Serious TEAEs were reported in 7 patients (14.0%). The only serious AE occurring in more than 1 patient was nervous system disorders (n = 3; 6.0%).

The MG0007 Study

Serious TEAEs were reported in 9 patients (9.2%). The serious AEs occurring in more than 1 patient were nervous system disorders (n = 3; 3.1%) and infections and infestations (n = 2; 2.0%).

Withdrawals Due to Adverse Events

The MG0004 Study

A total of 4 patients (8.0%) experienced TEAEs that led them to discontinue the study. Three of these patients (75.0%) experienced myasthenia gravis, while 1 patient (25.0%) experienced congestive cardiac failure. In patients who temporarily discontinued rozanolixizumab (n = 12; 24.0%), the main reasons were decreased blood IgG and hypogammaglobulinemia.

The MG0007 Study

A total of 6 patients (6.1%) permanently discontinued the study. Two patients (33.3%) had TEAEs with preferred-term myasthenia gravis, while 1 patient each reported TEAEs of adrenal disorder, pneumonia, tendon disorder, tenosynovitis, retroperitoneal neoplasm, thymoma, and subacute cutaneous lupus erythematosus. In patients who temporarily discontinued rozanolixizumab, the main reasons were decreased blood IgG, hypogammaglobulinemia, and COVID-19.

Mortality

The MG0004 Study

There were no AEs leading to death in this study.

The MG0007 Study

One death was reported due to a fatal TEAE (pneumonia).

Critical Appraisal

Patients who were enrolled in the pivotal trial (MyCarinG), were the ones entering the open-label extension studies (MG0004 and MG0007). The MG0004 and MG0007 studies were limited by their noncomparative open-label study designs. A lack of a control group precludes causal statements about benefit and harm compared with any comparator. The open-label and nonblinded nature of the study may increase the risk of bias in determining the magnitude of the subjective safety outcomes and all efficacy end points because these were subjective (e.g., MG-ADL, QMG, MG-QoL, and MG-C scores) as the lack of blinding may impact patients' expectations of the treatment. The direction and magnitude of these potential biases remains unclear. Concomitant treatments were intended to remain stable within treatment cycles but could be adjusted between cycles. These additional treatments could confound the relationship between rozanolixizumab and the efficacy and harm outcomes, but the degree of impact on the results cannot be predicted. Efficacy results were assessed by myasthenia gravis–specific antibody subgroups; however, these results should be interpreted with caution due to the small sample sizes (especially in the MuSK antibody-positive subgroup). Baseline MG-ADL, QMG, and MG-C scores indicated higher disease severity of patients entering the MG0007 study, potentially suggesting that there is a selection bias. Patients in the MG0007 study were allowed to switch between the 7mg/kg and 10mg/kg groups, based on the investigator's discretion before the start of each subsequent cycle of treatment. Therefore, it is difficult to differentiate the effect of the 7mg/kg dose (which is the focus of the reimbursement request) from that of the 10mg/kg dose on the efficacy outcomes. There is a high risk of attrition bias as the number of patients contributing to the analyses declined steadily over time.

Indirect Comparisons

The submission included an NMA and a MAIC. The comparator treatments included in the NMAs were zilucoplan, efgartigimod alfa, eculizumab, IVIg, PLEX, rituximab, and ravulizumab; the results from the comparisons with efgartigimod, eculizumab, IVIg, PLEX, and rituximab were included in the review. The comparator treatments included in the MAIC submission were efgartigimod, IVIg, and PLEX.

Description of Studies

The study selection methods were the same for the NMA and the MAIC. Briefly, a clinical systematic literature review based on studies identified from database searches from inception to May 1, 2023, was performed to inform both the NMA and MAIC. Results from the systematic literature review were then filtered by distinct population, intervention, comparison, outcomes, and study (PICOS) for the NMA or MAIC as part of the feasibility assessment.

Network Meta-Analysis Design

Homogeneity in the NMA network was assessed by visual inspection of the distribution of baseline characteristics for the trials comprising the network, as well as the time point at which study outcomes were reported. Plot digitization at 12 weeks was carried out to obtain data points from published figures. The NMAs were performed using a Bayesian approach with noninformative priors and fixed-effect models used. Change from baseline outcomes were assessed at the 12-week (± 2) time point using only phase III studies in the primary analysis, and the results were presented with estimates for treatment effects of each intervention relative to placebo as the reference treatment. Relative treatment effects (MG-ADL responders, defined as improvement of 3 points or more in score) were presented as odds ratios and continuous treatment effects (change in baseline in MG-ADL score) were reported as mean differences. An analysis was conducted in the overall population and refractory population (defined according to the RAISE trial). The sensitivity analyses were conducted by assessing the inclusion of different time points of reporting outcomes, as well as differences in study design (i.e., phase II versus phase III studies).

Matching-Adjusted Indirect Comparison Design

Before carrying out a feasibility assessment, the relative importance of all the baseline characteristics based on their impact on the outcomes was ranked by 2 clinical experts. The feasibility assessment consisted of comparing the relevant trials for each comparison in terms of their baseline characteristics and inclusion and/or exclusion criteria. In cases of differences in the inclusion and/or exclusion criteria, a subset of patients from the rozanolixizumab trial (MycarinG) were used to match the comparator trial. If feasibility was confirmed, the 2 studies were matched using a propensity score weighting method. A comparison of all potential analysis scenarios was presented to knowledge opinion leaders, and the base case was selected based on specific criteria. The comparisons of rozanolixizumab versus efgartigimod (ADAPT trial) were modelled using an anchored MAIC, and the results for rozanolixizumab versus IVIg (Barth et al., 2011) were modelled using an unanchored MAIC. Continuous outcomes (change from baseline in MG-ADL, MGC, MG-QoL, and QMG scores) were modelling using linear regression, with results presented as mean differences. Binary outcomes (2- or 3-point improvements in MG-ADL or QMG scores) were modelled using logistic regression, with the results presented as odds ratios.

Efficacy Results

Network Meta-Analysis

Heterogeneity was observed throughout the NMA network in disease severity, treatment history (where reported), trial eligibility criteria, placebo response, the definition of MG-ADL responders, the timing of end point evaluation, study designs, and baseline characteristics. The majority of patients enrolled in the trials

were AChR antibody-receptor positive, female, and had class II to IV gMG. The duration of disease ranged from 6.9 to 10.3 years. MuSK antibody status was reported in 2 trials (MycarinG [12% of patients] and ADAPT [4% of patients]). Study duration ranged from 12 to 48 weeks. The study network for the primary analysis showed that all included studies compared treatments to placebo, and each node in the network consisted of a single study.

The NMA primary analysis results for rozanolixizumab 7mg/kg indicated [redacted] for treatment and comparators with [redacted]. Rozanolixizumab 7mg/kg [redacted] placebo for MG-ADL responders.

Matching-Adjusted Indirect Comparison

There were some differences identified between the MycarinG (rozanolixizumab) trial and the ADAPT (efgartigimod) trial. Most notably, there were differences in the minimum MG-ADL scores required for enrolment, and that ADAPT required patients to be receiving stable doses of gMG therapy while the MycarinG trial required that patients were being considered for additional therapy. There were also differences noted between the inclusion criteria for the MycarinG trial and the inclusion criteria for the Barth et al. (2011) study (IVIg), most notably that the Barth et al. study was an active-controlled trial that did not require a specific MGFA class diagnosis or MG-ADL baseline score for enrolment, and the MycarinG trial was placebo controlled, and required weight and MG-ADL thresholds and AChR or MuSK antibody-positive status.

The results of the primary analysis for rozanolixizumab versus efgartigimod indicated that at 6 weeks, the results [redacted]. The [redacted] for the outcomes of 2- or 3-point improvements in MG-ADL score at 4 weeks, or 3-point improvements in QMG score at 4 weeks.

The results from the primary analysis for rozanolixizumab versus IVIg indicated that at 2 and 4 [redacted]; the results for QMG responders [redacted].

Harms Results

Harms outcomes were not analyzed as part of the indirect comparisons.

Critical Appraisal

Some limitations of the systematic literature review include the fact that the search was only run up until 2023 and therefore may miss more recent publications on comparators. In addition, the quality assessment was carried out at the level of the trial, which might not capture the fact that risks of some domains of bias (e.g., attrition bias) can vary by outcome. According to the clinical expert, the NMA included relevant comparators to the Canadian context and the outcome was of interest to clinicians. However, data from some relevant comparators, such as IVIg and rituximab, were not available in the primary analysis of the NMA, and additional limitations in the sensitivity analyses do not allow conclusions to be drawn regarding

these comparators. Likewise, the results from all comparators were not available in the submission for the MAIC.

There are important sources of heterogeneity in the NMA network that have clinical relevance and impact the certainty of the results. While all trials enrolled patients with class II to IV gMG, there were differences between the trials in the refractory status of the enrolled patients who were not accounted for in the analyses. For example, the trials for eculizumab and rituximab generally enrolled patients who were refractory and those who were newly diagnosed, respectively; the trial for zilucoplan included patients who were refractory; and the trial for rozanolixizumab required patients to be under consideration for additional therapy. In addition, MuSK antibody status was only reported in 2 of the 6 included trials, and the trials in the network used MG-ADL score thresholds ranging from 3 to 6 points. Sensitivity analyses were conducted, but they do not address the heterogeneity concerns. Taken together, these could represent clinically meaningful differences in patient disease status and affect confidence that the transitivity assumption underpinning the NMA was met.

With regards to the MAICs, while the clinical expert consulted for the review noted that the list of known prognostic and/or effect modifying variables used for weighting in both MAICs was comprehensive, not all baseline characteristics were reported before and after weighting; therefore, it is not known whether there were other potential sources of heterogeneity in the trial populations remaining after weighting. Weighting controlled for the differences in the reported baseline characteristics for the anchored MAIC comparing rozanolixizumab to efgartigimod. However, the effective sample size was considerably smaller than the sample sizes of the 2 trials prematching, suggesting that a small proportion of the patient population may be driving the results, and the findings could be unstable. This suggests that there remains uncertainty in the results for the comparison of rozanolixizumab to efgartigimod. The comparison of rozanolixizumab to IVIg was carried out using an unanchored MAIC, which relied on the assumption that all possible prognostic factors and treatment effect modifiers are controlled for, an assumption that is largely considered impossible to meet. The scenario used in the current MAIC did not include all baseline characteristics in the weighting process, resulting in a high risk of residual confounding. Confidence in the results is therefore highly uncertain. Furthermore, there are important study differences that were not controlled for by the weighting process, such as the lack of placebo comparator in the Barth et al. trial, the timing of the primary end point, and the proportion of patients with MuSK antibody-positive status. Taken as a whole, conclusions on the efficacy of rozanolixizumab versus IVIg are challenging to draw.

The indirect evidence as a whole is also subject to some limitations impacting generalizability. First, the study population of the MycarinG trial included patients who were AChR antibody positive or MuSK antibody positive. To improve similarity to the efgartigimod trial population, only the patients who were MuSK antibody negative, AChR antibody positive from the MyCarinG trial were included in the unanchored MAIC for rozanolixizumab versus efgartigimod (i.e., a subset of the full trial population). This adversely impacts the generalizability of those results to the MuSK antibody-positive gMG population. Furthermore, the results of the MAIC were assessed as early as 2 to 6 weeks, which the clinical expert noted is early to assess treatment response and might not capture maximal treatment response. Lastly, long-term comparative efficacy and harms information is unavailable.

Economic Evidence

Cost and Cost-Effectiveness

Table 4: Summary of Economic Evaluation

Component	Description
Type of economic evaluation	Cost-utility analysis Markov model
Target population	Adults with AChR antibody-positive or MuSK antibody-positive gMG for whom symptoms persist despite conventional therapy with AChEIs, corticosteroids, and/or NSISTs.
Treatment	Rozanolixizumab (Rystiggo) plus CT
Dose regimen	Dose weekly for 6 weeks. Subsequent treatment cycles are based on clinical evaluation and may vary by patient. Body weight ≥ 35 to < 50 kg: 280 mg Body weight ≥ 50 kg to < 70: 420 mg Body weight ≥ 70 to < 100 kg: 560 mg Body weight ≥ 100 kg: 840 mg
Submitted price	Rozanolixizumab 280 mg/2 mL single-dose vial: $12,260
Submitted treatment cost	$436,956 per year, assuming a patient weighing ≥ 70 and < 100 kg, and 2.97 treatment cycles per year
Comparators	• CT[a] • Eculizumab plus CT • Efgartigimod alfa plus CT • IVIg or SCIg plus CT • PLEX plus CT • Rituximab plus CT
Perspective	Canadian publicly funded health care payer
Outcomes	QALYs, LYs
Time horizon	Lifetime (52.5 years)
Key data sources	• The sponsor-submitted NMA informed the comparative efficacy of rozanolixizumab, conventional therapy, eculizumab, and efgartigimod alpha; individual trials informed the comparative efficacy of chronic IVIg and SCIg, chronic plasma exchange (Barth et al., 2011), and rituximab (Nowak et al., 2021)
Submitted results	• Rozanolixizumab plus CT was associated with an ICER of $2,676,135 per QALY gained (incremental cost = $21,998; incremental QALYs = 0.01) compared to efgartigimod alfa plus CT. • CT alone and rituximab plus CT were also on the efficacy frontier but were less costly and less effective treatments.
Key limitations	• The modelled population reflects the MycarinG trial, which is narrower than the proposed Health Canada indication of adults with gMG. The trial excluded patients with MGFA class I, IVb, and V gMG; those who did not meet specific disease severity score cutoffs; and those who did not show persistent symptoms despite CT. • Due to the lack of direct clinical evidence, limitations with the sponsor-submitted NMA (e.g., imprecision of estimates, heterogeneity in the patient and study characteristics), and the

Component	Description
	sponsor's use of naive comparisons to inform the economic evaluation, conclusions regarding the comparative efficacy and safety of rozanolixizumab relative to its comparators largely cannot be drawn. • The relevance of some comparators varies by serotype as some are currently only used for AChR antibody-positive gMG (e.g., efgartigimod alfa), while others are primarily used for MuSK antibody-positive gMG (i.e., rituximab). • The sponsor assumed maintenance of clinical effects beyond treatment discontinuation, which is not appropriate as this assumption underestimated treatment costs and overestimated benefits. • The sponsor-assumed reductions in corticosteroid use based on treatment response were not supported by the available clinical data. This likely overestimated the extent to which corticosteroid use may be reduced and overestimated the cost and HRQoL associated with reductions in use. • The model lacked transparency and reliability, limiting the ability of CDA-AMC to properly validate results within the time frame of this review.
CDA-AMC reanalysis results	• Given the clinical limitations identified with the sponsor's economic submission, including uncertainty in comparative treatment effect, CDA-AMC was unable to derive a more reliable estimate of the cost-effectiveness of rozanolixizumab as an add-on therapy to CT. • While the sponsor's base case suggested differences in treatment benefits between rozanolixizumab and other add-on therapies used for the treatment of adults with AChR antibody-positive or MuSK antibody-positive gMG whose symptoms persist despite CT, there is no robust evidence to support this claim. If the sponsor's claim of added benefit (0.008 QALYs, 3 quality-adjusted days) is realized, the probability that rozanolixizumab is cost-effective at a willingness-to-pay threshold of $50,000 per QALY gained is 0%. • CDA-AMC undertook several scenarios that suggested that the ICER for rozanolixizumab is likely higher than estimated by the sponsor due to underestimation of drug acquisition costs. • A price reduction of at least 87.5% (from $12,260 to $1,533 per 280 mg vial) is required for rozanolixizumab to achieve an ICER of $50,000 per QALY gained.

AChEI = acetylcholinesterase inhibitor; CDA-AMC = Canada's Drug Agency; CT = conventional therapy; gMG = generalized myasthenia gravis; HRQoL = health-related quality of life; ICER = incremental cost-effectiveness ratio; IVIg = IV immunoglobulin; LY = life-year; NMA = network meta-analysis; NSIST = nonsteroidal immunosuppressive therapy; PLEX = plasma exchange; QALY = quality-adjusted life-year; SCIg = subcutaneous immunoglobulin.

[a]Conventional therapy is defined as consisting of a 12.5% mix of each of the following: prednisone, azathioprine, mycophenolate mofetil, cyclosporine, tacrolimus, methotrexate, pyridostigmine, and cyclophosphamide.

Budget Impact

CDA-AMC identified the following key limitations with the sponsor's analysis:

- Reference scenario market shares are uncertain as the proportion of patients receiving PLEX is likely overestimated and eculizumab is not a funded comparator for the treatment of gMG.
- The analyses were not conducted from a drug plan payer perspective as the costs of blood products were included.
- The uptake of rozanolixizumab is underestimated when considering funding for its Health Canada–indicated population (i.e., adults with gMG).
- Different body weight distributions were assumed when calculating the total treatment cost of rozanolixizumab and efgartigimod alfa.

CDA-AMC reanalyses revised the sponsor's submitted analysis by assuming eculizumab has 0% of the public market, by redistributing half the market share assigned to chronic IVIg or SCIg to other comparators, by removing the cost of blood products from the analysis, and by revising the distribution of patient body

weights used to estimate dosing for rozanolixizumab and efgartigimod alfa. In addition to these changes, CDA-AMC increased the uptake of rozanolixizumab in the analysis based on the Health Canada–indicated population.

The results of the CDA-AMC reanalyses suggest that the reimbursement of rozanolixizumab in combination with conventional therapy for the treatment of adults with AChR antibody-positive or MuSK antibody-positive gMG whose symptoms persist despite conventional therapy may be associated with a 3-year incremental budgetary cost of $132,461,365 (year 1: $24,638,709; year 2: $42,950,784; year 3: $64,871,872).

CDEC Information

Members of the Committee

Dr. Peter Jamieson (Chair), Dr. Sally Bean, Daryl Bell, Dan Dunsky, Dr. Trudy Huyghebaert, Morris Joseph, Dr. Dennis Ko, Dr. Christine Leong, Dr. Kerry Mansell, Dr. Alicia McCallum, Dr. Srinivas Murthy, Dr. Nicholas Myers, Dr. Krishnan Ramanathan, Dr. Marco Solmi, Dr. Edward Xie, and Dr. Peter Zed

Meeting date: January 22, 2025

Regrets: Two expert committee members did not attend.

Conflicts of interest: One expert committee member did not participate due to considerations of conflict of interest.

Canada's Drug Agency
L'Agence des médicaments du Canada
Drugs. Health Technologies and Systems. Médicaments, technologies de la santé et systèmes.

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Questions or requests for information about this report can be directed to Requests@CDA-AMC.ca.