

Reimbursement Recommendation

Nipocalimab (Imaavy)

Indication: As an add-on to standard therapy for the treatment of generalized myasthenia gravis in adult and adolescent patients aged 12 years and older who are anti-acetylcholine receptor or anti-muscle-specific tyrosine kinase antibody positive.

Sponsor: Janssen Inc.

Final recommendation: Do not reimburse

Summary

What Is the Reimbursement Recommendation for Imaavy?

Canada's Drug Agency (CDA-AMC) recommends that Imaavy not be reimbursed by public drug plans "as an add-on to standard therapy for the treatment of generalized myasthenia gravis in adult and adolescent patients aged 12 years and older who are anti-acetylcholine receptor or anti-muscle-specific tyrosine kinase antibody positive."

Why Did CDA-AMC Not Recommend Reimbursement?

- The Canadian Drug Expert Committee (CDEC) determined that it is uncertain whether Imaavy demonstrates acceptable clinical value versus appropriate comparators when used as an add-on to standard therapy for the treatment of generalized myasthenia gravis (gMG) in adult and adolescent patients with antiacetylcholine receptor (AChR) or antimuscle-specific tyrosine kinase (MuSK) antibody-positive disease. Appropriate comparators in the adult population refer to rituximab, efgartigimod alfa, ravulizumab, zilucoplan, and rozanolixizumab. Appropriate comparators in the adolescent population refer to IV immunoglobulin (IVIg), plasma exchange (PLEX), and rituximab. Given that Imaavy is expected to be an alternative treatment to the comparators, acceptable clinical value refers to at least comparable value versus the comparators relevant to each age group.
- Evidence from 1 clinical trial in adult patients with gMG showed that compared with placebo, treatment with Imaavy likely improves daily function, disease severity, and may improve health-related quality of life (HRQoL) at 22 to 24 weeks. However, it is uncertain whether the improvements are clinically meaningful. Further, there appears to be little to no clinically meaningful difference between Imaavy and placebo in the proportion of patients who had treatment response and fatigue. The evidence for the subgroup with anti-MuSK antibody-positive disease was uncertain due to the small number of patients enrolled in the trial.
- Evidence from 1 trial of 8 adolescents with gMG was highly uncertain due to small sample size and single-arm trial design.
- Evidence from 1 indirect treatment comparison (ITC) of adults with anti-AChR antibody-positive disease was associated with important methodological limitations that precluded CDEC from drawing firm conclusions regarding the comparative efficacy and safety of Imaavy versus efgartigimod alfa, ravulizumab, zilucoplan, and rozanolixizumab. Rituximab was also not included in the efficacy comparison. Additionally,

Summary

no comparative evidence versus relevant comparators was submitted for adolescents and for the subpopulation with anti-MuSK antibody-positive disease.

- CDEC acknowledged a significant unmet need in adolescent patients and patients with anti-MuSK antibody-positive disease based on disease severity, limited treatment options, and potential challenges with evidence generation due to the rarity of gMG. However, CDEC was unable to determine that Imaavy addresses the significant unmet need with an acceptable level of certainty in clinical value based on the evidence reviewed. CDEC did not identify a significant unmet need in the adult population with anti-AChR antibody-positive disease given the availability of multiple advanced therapies.
- CDEC acknowledged that there is a significant unmet nonclinical need and health inequity, including geographic barriers or inequitable access to infusion services across Canada. However, the committee was unable to determine if Imaavy addresses this significant unmet nonclinical need and health inequity, since similar to many existing treatments, Imaavy is administered as an IV infusion and requires access to infusion centres or home infusion programs, which remain limited in many rural and remote regions.
- Based on all of the preceding considerations, CDEC recommended that Imaavy not be reimbursed.

Review Background

- **Disease background:** gMG is a rare, chronic autoimmune disorder characterized by fluctuating skeletal-muscle weakness due to impaired neuromuscular transmission. gMG typically affects ocular, bulbar, limb, and respiratory muscles, impacting daily function. In severe cases, the disease can progress to myasthenic crisis, a life-threatening event that may require ventilatory support. It was estimated that in 2016, the prevalence of myasthenia gravis (MG) in Canada is about 32 per 100,000 individuals.
- **Indication and reimbursement request:** Nipocalimab (Imaavy) has been approved by Health Canada “as an add-on to standard therapy for the treatment of generalized myasthenia gravis in adult and adolescent patients aged 12 years and older who are anti-acetylcholine receptor or anti-muscle-specific tyrosine kinase antibody positive.” The sponsor is seeking reimbursement of nipocalimab as an add-on therapy for AChR or MuSK antibody-positive adult (≥ 18 years) and adolescent (aged 12 years to < 18 years) patients with gMG whose symptoms persist despite adequate treatment with acetylcholinesterase (AChE) inhibitors, corticosteroids, and/or nonsteroidal immunosuppressant therapy (NSISTs).
- **Drug under review:** Nipocalimab is a fully human IgG1 monoclonal antibody that inhibits the FcRn. It is available as 300 mg/1.62 mL and 1,200 mg/6.5 mL solution, for IV use and the dosage recommended in the product monograph is 30 mg/kg administered over approximately 30 minutes, followed by a maintenance dose of 15 mg/kg administered over approximately 15 minutes every 2 weeks thereafter.
- **Treatment costs:** At the submitted price of \$3,646.14 and \$14,584.56 per 300 mg and 1,200 mg vial, respectively, the cost of nipocalimab is expected to be \$395,085 per patient in the first year, and \$380,501 in subsequent years, based on the Health Canada–recommended dosage (assuming a patient weighs 76 kg and including wastage of excess medication in vials, where applicable).

Highlights of Input From Interested Parties

The patient group (Muscular Dystrophy Canada) noted the following regarding impacts of the disease, unmet needs, and important outcomes:

- Patients with gMG reported substantial impacts on daily life, including reduced productivity and employment challenges, fatigue, poor sleep, respiratory, and mobility limitations. Patients emphasized that gMG affects not only physical functioning but also mental health, quality of life, and family well-being.
- Important treatment goals identified by patients are to decrease exacerbations, maintain disease control, including experiencing less weakness, fatigue, difficulty breathing, and maintaining quality of life.
- While current treatment options for gMG can be effective and patients expressed positive experiences with some treatments such as IVIg for managing their disease, there are concerns about

the long-term and sustained benefits of these treatments. Patients expressed the need for treatments that result in improved disease control, less serious adverse effects, maintenance of independence, and reduced hospital admission.

The clinician group (Neuromuscular Disease Network) for Canada and the clinical experts consulted by CDA-AMC noted the following regarding unmet needs arising from the disease and place in therapy for the drug under review:

- Standard therapy (AChE inhibitors, corticosteroids, and/or NSiSTs), IVIg, and PLEX are effective but limited by delayed onset, adverse events (AEs), and monitoring requirements. Approximately 10% of patients with gMG remain refractory despite standard therapy. Adolescents, pregnant patients, older adults, patients with pure ocular symptoms, seronegative MG, anti-MuSK antibody-positive disease, or recent thymectomy have fewer effective treatment options. There is also an absence of biomarkers to select the most appropriate therapy for each patient.
- Treatment access and equity related challenges remain substantial. IVIg is costly and not consistently available, with unequal access in rural areas, and PLEX is offered only in a small number of hospitals. These rescue treatments (IVIg and PLEX) require repeated hospital visits and impose substantial patient and caregiver burden due to long infusion or apheresis sessions, frequent visits, transportation needs, and the requirement for caregiver accompaniment. There are significant challenges including the high cost of infusion treatments and insurance restrictions that limit access to advanced therapies. IVIg is costly and not consistently available, with unequal access in rural areas, and PLEX is offered only in a small number of hospitals.
- The clinical experts consulted by CDA-AMC noted that, similar to other FcRn inhibitors, nivalimab is expected to be used as a second-line or third-line therapy in patients whose disease is not adequately controlled with standard therapy (AChE inhibitors, corticosteroids, and/or NSiSTs).

The participating public drug programs raised potential implementation issues related to considerations for initiation and prescribing of therapy, generalizability of trial populations to broader populations, care provision issues, and system and economic issues.

Recommendation

With a vote of 12 to 2, CDEC recommends that nivalimab not be reimbursed “as an add-on to standard therapy for the treatment of generalized myasthenia gravis in adult and adolescent patients aged 12 years and older who are anti-acetylcholine receptor or anti-muscle-specific tyrosine kinase antibody positive.”

Rationale for the Recommendation

Clinical Value

Based on the totality of the presented clinical evidence, CDEC concluded that it is uncertain whether nipocalimab demonstrates acceptable clinical value compared with appropriate comparators when the treatments are used as an add-on to standard therapy for the treatment of gMG in adults and adolescents with anti-AChR or anti-MuSK antibody-positive disease. Appropriate comparators in the adult population refer to rituximab, efgartigimod alfa, ravulizumab, zilucoplan, and rozanolixizumab. Appropriate comparators in the adolescent population refer to IVIg, PLEX, and rituximab. Given that nipocalimab is expected to be an alternative treatment to the appropriate comparators, acceptable clinical value refers to at least comparable value versus the comparators relevant to each age group.

Evidence from 1 double-blind, randomized controlled trial (RCT) (VIVACITY-MG3; N = 199) in the adult population demonstrated that, when used as an add-on to standard therapy (AChE inhibitors, corticosteroids, and/or NSISTs), treatment with nipocalimab likely results in an improvement in Myasthenia Gravis–Activities of Daily Living (MG-ADL) and Quantitative Myasthenia Gravis (QMG) scores at weeks 22 to 24 compared with placebo in patients with gMG who have anti-AChR or anti-MuSK antibody-positive disease and respond inadequately to standard therapy. However, the clinical importance of this improvement is uncertain. Further, there is moderate certainty evidence that nipocalimab likely results in little to no clinically important difference in the proportion of patients achieving MG-ADL and QMG responses at weeks 22 to 24 compared to placebo. There is low-certainty evidence that nipocalimab may improve HRQoL compared with placebo; however, the clinical importance of this improvement is uncertain. The evidence also suggested that nipocalimab may result in little to no clinically important difference in fatigue compared to placebo. The evidence for the subgroup with anti-MuSK antibody-positive disease was uncertain, with wide confidence intervals reflecting imprecision due to small sample size.

Evidence from 1 open-label, single-arm trial (VIBRANCE-MG; N = 8) in adolescents with gMG who had anti-AChR antibody-positive disease and responded inadequately to standard therapy was reviewed. The certainty of the evidence compared to any comparator was very low owing to the noncomparative study design and small sample size.

No head-to-head comparisons between nipocalimab and relevant comparators were submitted. The sponsor-submitted indirect evidence, consisting of 1 network meta-analysis (NMA) comparing the efficacy and safety of nipocalimab versus efgartigimod alfa, ravulizumab, zilucoplan, and rozanolixizumab in adults with gMG who had anti-AChR antibody-positive disease. This NMA was associated with important methodological limitations that precluded CDEC from drawing firm conclusions regarding the comparative effects between the treatments in this population. As a result, the comparative clinical effectiveness of nipocalimab relative to available reimbursed therapies remains unclear. Further, rituximab, which is considered a relevant comparator, was not included in the efficacy comparison. No direct and indirect comparative evidence was submitted versus appropriate comparators for adults with anti-MuSK antibody-positive gMG and for adolescents, representing important evidence gaps. CDEC considered that the reviewed evidence was

insufficient to demonstrate at least comparable outcomes between nipocalimab and the comparators in the population under review.

Further information on the committee's discussion around clinical value is provided in the Summary of Deliberation section.

Considering Significant Unmet Clinical Need

gMG is a chronic condition often associated with muscle weakness impacting vision, speech, swallowing, and breathing. CDEC acknowledged there is a significant unmet clinical need among subpopulations of patients with gMG, including adolescents and patients with anti-MuSK antibody-positive disease, due to limited treatment options available for these patients. CDEC also acknowledged that, because gMG is a rare disease, there may be practical challenges in generating evidence — particularly for adolescents and patients with anti-MuSK antibody-positive disease, for whom clinical data are especially limited. CDEC acknowledged that these subpopulations were part of the Health Canada indication. However, even when taking the significant unmet clinical need into account, CDEC was unable to conclude that there was an acceptable level of certainty in the clinical value of nipocalimab in these subpopulations compared to relevant alternatives, based on the evidence reviewed. CDEC did not identify a significant unmet need in the adult population with anti-AChR antibody-positive disease given the availability of multiple advanced therapies, albeit variability in access across the jurisdictions.

Further information on the committee's discussion around unmet clinical need is provided in the Summary of Deliberation section.

Considering Significant Unmet Nonclinical Need or Health Inequity

CDEC acknowledged that there is a significant unmet nonclinical need and health inequity, including geographic barriers or inequitable access to infusion services across Canada as noted in both patient and clinician input. The committee was unable to conclude that nipocalimab addresses this significant unmet nonclinical need and health inequity, since similar to many existing treatments, nipocalimab is an IV infusion therapy requiring access to infusion centres or home infusion programs, which remain limited in many rural and remote regions.

Further information on the committee's discussion around unmet nonclinical need is provided in the Distinct Social and Ethical Considerations domain in the Summary of Deliberation section.

Developing the Recommendation

Due to the uncertainty in clinical value, CDEC could not recommend whether to reimburse nipocalimab or not based on clinical value alone. Therefore, they also considered whether nipocalimab addressed a significant unmet clinical need with an acceptable level of certainty in clinical value. CDEC was not able to recommend reimbursement even after taking this into account. Finally, they considered whether nipocalimab addresses a significant unmet nonclinical need or health inequity. CDEC was unable to conclude that nipocalimab addresses a significant unmet nonclinical need or health inequity to a degree that overcomes the uncertainty

in clinical value and potential risks. Based on all of the preceding considerations, CDEC recommended that nipocalimab not be reimbursed.

Because CDEC recommended that nipocalimab not be reimbursed, further deliberation was not required on whether reimbursement conditions should be added to address important economic considerations, health system impacts, or social and ethical considerations, or to ensure clinical value is realized.

Summary of Deliberation

CDEC considered all domains of value of the deliberative framework before developing its recommendation: clinical value, unmet clinical need, distinct social and ethical considerations, economic considerations, and impacts on health systems. For further information on the domains of value, refer to [Expert Committee Deliberation at CDA-AMC](#).

The committee considered the following key discussion points, organized by the 5 domains of value.

The sponsor requested a reconsideration of the initial draft recommendation not to reimburse nipocalimab “as an add-on to standard therapy for the treatment of generalized myasthenia gravis in adult and adolescent patients aged 12 years and older who are anti-acetylcholine receptor or anti-muscle-specific tyrosine kinase antibody positive.” There were 4 issues outlined by the sponsor in the request for reconsideration that were discussed by CDEC.



Clinical Value

- **Efficacy versus placebo in adults:** During the initial and reconsideration meetings, CDEC discussed that evidence from 1 double-blind, RCT (VIVACITY-MG3, N = 199) supported an improvement with nipocalimab versus placebo in daily function and disease severity in adults with gMG who have anti-AChR or anti-MuSK antibody-positive disease and that responds inadequately to standard therapy. The between-group difference in least-square mean change from baseline in MG-ADL score (primary end point) and QMG score (key secondary end point) at weeks 22 to 24 was -1.45 (95% confidence interval [CI], -2.38 to -0.52) and -2.81 (95% CI, -4.22 to -1.41), respectively. There is moderate certainty evidence that nipocalimab likely results in little to no clinically important difference in the proportion of patients achieving MG-ADL (key secondary end point) and QMG responses at weeks 22 to 24 compared to placebo. The evidence suggests that nipocalimab may improve HRQoL, as assessed by Myasthenia Gravis Quality of Life 15-item scale revised (MG-QoL15r) score, and has little to no clinically important difference in fatigue, as assessed by the Quality of Life in Neurological Disorders (Neuro-QoL) fatigue score, at weeks 22 and 24. Additionally, the long-term extension study of the VIVACITY-MG3 trial suggested potential for maintained improvements in MG-ADL and QMG scores for at least 60 weeks following the 24-week double-blind RCT; however, no firm conclusions could be drawn on the long-term effects of nipocalimab due to the open-label single-arm design, missing data, and risk of selection bias.

- Depth of response and dosing schedule:** During the reconsideration meeting, CDEC discussed the dosing schedule of nipocalimab relative to other advanced therapies. Nipocalimab is administered at a consistent 2-week interval, whereas other FcRn inhibitors use cyclical dosing. While a consistent dosing schedule may be perceived as advantageous for maintaining more disease control stability, clinical expert input indicated that it is uncertain whether this translates into improved outcomes. CDEC further reviewed evidence from the VIVACITY-MG3 trial on the depth of response in MG-ADL and QMG scores. Although results favoured nipocalimab, CDEC noted that comparisons were limited to placebo, and that comparative evidence versus other FcRn inhibitors on depth of response is lacking. CDEC also noted that complement inhibitors are also administered on a consistent dosing schedule.
- Efficacy in adolescents:** During the initial and reconsideration meetings, CDEC discussed evidence from 1 open-label, single-arm trial (VIBRANCE-MG, N = 8) which suggested that treatment with nipocalimab may result in within-group improvements from baseline in daily function and disease severity in adolescents with gMG who have anti-AChR antibody-positive disease and that responds inadequately to standard therapy. The within-group change from baseline in MG-ADL and QMG scores at week 24 were [REDACTED] and [REDACTED], respectively. All patients had an at least 2-point improvement in MG-ADL score at week 24. However, the evidence is very uncertain about the effects of nipocalimab when compared with any comparator due to the noncomparative study design and small sample size. Clinical experts consulted by the review team indicated that extrapolation of results from the adult population to the adolescent population is biologically plausible; however, based on the submitted evidence, CDEC considered the effects of nipocalimab to be inconclusive. A long-term study in adolescent patients is ongoing, and results were immature and thus, not submitted for review.
- Limited evidence in the population with anti-MuSK antibody-positive disease:** During the initial meeting, CDEC discussed that while the VIVACITY-MG3 trial included patients with anti-AChR or anti-MuSK antibody-positive disease, the proportion of patients with anti-MuSK antibody-positive disease was low at 10.5%. This is in line with the distribution of anti-MuSK antibody status in patients with gMG reported in the literature. However, the small sample size limits any firm conclusions about the efficacy and safety of nipocalimab in the subpopulation of adults with anti-MuSK antibody-positive disease. As well, no patients with anti-MuSK antibody-positive disease were included in the VIBRANCE-MG trial; the effects of nipocalimab in adolescents with anti-MuSK antibody-positive disease is therefore unknown.
- Clinical importance of treatment effects:** Improving daily function, reducing muscle weakness, preventing exacerbations or myasthenic crises, minimizing long-term corticosteroid toxicity, and improving HRQoL were highlighted as important outcomes to patients and clinicians, based on the input received for this review. During the initial and reconsideration meetings, CDEC noted uncertainty regarding the clinical importance of the benefits of nipocalimab on daily function and muscle weakness in adult patients. Although the change from baseline analyses in MG-ADL and QMG scores at weeks 22 to 24 favoured nipocalimab versus placebo (between-group differences:

–1.45 and –2.81 points, respectively), the clinical importance of these findings is uncertain. CDEC acknowledged limitations in applying commonly cited within-group minimal important differences (MIDs) (2 points for MG-ADL; 3 points for QMG), and clinical expert input suggested the observed effects may be marginally clinically important. This uncertainty was also reflected in the MG-ADL and QMG responder analyses, where between-group differences did not consistently meet the 20% threshold considered clinically meaningful. Overall, CDEC noted that both change from baseline and responder analyses did not consistently demonstrate a clinically meaningful benefit relative to placebo. Clinical deterioration requiring hospitalization or rescue therapy, and changes to steroid use were measured in the VIVACITY-MG3 trial and its long-term extension, respectively, although no formal statistical testing was conducted and therefore, no definitive conclusions can be drawn on these outcomes. CDEC further discussed that it is uncertain whether the improvements in HRQoL (assessed by MG-QoL15r score) is clinically important in the absence of an MID estimate and that the change in fatigue level appears to be of little to no clinical importance.

- Placebo effect:** During the reconsideration meeting, in discussing the clinical importance of treatment effects, CDEC noted that the MG-ADL response rate in the nipocalimab group in the VIVACITY-MG3 trial (68.6%) was similar to rates observed in pivotal trials of other advanced therapies (64% to 78%). However, placebo response rate varied across trials, with a notably higher rate observed in trials of nipocalimab and complement inhibitors (53% to 67%). Clinical expert input suggested that the increased availability of effective therapies may raise patient expectations of benefit in more recent trials, potentially contributing to higher placebo response rates compared with earlier studies. The committee noted that variability in placebo responses may be partly attributable to differences in assessment time points across trials, as well as the waxing and waning nature of gMG. However, the submission did not adequately explain the observed differences in placebo response rates across studies. Overall, CDEC noted that the reasons for variability in placebo response rates across trials remain unclear. The committee also highlighted that naive comparisons of data across trials are subject to a critical risk of bias, due to differences in study design, patient populations, baseline characteristics, outcome assessment, and timing of end points. A sponsor-submitted NMA was reviewed to inform the comparative effects of nipocalimab versus relevant comparators in adults with anti-AChR antibody-positive gMG.
- Harms findings:** During the initial meeting, CDEC discussed that no notable safety signals for nipocalimab were identified from the VIVACITY-MG3 and VIBRANCE-MG trials. The safety profile was broadly consistent with the FcRn inhibitor class, with similar rates of AEs and serious AEs compared with placebo in the VIVACITY-MG3 trial. However, the small sample size and uncontrolled design of the adolescent study preclude meaningful conclusions about safety in adolescent patients.
- Certainty of the evidence:** During the initial and reconsideration meetings, CDEC discussed the Grading of Recommendations Assessment, Development and Evaluation (GRADE) assessment of selected outcomes from the VIVACITY-MG3 trial and noted that the certainty of the outcomes, compared to placebo, of MG-ADL and QMG were considered “moderate” due to concern for serious imprecision, while the certainty of the outcomes of the MG-QoL15r and Neuro-QoL fatigue scores

were considered “low” due to concern for serious study limitations and imprecisions, and the proportion of patients with 1 or more serious or severe infection or hypoalbuminemia was “low” due to concern for very serious imprecision. The certainty of these outcomes in the VIBRANCE-MG trial was “very low” due to the noncomparative design and small sample size.

- Efficacy and harms versus appropriate comparators:** During the initial and reconsideration meetings, CDEC noted that rituximab, efgartigimod alfa, ravulizumab, zilucoplan, and rozanolixizumab are the appropriate comparators in the adult population and that IVIg, PLEX, and rituximab are the appropriate comparators in the adolescent population. Direct comparative evidence for nipocalimab versus appropriate comparators was not submitted. CDEC discussed the sponsor-submitted NMA, which indirectly compared the efficacy and safety of nipocalimab with efgartigimod alfa, ravulizumab, zilucoplan, and rozanolixizumab in adult patients with gMG who have anti-AChR antibody-positive disease. CDEC noted that due to trial heterogeneity, moderate risk of bias in some included trials, sparse networks, reliance on a fixed-effect model, and indirect evidence from the NMA was insufficient to definitively conclude whether treatment with nipocalimab is at least comparable to the comparators in terms of change in the MG-ADL and QMG scores from baseline, and the risk of experiencing any AEs or serious AEs in the treatment of adult patients. Moreover, no comparisons against rituximab for populations with anti-AChR or anti-MuSK antibody-positive disease, or against rozanolixizumab for the population with anti-MuSK antibody-positive disease, were included in the direct or indirect comparative evidence submitted. Two additional ITCs, including an unanchored matching-adjusted indirect comparison and a placebo-anchored Bucher ITC, were included in the submission as supporting evidence. However, these were provided by the sponsor as poster presentations within a slide presentation and lacked sufficient supporting documentation to meet CDA-AMC appraisal requirements, as detailed in the [Procedures for Reimbursement Reviews](#). Consequently, only the sponsor-submitted NMA was appraised by CDA-AMC and informed conclusions for CDEC on the comparative effects of nipocalimab and relevant comparators.
- Subgroup with anti-AChR antibody-positive disease:** During the reconsideration meeting, CDEC discussed the sponsor’s request to focus on the evidence for adults and adolescents with anti-AChR antibody-positive disease. While most patients enrolled in the pivotal adult trial had anti-AChR antibody-positive disease, and subgroup analyses showed results broadly consistent with the overall trial population, CDEC noted that these findings remain subject to the same limitations as the primary analysis, including modest and imprecise between-group effects and uncertainty regarding clinical importance. In addition, subgroup analyses were not powered to support definitive conclusions, and the comparative evidence versus relevant therapies in the adult population with anti-AChR antibody-positive disease is uncertain. Also, no comparative evidence for the adolescent population with anti-AChR antibody-positive disease was submitted. As such, CDEC concluded that focusing on the subgroup with anti-AChR antibody-positive disease did not meaningfully reduce uncertainty regarding the magnitude, clinical relevance, or comparative effectiveness of nipocalimab.
- Evidence gaps:** During the initial meeting, CDEC discussed that multiple evidence gaps remain in this submission, which include the absence of direct and indirect comparative evidence versus

appropriate comparators for adults with anti-MuSK antibody-positive disease, for adolescents, and for HRQoL outcomes. No long-term data to inform the efficacy and safety of nipocalimab in adolescents was submitted.

- **Clinical value:** During the initial and reconsideration meetings, based on all of the preceding considerations, the committee was unable to determine there was at least similar clinical value between nipocalimab and the appropriate comparators in the population under review.



Unmet Clinical Need

- **Input on unmet clinical need:** Patients and clinicians reported that many individuals continue to experience persistent symptoms, delayed response to standard therapy, and substantial impacts on daily functioning and quality of life. Patients highlighted reliance on frequent hospital visits for rescue treatments, variable access to these treatments, and the burden of long-term steroid toxicity. Clinicians noted unmet needs in refractory disease, intolerance to existing therapies, and limited options for adolescents, those with anti-MuSK antibody-positive disease, those who were seronegative, or living with ocular MG.
- **Severity of the disease:** During the initial and reconsideration meetings, CDEC acknowledged that gMG is a serious and chronic neuromuscular disease, with fluctuating muscle weakness in multiple areas of the body, resulting in substantial morbidity. Clinicians and patients emphasized that substantial symptoms persist despite standard therapy, and approximately 10% of patients remain with refractory disease.
- **Availability of treatment options:** During the initial and reconsideration meetings, CDEC discussed that in addition to standard therapy, IVIg, PLEX, and advanced therapies including rituximab, efgartigimod, rozanolixizumab, zilucoplan, and ravulizumab can be used for the treatment of adults with gMG. Advanced therapies are typically offered to those whose disease responds inadequately to standard therapy. CDEC noted that nipocalimab is the only advanced therapy currently approved for adolescents; other available off-label treatments for adolescents with disease that responds inadequately to standard therapy are limited to IVIg, PLEX, and rituximab. As well, only 2 advanced therapies (rozanolixizumab and off-label rituximab) are available for the treatment of adults with anti-MuSK antibody-positive disease.
- **Reimbursement status of appropriate comparators in adults:** During the initial meeting, CDEC noted that multiple advanced therapies are approved for adults although access varies by jurisdiction. The pan-Canadian Pharmaceutical Alliance (pCPA) negotiations for efgartigimod, ravulizumab, rozanolixizumab, and zilucoplan successfully concluded with an agreement; funding is pending consideration by some jurisdictions. Reimbursement of rituximab varies across jurisdictions.
- **Significant unmet clinical need:** During the initial and reconsideration meetings, CDEC acknowledged that there is significant unmet clinical need (as described in the recommendation framework in the [Procedures for Reimbursement Reviews](#)) in specific subpopulations, including patients with anti-MuSK antibody-positive disease and adolescents, for whom treatment options are

limited. CDEC also acknowledged that there may be challenges with evidence generation given the rarity of these subpopulations. While CDEC acknowledged that these subpopulations were included in the Health Canada indication, based on the proceeding considerations, CDEC was unable to conclude that nipocalimab addresses a significant unmet clinical need with an acceptable level of certainty in clinical value for these subpopulations. CDEC did not identify a significant unmet need in the adult population with anti-AChR antibody-positive gMG given the availability of multiple advanced therapies, albeit variability in access across the jurisdictions.



Distinct Social and Ethical Considerations

- **Input on unmet nonclinical need:** Patients and clinicians highlighted several unmet nonclinical needs, including geographic barriers to accessing IVIg and PLEX, with some patients travelling long distances for treatment, high cost of infusion treatments, and variable availability of community infusion programs across jurisdictions. Caregivers often bear substantial burden when patients experience symptoms or mobility limitations.
- **Equity considerations:** During the initial meeting, CDEC discussed that gMG disproportionately affects African American and Black population groups and those who were underrepresented in the clinical evidence, limiting certainty regarding effectiveness and safety for these communities. Geographic disparities were also noted, as access to infusion therapies is more limited in rural and remote regions, creating differential access compared to urban settings.
- **Significant unmet nonclinical need or health inequity:** During the initial and reconsideration meetings, CDEC discussed that there is a significant unmet nonclinical need and health inequity. Input from patients and clinicians highlighted ongoing nonclinical barriers, including inequitable access to IVIg, PLEX, and other infusion services across Canada, particularly in rural and remote regions. CDEC noted that while these access challenges contribute to health inequities, nipocalimab is unlikely to mitigate them, as it requires administration via infusion, similar to many other advanced treatments.
- **Ethical implications:** During the initial meeting, CDEC noted that clinicians and patients identified the high cost of infusion therapies as an unmet nonclinical need, and emphasized that the uniform, high list price of advanced therapies raises ethical challenges related to equitable access. These cost pressures raise concerns about fair access, because people should be able to receive treatment based on their medical needs, not their ability to pay. There are also concerns about the impact on future patients and health care budgets, given the high costs of advanced therapies.
- **Deliberation on social and ethical implications:** During the initial meeting, the committee considered the social and ethical implications of nipocalimab; however, the recommendation not to reimburse meant that further deliberation on measures to address these implications was not required.



Economic Considerations

- **Deliberation on economic considerations:** During the initial meeting, the committee reviewed the economic considerations for nipocalimab plus standard therapy; however, the recommendation not to reimburse meant that further deliberation on the considerations was not required.



Impacts on Health Systems

- **Deliberation on impacts on health systems:** During the initial meeting, the committee considered the impacts on health systems when implementing nipocalimab; however, the recommendation not to reimburse meant that further deliberation on measures to address these impacts was not required.

Sources of Information Used by the Committee

To make its recommendation, the committee considered the following information (links to the full documents for the review can be found on the [project webpage](#)):

- the CDA-AMC review of the clinical and pharmacoeconomic evidence submitted by the sponsor, as well as relevant ethical issues related to nipocalimab (refer to the main report and Supplemental Material document)
- the sponsor's comments on the draft report and the CDA-AMC responses
- patients' perspectives gathered by 1 patient group, Muscular Dystrophy Canada (refer to the Patient and Clinician Group Input document)
- input from 1 clinician group, Neuromuscular Disease Network (refer to the Patient and Clinician Group Input document)
- input from public drug programs that participate in the reimbursement review process (refer to the Supplemental Material document)
- input from 2 clinical experts with expertise in the management of gMG consulted by CDA-AMC.

Request for Reconsideration

The sponsor filed a request for reconsideration of the draft recommendation for nipocalimab “as an add-on to standard therapy for the treatment of generalized myasthenia gravis in adult and adolescent patients aged 12 years and older who are anti-acetylcholine receptor or anti-muscle-specific tyrosine kinase antibody positive.” In their request, the sponsor identified the following issues:

- The sponsor noted that a negative recommendation disproportionately affects adolescents who represent an equity deserving group for which nipocalimab is the only on-label gMG treatment. As such, the sponsor was of the view that the recommendation is misaligned with the stated recognition of CDA-AMC of balancing unmet need and equity with clinical value. The sponsor requested CDEC to reconsider the reimbursement of nipocalimab specifically for adult and adolescent patients

with anti-AChR antibody-positive gMG, as the evidence base for this population is supported by concordant findings from the VIVACITY-MG (adult) and VIBRANCE-MG (adolescent) trials.

- The sponsor noted that key secondary end points were not considered by CDEC. The sponsor requested CDEC to fully consider key secondary end points (i.e., MG-ADL response rates) based on the VIVACITY-MG3 trial together with the depth of the MG-ADL and QMG responses provided to CDA-AMC during the review specifically for adult and adolescent patients with anti-AChR antibody-positive gMG.
- The sponsor noted that the recommendation by CDEC for adults with anti-AChR antibody-positive gMG is inconsistent with previous reviews. The sponsor noted that the recommendation by CDEC is largely based on an improper interpretation of MID for MG-ADL and QMG and is not consistent with the interpretation acknowledged in the Clinical Review report. The sponsor requested CDEC to reconsider its interpretation of clinical value based on the proper application of validated MIDs, and in consideration of the totality of the evidence.
- The sponsor noted that multiple ITCs demonstrate comparable efficacy across therapies for anti-AChR antibody-positive gMG. The sponsor requested CDEC to reconsider its conclusion regarding nipocalimab's comparative clinical benefit relative to other advanced therapies specifically for adult and adolescent patients with anti-AChR antibody-positive gMG, considering the NMA for adult patients with anti-AChR antibody-positive gMG together with additional ITCs methods (unanchored matching-adjusted indirect comparison and placebo-anchored Bucher ITC) provided to CDA-AMC as supportive evidence.

In the meeting to discuss the sponsor's request for reconsideration, CDEC considered the following information:

- information submitted as part of the sponsor's request for reconsideration
- information from the initial submission related to the issues identified by the sponsor
- feedback from 2 clinical specialists with expertise in diagnosing and treating patients with MG
- feedback on the draft recommendation from 1 patient group (Muscular Dystrophy Canada)
- feedback on the draft recommendation from 2 clinician groups (Neuromuscular Disease Network for Canada and Western Canada Neuromuscular)
- feedback on the draft recommendation from the public drug program that participate in the reimbursement review process
- feedback on the draft recommendation from the sponsor.

All feedback received in response to the draft recommendation is available on the CDA-AMC [project webpage](#).

CDEC Information

Members of the Committee

Dr. Peter Jamieson (Chair), Dr. Kerry Mansell (Vice-Chair), Sally Bean, Daryl Bell, Dan Dunskey, Dr. Ran Goldman, Dr. Trudy Huyghebaert, Dr. Dennis Ko, Dr. Christine Leong, Dr. Alicia McCallum, Dr. Srinivas Murthy, Dr. Nicholas Myers, Dr. Krishnan Ramanathan, Dr. Marco Solmi, Carla Velastegui, Dr. Edward Xie, and Dr. Peter Zed.

Initial meeting date: January 28, 2026

Regrets: Four expert committee members did not attend.

Conflicts of interest: None

Reconsideration meeting date: May 27, 2026

Regrets: One expert committee member did not attend.

Conflicts of interest: None



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