Policy Number	**RX501.188**
Policy Effective Date	**08/01/2026**

Nipocalimab-aahu

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Disclaimer

Medical policies are a set of written guidelines that support current standards of practice. They are based on current generally accepted standards of care developed by: nonprofit professional association(s) for the relevant clinical specialty, third-party entities that develop treatment criteria, or other federal or state governmental agencies. A requested therapy must be proven effective for the relevant diagnosis or procedure. For drug therapy, the proposed dose, frequency and duration of therapy must be consistent with recommendations in at least one authoritative source. This medical policy is supported by FDA-approved labeling and/or nationally recognized authoritative references to major drug compendia, peer reviewed scientific literature and generally accepted standards of medical care. These references include, but are not limited to: MCG care guidelines, DrugDex (IIa level of evidence or higher), NCCN Guidelines (IIb level of evidence or higher), NCCN Compendia (IIb level of evidence or higher), professional society guidelines, and CMS coverage policy.

Carefully check state regulations and/or the member contract.

Each benefit plan, summary plan description or contract defines which services are covered, which services are excluded, and which services are subject to dollar caps or other limitations, conditions or exclusions. Members and their providers have the responsibility for consulting the member's benefit plan, summary plan description or contract to determine if there are any exclusions or other benefit limitations applicable to this service or supply. **If there is a discrepancy between a Medical Policy and a member's benefit plan, summary plan description or contract, the benefit plan, summary plan description or contract will govern.**

Legislative Mandates

EXCEPTION: For members residing in the state of Ohio, § 3923.60 requires any group or individual policy (Small, Mid-Market, Large Groups, Municipalities/Counties/Schools, State Employees, Fully-Insured, PPO, HMO, POS, EPO) that covers prescription drugs to provide for the coverage of any drug approved by the U. S. Food and Drug Administration (FDA) when it is prescribed for a use recognized as safe and effective for the treatment of a given indication in one or more of the standard medical reference compendia adopted by the United States Department of Health and Human Services or in medical literature even if the FDA has not approved the drug for that indication. Medical literature support is only satisfied when safety and efficacy has been confirmed in two articles from major peer-reviewed professional medical journals that present data supporting the proposed off-label use or uses as generally safe and effective. Examples of accepted journals include, but are not limited to, Journal of

American Medical Association (JAMA), New England Journal of Medicine (NEJM), and Lancet. Accepted study designs may include, but are not limited to, randomized, double blind, placebo controlled clinical trials. Evidence limited to case studies or case series is not sufficient to meet the standard of this criterion. Coverage is never required where the FDA has recognized a use to be contraindicated, and coverage is not required for non-formulary drugs.

Coverage

Nipocalimab-aahu (Imaavy™) **may be considered medically necessary** for the treatment of individuals with generalized myasthenia gravis (gMG) who meet the following criteria:

1. 12 years of age or older.
2. Diagnosis of gMG with class II to IV disease per the Myasthenia Gravis Foundation of America (MGFA) classification system (see Policy Guidelines).
3. Anti-acetylcholine receptor antibody (Anti-AChR) antibody positive or anti-muscle-specific tyrosine kinase (MuSK) antibody positive.
4. Individual is currently receiving one of the following:
   - Acetycholinesterase (AChE) inhibitors, or
   - Steroids or non-steroidal immunosuppressive therapies (NSISTS), either in combination or alone.
5. If individual is over 18 years of age -- Impaired activities of daily living defined as a myasthenia gravis activities of daily living (MG-ADL) total score of at least 6 (see Policy Guidelines).

Nipocalimab-aahu (Imaavy™) **is considered experimental, investigational and/or unproven** for all other non-Food and Drug Administration approved indications, and when the above criteria are not met.

Policy Guidelines

Myasthenia Gravis Foundation of America (MGFA) Clinical Classification

In 1997, the Medical Scientific Advisory Board of the MGFA formed a task force to address the need for universally accepted classifications, grading systems, and analytic methods for the management of individuals undergoing therapy and for use in therapeutic research trials. As a result, the MGFA Clinical Classification was created. This classification divides myasthenia gravis (MG) into 5 main classes and several subclasses, as follows (11):

- Class I: Any ocular muscle weakness; may have weakness of eye closure. All other muscle strength is normal.
- Class II: Mild weakness affecting muscles other than ocular muscles; may also have ocular muscle weakness of any severity.
  - IIa. Predominantly affecting limb, axial muscles, or both. May also have lesser involvement of oropharyngeal muscles.
  - IIb. Predominantly affecting oropharyngeal, respiratory muscles, or both. May also have lesser or equal involvement of limb, axial muscles, or both.

- Class III: Moderate weakness affecting muscles other than ocular muscles; may also have ocular muscle weakness of any severity.
  - IIIa. Predominantly affecting limb, axial muscles, or both. May also have lesser involvement of oropharyngeal muscles.
  - IIIb. Predominantly affecting oropharyngeal, respiratory muscles, or both. May also have lesser or equal involvement of limb, axial muscles, or both.
- Class IV: Severe weakness affecting muscles other than ocular muscles; may also have ocular muscle weakness of any severity.
  - IVa. Predominantly affecting limb, axial muscles, or both. May also have lesser involvement of oropharyngeal muscles.
  - IVb. Predominantly affecting oropharyngeal, respiratory muscles, or both. May also have lesser or equal involvement of limb, axial muscles, or both.
- Class V: Defined as intubation, with or without mechanical ventilation, except when employed during routine postoperative management. The use of a feeding tube without intubation places the individual in class IVb.

<u>The Myasthenia Gravis–Specific Activities of Daily Living Scale (MG-ADL)</u>

The Myasthenia Gravis–specific Activities of Daily Living scale (MG-ADL) was developed in the late 1990s to measure Myasthenia Gravis symptoms and functional status. (12) It is an 8-item, patient reported questionnaire that is easy to administer (less than 10 minutes) and can be used in clinical trials. See Table PG1.

Table PG1. MG Activities of Daily Living (MG-ADL) Profile

Grade	**0**	**1**	**2**	**3**
Talking	Normal	Intermittent slurring or nasal speech	Constant slurring or nasal, but can be understood	Difficult to understand speech
Chewing	Normal	Fatigue with solid food	Fatigue with soft food	Gastric tube
Swallowing	Normal	Rare episode of choking	Frequent choking necessitating changes in diet	Gastric tube
Breathing	Normal	Shortness of breath with exertion	Shortness of breath at rest	Ventilator dependent
Impairment of ability to brush teeth or comb hair	None	Extra effort, but no rest periods needed	Rest periods needed	Cannot do one of these functions

Impairment of ability to arise from a chair	None	Mild, sometimes uses arms	Moderate, always uses arms	Severe, requires assistance
Double vision	None	Occurs, but not daily	Daily, but not constant	Constant
Eyelid droop	None	Occurs, but not daily	Daily, but not constant	Constant

Each activity is scored 0-3; and all scores are totaled to represent the overall MG-ADL score.

Description

Myasthenia gravis is an acquired, autoimmune disorder that affects the neuromuscular junction of the skeletal muscles. Eighty to 90 percent of individuals with myasthenia gravis have autoantibodies against the acetylcholine receptor (AChR) detectable in serum, and these antibodies are believed to play a central role in disease pathomechanism. The AChR antibodies in myasthenia gravis are primarily immunoglobulin G1 (IgG1) and G3 (IgG3). In addition to blocking ACh binding to the AChR and cross-linking and internalizing the AChRs, these antibodies act through complement activation. (2) Some individuals with myasthenia gravis who are seronegative for AChR antibodies have antibodies directed against another target on the surface of the muscle membrane, muscle-specific receptor tyrosine kinase. (3) In contrast with AChR antibody-positive myasthenia gravis, in which complement-fixing immunoglobulin G1 (IgG1) and G3 (IgG3) subclasses predominate (4) muscle-specific kinase antibodies are mainly IgG4, (5) the IgG subtype that does not activate complement.

The clinical manifestations can vary from mild and focal weakness in some individuals to severe tetraparesis with respiratory failure in others. Symptom severity may also vary substantially in an individual patient throughout the day and over the course of the condition. Classification systems stratify individuals by symptoms or diagnostic findings to specify the severity of impairment and to aid with management. There are 2 clinical forms - ocular and generalized. In ocular form, weakness is limited to the eyelids and extraocular muscles while in generalized form, weakness involves a variable combination of ocular, bulbar, limb, and respiratory muscles. Myasthenia gravis may be categorized by symptom severity to guide treatment decisions, determine eligibility for clinical trials, and help with prognostication.

A widely used classification system from a task force of the Myasthenia Gravis Foundation of America stratifies individuals by the extent and severity of muscle weakness (6) and is summarized in the Policy Guideline section. Myasthenia gravis is a relatively uncommon disorder. Both incidence and prevalence have significant geographical variations. Reported prevalence rates range from 150 to 200 cases per million, and they have steadily increased over the past 50 years, at least partly due to improvements in recognition, diagnosis, treatment, and an overall increase in life expectancy. (7) More recent studies addressing incidence rates have been conducted in Europe and show a wide range from 4.1 to 30 cases per million person-

years. (8, 9) The annual rate is lower in studies coming from North America and Japan, with the incidence ranging from 3 to 9.1 cases per million. (10)

The diagnosis is primarily based on clinical testing. Laboratory investigations and procedures can aid the clinician in confirming clinical findings. These may include serologic tests, electrophysiologic exams (e.g., repetitive nerve stimulation test and single-fiber electromyography), an edrophonium test, an ice-pack test, imaging, and laboratory testing for other coexisting autoimmune disorders (e.g., anti-nuclear antibodies, rheumatoid factor, and thyroid function). For most individuals with clinical features of myasthenia gravis, the diagnosis is confirmed by the presence of autoantibodies against the AChRs or against other muscle receptor-associated proteins. A positive anti-AChR antibody is present in 80% of individuals with gMG and confirms the diagnosis in an individual with classical clinical findings. About 5 to 10% of individuals will demonstrate anti-muscle specific kinase antibodies. Individuals who are seronegative for either of these antibodies will have anti-LRP4 antibodies.

Treatment

The goals of therapy are to render individuals minimally symptomatic or better while minimizing side effects from medications. The 4 basic therapies for myasthenia gravis include:
1) Symptomatic therapy with an acetylcholinesterase inhibitor such as pyridostigmine and neostigmine;
2) Chronic immunotherapies (such as glucocorticosteroids, eculizumab, rituximab, maintenance intravenous immunoglobulin [IVIG] or plasma exchange, and cyclophosphamide);
3) Rapid but transient immunomodulatory therapies (plasma exchange and intravenous immune globulin); and
4) Thymectomy. Approximately 10 percent of individuals with gMG have symptoms that are refractory or limited by specific toxicities of conventional immunomodulatory therapies (e.g., high-dose glucocorticoids). Therapeutic options for refractory disease include azathioprine, cyclosporine, eculizumab, efgartigimod, mycophenolate, ravulizumab, and tacrolimus.

In order to stabilize a patient with myasthenia gravis an operative procedure, IVIG or plasmapheresis may be utilized. These interventions are also the treatment of choice during a myasthenic crisis and in individuals who are resistant to immunosuppressive medications. Thymectomy may be employed as a therapeutic approach for certain individuals with myasthenia gravis.

Regulatory Status

Nipocalimab-aahu (Imaavy™) was approved by the U.S. Food and Drug Administration (FDA) in 2025.

Imaavy™ is a neonatal Fc receptor blocker indicated for the treatment of generalized myasthenia gravis (gMG) in adult and pediatric patients 12 years of age and older who are anti-acetylcholine receptor (AChR) or anti-muscle-specific tyrosine kinase (MuSK) antibody positive. Imaavy™ is administered via intravenous infusion. (1)

The safety and effectiveness of Imavvy for the treatment of gMG in pediatric patients below the age of 12 years have not been established.

Rationale

This policy is based on the U.S. Food and Drug Administration (FDA) labeled indications for Nipocalimab-aahu (Imaavy™).

Nipocalimab-aahu (Imaavy™) (1)
The efficacy of Imaavy for the treatment of generalized myasthenia gravis (gMG) in adults who are anti-acetylcholine receptor (AChR) or anti-muscle-specific tyrosine kinase (MuSK) antibody positive was established in a 24-week, multicenter, randomized, double-blind, placebo-controlled study (Study 1; NCT04951622). Patients were treated with Imaavy with the recommended dosage regimen.

Study 1 enrolled patients with gMG who met the following criteria:

- Myasthenia Gravis Foundation of America (MGFA) Clinical Classification Class II to IV
- Myasthenia Gravis-Activities of Daily Living (MG-ADL) total score of at least 6
- On stable dose of standard of care MG therapy prior to baseline that included acetylcholinesterase (AChE) inhibitors, steroids or non-steroidal immunosuppressive therapies (NSISTs), either in combination or alone.

In Study 1, a total of 196 patients were randomized 1:1 to receive Imaavy (n=98) or placebo (n=98). Baseline characteristics were similar between treatment groups. For the primary efficacy analysis population (n=153), patients had a median age of 52 years at screening (range 20 to 81 years) and a median time since diagnosis of 6 years. Sixty percent of patients were female; 63% were White; 32% were Asian; 1% were Black or African American; and <1% were American Indian or Alaskan Native. At baseline, median MG-ADL total score was 9, and median Quantitative Myasthenia Gravis (QMG) total score was 15. Eighty-eight percent (n=134) of patients were positive for AChR antibodies and 10% (n=16) were positive for MuSK antibodies.

At baseline, in each group, 85% of patients received AChE inhibitors, 66% of patients received steroids, and 54% of patients received NSISTs at stable doses.

The efficacy of Imaavy was measured using the MG-ADL scale, which assesses the impact of gMG on daily functions of 8 signs and symptoms that are typically affected in gMG. Each item is assessed on a 4-point scale, where a score of 0 represents normal function and a score of 3 represents loss of ability to perform that function. A total score ranges from 0 to 24, with the higher scores indicating more impairment.

The primary efficacy endpoint was the comparison of the mean change from baseline to Weeks 22, 23, and 24 between treatment groups in the MG-ADL total score. A statistically significant

difference favoring Imaavy was observed in MG-ADL total score change from baseline (p=0.002; see Table 1 and Figure 1).

The efficacy of Imaavy was also measured using the QMG total score, which is a 13-item categorial grading system that assesses muscle weakness. Each item is assessed on a 4 -point scale, where a score of 0 represents no weakness, and a score of 3 represents severe weakness. A total possible score ranges from 0 to 39, where higher scores indicate more severe impairment.

The secondary endpoint was the comparison of the mean change from baseline to Weeks 22 and 24 between treatment groups in the QMG total score. A statistically significant difference favoring Imaavy was observed in the QMG total score change from baseline (p<0.001; see Table 1).

The results are presented in Table 1.

Table 1. Least Squares Mean Change from Baseline to Week 24 in MG-ADL and QMG Total Scores in Study 1

Efficacy Endpoints	**Imaavy N = 77 LS Mean (SE)**	**Placebo N = 76 LS Mean (SE)**	**Imaavy Change Relative to Placebo LS Mean Difference (95% CI)**	**p-value**
Primary Endpoint				
MG-ADL Total Score[1]	-4.7 (0.33)	-3.3 (0.34)	-1.5 (-2.4, -0.5)	0.002
Secondary Endpoint				
QMG Total Score[2]	-4.9 (0.5)	-2.1 (0.5)	-2.8 (-4.2, -1.4)	<0.001

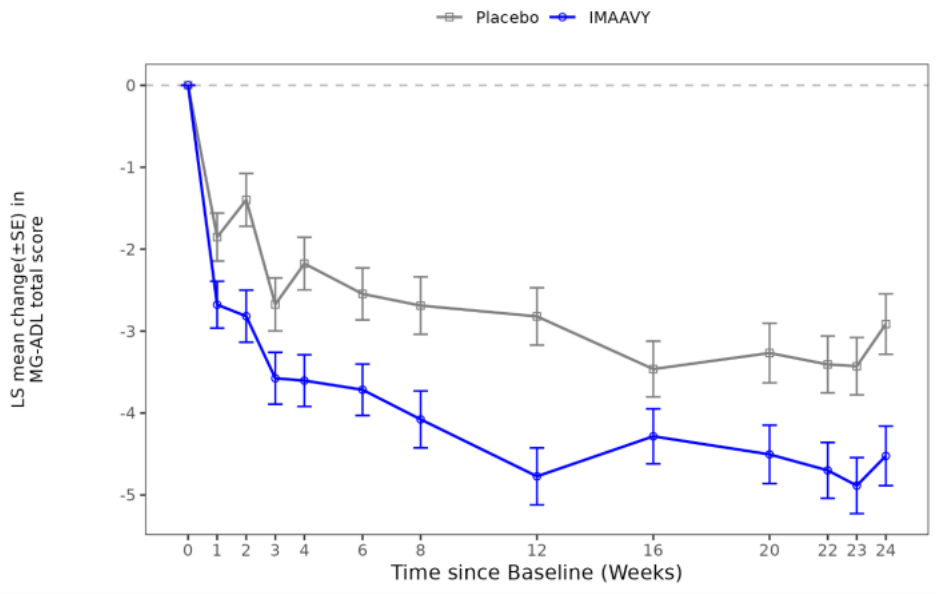
1CI: confidence interval; MG-ADL: Myasthenia Gravis – Activities of Daily Living; QMG: Quantitative Myasthenia Gravis; LS mean: Least squares mean; SE: standard error.

[1] Mean change from baseline over weeks 22, 23, and 24

[2] Mean change from baseline over weeks 22 and 24

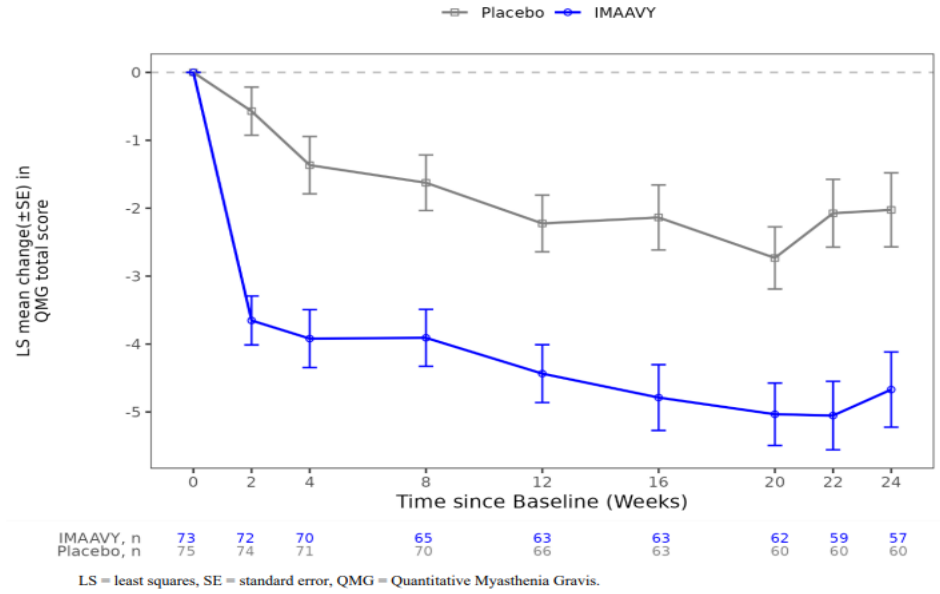
Figure 1 shows the mean change from baseline to Week 24 in MG-ADL total score in Study 1, and Figure 2 shows the mean change from baseline to Week 24 in QMG total score in Study 1.

Figure 1: Least Squares Mean Change from Baseline in MG-ADL Total Score Over 24 Weeks in Study 1



LS = least squares, SE = standard error, MG-ADL = Myasthenia Gravis Activities of Daily Living

Figure 2: Least Squares Mean Change from Baseline in QMG Total Score Over 24 Weeks in Study 1



LS = least squares, SE = standard error, QMG = Quantitative Myasthenia Gravis.

Pediatric Use

The safety and effectiveness of Imaavy for the treatment of gMG have been established in pediatric patients 12 years of age and older. Use of Imaavy in pediatric patients for this indication is supported by evidence from an adequate and well-controlled trial in adults with

additional pharmacokinetic and safety data in pediatric patients who are 12 years of age and older.

In a 24-week, single arm study evaluating the safety of Imaavy in 7 pediatric patients aged 12 to 16 years with gMG who were AChR positive, adverse reactions were consistent with those observed in adult patients with gMG.

Coding

Procedure codes on Medical Policy documents are included **only** as a general reference tool for each policy. **They may not be all-inclusive.**

The presence or absence of procedure, service, supply, or device codes in a Medical Policy document has no relevance for determination of benefit coverage for members or reimbursement for providers. **Only the written coverage position in a Medical Policy should be used for such determinations.**

Benefit coverage determinations based on written Medical Policy coverage positions must include review of the member's benefit contract or Summary Plan Description (SPD) for defined coverage vs. non-coverage, benefit exclusions, and benefit limitations such as dollar or duration caps.

CPT Codes	None
HCPCS Codes	J9256

*Current Procedural Terminology (CPT®) ©2025 American Medical Association: Chicago, IL.

References

U.S. Food and Drug Administration Label:

1. Prescribing Label: Imaavy™ (nipocalimab-aahu) injection, for intravenous use. April 2025. Available at <https://www.accessdata.fda.gov> (accessed February 2, 2026).

Other:

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Centers for Medicare and Medicaid Services (CMS)

The information contained in this section is for informational purposes only. HCSC makes no representation as to the accuracy of this information. It is not to be used for claims adjudication for HCSC Plans.

The Centers for Medicare and Medicaid Services (CMS) does not have a national Medicare coverage position. Coverage may be subject to local carrier discretion.

A national coverage position for Medicare may have been developed since this medical policy document was written. See Medicare's National Coverage at <https://www.cms.hhs.gov>.

Policy History/Revision

Date	Description of Change
08/01/2026	New medical document. Nipocalimab-aahu (Imaavy™) may be considered medically necessary for the treatment of individuals with generalized myasthenia gravis (gMG) who meet the following criteria: 12 years of age or older; Diagnosis of gMG with class II to IV disease per the Myasthenia Gravis Foundation of America (MGFA) classification system (see Policy Guidelines); Anti-acetylcholine receptor antibody (Anti-AChR) antibody positive or anti-muscle-specific tyrosine kinase (MuSK) antibody positive; Individual is currently receiving one of the following: Acetycholinesterase (AChE) inhibitors, or Steroids or non-steroidal immunosuppressive therapies (NSISTS), either in combination or alone; If individual is over 18 year of age -- Impaired activities of daily living defined as a myasthenia gravis activities of daily living (MG-ADL) total score of at least 6 (see Policy Guidelines). Nipocalimab-aahu (Imaavy™) is considered experimental, investigational

	and/or unproven for all other non-Food and Drug Administration approved indications, and when the above criteria are not met.