Utilization Review Policy 367

POLICY: Neurology – Imaavy Utilization Management Medical Policy
- Imaavy™ (nipocalimab-aahu intravenous infusion – Johnson & Johnson)

EFFECTIVE DATE: 08/01/2025
LAST REVISION DATE: 05/14/2025

COVERAGE CRITERIA FOR: All UCare Plans

OVERVIEW

Imaavy, a neonatal Fc receptor blocker, is indicated for the treatment of **generalized myasthenia gravis** in adults and pediatric patients ≥ 12 years of age who are anti-acetylcholine receptor (AChR) or anti-muscle-specific tyrosine kinase (MuSK) antibody positive.[1]

Disease Overview

Myasthenia gravis is a chronic autoimmune neuromuscular disease that causes weakness in the skeletal muscles, which are responsible for breathing and moving parts of the body, including the arms and legs.[2] Myasthenia gravis is caused by the production of pathogenic immunoglobulin G (IgG) autoantibodies against neuromuscular junction components (AChR, MuSK, and low density lipoprotein receptor-related protein 4 [LRP4]).[3] Approximately 85% of patients with myasthenia gravis are anti-AChR antibody-positive and approximately 5% to 8% of patients are anti-MuSK antibody-positive.[4] The result of the antibodies at the junction is unsuccessful nerve transmission and deficiency or weakness of muscle contractions.[3] The hallmark of myasthenia gravis is muscle weakness that worsens after periods of activity and improves after periods of rest.[2] Certain muscles such as those that control eye and eyelid movement, facial expression, chewing, talking, and swallowing are often involved in the disorder; however, the muscles that control breathing and neck and limb movements may also be affected.

Clinical Efficacy

The efficacy of Imaavy was evaluated in one randomized, double-blind, multicenter, placebo-controlled Phase III pivotal study, Vivacity-MG3 (published) [n = 196].[5] Enrolled patients were ≥ 18 years of age with symptoms of gMG categorized as Myasthenia Gravis Foundation of America (MGFA) Class II to IV at screening. In addition, patients had a suboptimal response (defined as myasthenia gravis-activities of daily living [MG-ADL] score of ≥ 6 at baseline) to their current, stable standard-of care therapy for gMG (e.g., acetylcholinesterase inhibitor, corticosteroid, immunosuppressant). Patients were randomized to receive Imaavy (at the FDA-approved regimen) or placebo in addition to their stable gMG regimen. The majority of patients were anti-AChR antibody positive (82% in the Imaavy group vs. 93% in the placebo group), followed by anti-MuSK antibody-positive (16% vs. 5%, respectively) and anti-lipoprotein receptor-related protein 4 (LRP4) antibody positive (3% vs. 1%, respectively). The efficacy analysis dataset included all randomly assigned patients who received at least one dose (partial or complete) of study drug in the double-blind phase and were antibody-positive for a gMG-related pathogenic antibody (anti-AChR, anti-MuSK, or anti-LRP4). The primary efficacy endpoint was the difference between Imaavy and placebo in the least-squares (LS) mean change from baseline in the MG-ADL total score averaged over Weeks 22, 23, and 24. A significantly greater reduction in the MG-ADL total score was observed in the Imaavy group compared with placebo (LS mean change from baseline was -4.70 vs. -3.25, respectively; difference of -1.45; P = 0.0024). The first key secondary endpoint was the difference in the LS mean change in the quantitative myasthenia gravis (QMG) total score from baseline over Weeks 22 and 24; the results favored Imaavy (-4.86 for Imaavy vs. -2.05 for placebo; difference of -2.81; P = 0.00012). The second key

secondary endpoint was the percentage of patients with at least a 2-point improvement in the MG-ADL score over Weeks 22, 23, and 24 and significantly more patients in the Imaavy group achieved this endpoint compared with placebo (69% vs. 53%, respectively; difference of 16.2%; P = 0.021).
Clinical Pediatric Data: Use in pediatric patients ≥ 12 years of age for this indication is supported by evidence from an adequate and well-controlled trial in adults and additional pharmacokinetic and safety data in pediatric patients who are ≥ 12 years of age.[1] There is an ongoing Phase II/III open-label study to evaluate the efficacy of Imaavy in pediatric patients 2 to < 18 years of age with gMG who are anti-AChR or anti-MuSK antibody positive.[6] Data are not yet available.

Dosing Information

The initial dose of Imaavy is 30 mg/kg administered once via intravenous (IV) infusion over at least 30 minutes.[1] Two weeks after the initial dose, administer a maintenance dose of 15 mg/kg via IV infusion over at least 15 minutes. Continue the maintenance dose every 2 weeks thereafter.

Guidelines

An international consensus guidance for the management of myasthenia gravis was published in 2016.[7] The guidelines recommend pyridostigmine for the initial treatment in most patients with myasthenia gravis. The ability to discontinue pyridostigmine can indicate that the patient has met treatment goals and may guide the tapering of other therapies. Corticosteroids or immunosuppressant therapy should be used in all patients with myasthenia gravis who have not met treatment goals after an adequate trial of pyridostigmine. Nonsteroidal immunosuppressant agents include azathioprine, cyclosporine, mycophenolate mofetil, methotrexate, and tacrolimus. It is usually necessary to maintain some immunosuppression for many years, sometimes for life. Plasma exchange and intravenous immunoglobulin can be used as short-term treatments in certain patients. A 2020 update to these guidelines provides new recommendations for methotrexate, rituximab, and eculizumab intravenous infusion (Soliris®, biosimilars).[8] All recommendations should be considered extensions or additions to recommendations made in the initial international consensus guidance (2016). Oral methotrexate may be considered as a steroid-sparing agent in patients with generalized myasthenia gravis who have not tolerated or responded to steroid-sparing agents. Rituximab should be considered as an early therapeutic option in patients with anti-MuSK antibody-positive myasthenia gravis who have an unsatisfactory response to initial immunotherapy. Eculizumab should be considered in the treatment of severe, refractory, anti-AChR antibody-positive generalized myasthenia gravis.

Pediatric patients with generalized myasthenia gravis. Cholinesterase inhibitors are used first-line for the symptomatic treatment of juvenile myasthenia gravis (JMG); pyridostigmine is the most widely used cholinesterase inhibitor for JMG.[8] There are no formal guidelines for the use of immunosuppressive therapy in JMG and current practice has been taken from adult guidelines and expert opinions based on individual experience. Prednisolone is accepted as the first-line immunosuppressive therapy in JMG. Second-line therapies or steroid-sparing agents include, but are not limited to, azathioprine, mycophenolate mofetil, tacrolimus, rituximab, cyclosporine, and cyclophosphamide.

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of Imaavy. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indication. Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. Because of the specialized skills required for evaluation and diagnosis of patients treated with Imaavy as well as the monitoring required for adverse events and

long-term efficacy, approval requires Imaavy to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Imaavy is recommended in those who meet the following criteria:

FDA-Approved Indication

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1. Generalized Myasthenia Gravis. Approve for the duration noted if the patient meets ONE of the following (A or B):

A) Initial Therapy. Approve for 6 months if the patient meets ALL of the following (i, ii, iii, iv, v, and vi):

- **i.** Patient is ≥ 12 years of age; AND
- **ii.** If patient is ≥ 18 years of age, patient meets BOTH of the following (a and b):
  - **a)** Myasthenia Gravis Foundation of America classification of II to IV; AND
  - **b)** Myasthenia Gravis Activities of Daily Living (MG-ADL) score of ≥ 6; AND
- **iii.** Patient meets ONE of the following (a or b):
  - **a)** Patient has confirmed anti-acetylcholine receptor antibody-positive generalized myasthenia gravis; OR
  - **b)** Patient has confirmed anti-muscle-specific tyrosine kinase antibody-positive generalized myasthenia gravis; AND
- **iv.** Patient meets ONE of the following (a or b):
  - **a)** Patient previously received or is currently receiving pyridostigmine; OR
  - **b)** Patient has had inadequate efficacy, a contraindication, or significant intolerance to pyridostigmine; AND
- **v.** Patient has evidence of unresolved symptoms of generalized myasthenia gravis; AND
  Note: Examples of unresolved symptoms include difficulty swallowing, difficulty breathing, or a functional disability resulting in the discontinuation of physical activity (e.g., double vision, talking, impairment of mobility).
- **vi.** The medication is being prescribed by or in consultation with a neurologist; OR

B) Patient is Currently Receiving Imaavy. Approve for 1 year if the patient meets ALL of the following (i, ii, and iii):

- **i.** Patient is ≥ 12 years of age; AND
- **ii.** According to the prescriber, patient is continuing to derive benefit from Imaavy; AND
  Note: Examples of derived benefit include reductions in exacerbations of myasthenia gravis; improvements in speech, swallowing, mobility, and respiratory function.
- **iii.** The medication is being prescribed by or in consultation with a neurologist.

Dosing. Approve the following (A or B):

A) Initial Therapy. Approve initial dose of 30 mg/kg administered once vial intravenous infusion; followed by maintenance dose of 15 mg/kg administered via intravenous infusion (starting 2 weeks after the initial dose and administer every 2 weeks thereafter); AND

B) Patient is Currently Receiving Imaavy. Approve maintenance dose of 15 mg/kg administered via intravenous infusion every 2 weeks.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Imaavy is not recommended in the following situations:

1. **Concomitant Use with Another Neonatal Fc Receptor Blocker, a Complement Inhibitor, or a Rituximab Product.** There is no evidence to support concomitant use of Imavavy with another neonatal Fc receptor blocker, a complement inhibitor, or a rituximab product.
   Note: Examples of neonatal Fc receptor blockers are Rystiggo (rozanolixizumab-noli subcutaneous infusion), Vyvgart (efgartigimod alfa-fcab intravenous infusion) and Vyvgart Hytrulo (efgartigimod alfa and hyaluronidase-qvfc subcutaneous injection).
   Note: Examples of complement inhibitors are eculizumab intravenous infusion (Soliris, biosimilars), Ultomiris (ravulizumab-cwvz intravenous infusion), and Zilbrysq (zilucoplan subcutaneous injection).

2. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

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3. Cleanthous S, Mork AC, Regnault A, et al. Development of the myasthenia gravis (MG) symptoms PRO: a case study of a patient-centred outcome measure in rare disease. *Orphanet J Rare Dis.* 2021;16:457.
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5. Antozzi C, Vu T, Ramchandren S, et al. Safety and efficacy of nipocalimab in adults with generalised myasthenia gravis (Vivacity-MG3): a phase 3, randomized, double-blind, placebo-controlled study. *Lancet Neurol*. 2025;24:105-116.
6. An open-label uncontrolled multicenter study to evaluate the pharmacokinetics, pharmacodynamics, and safety and activity of nipocalimab in children aged 2 to less than 18 years with generalized myasthenia gravis (NCT05265273). Available at: https://clinicaltrials.gov/study/NCT05265273. Accessed on May 2, 2025.
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8. Narayanaswami P, Sanders DB, Wolfe G, et al. International Consensus Guidance for Management of Myasthenia Gravis: 2020 Update. *Neurology*. 2021;96(3):114-122.
9. O'Connell K, Ramdas S, Palace J. Management of juvenile myasthenia gravis. *Front Neurol*. 2020;11:743. Doi: 10.3389/fneuro.2020.00743.

HISTORY

Type of Revision	Summary of Changes	Review Date
New Policy	--	05/14/2025
UCare P&T Review	Policy reviewed and approved by UCare P&T committee. Annual review process	06/17/2025