Blue Cross Blue Shield Blue Care Network of Michigan

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P&T Date: 06/05/2025

Imaavy™ (nipocalimab-aahu)

HCPCS: J3590

Policy:

Requests must be supported by submission of chart notes and patient specific documentation.

A. Coverage of the requested drug is provided when all the following are met:
   a. FDA approved indication
   b. FDA approved age
   c. Documented anti-acetylcholine receptor (AChR) antibody positive myasthenia gravis (MG) identified by:
      i. Lab record or chart notes identifying the patient is positive for anti-AChR antibodies
      AND
      ii. One of the following confirmatory tests:
         1. Positive edrophonium test
         2. History of clinical response to oral cholinesterase inhibitors (for example: pyridostigmine)
         3. Electrophysiological evidence of abnormal neuromuscular transmission by repetitive nerve stimulation (RNS) or single-fiber electromyography (SFEMG)
         OR
   d. Documented anti-muscle-specific tyrosine kinase (MuSK) antibody positive MG identified by:
      i. Lab record or chart notes identifying the patient is positive for anti-MuSK antibodies
      AND
      ii. Electrophysiological evidence of abnormal neuromuscular transmission by repetitive nerve stimulation (RNS) or single-fiber electromyography (SFEMG)
   e. Patients must NOT have a history of:
      i. Thymectomy within 6 months
      ii. Current thymoma
      iii. Other neoplasms of the thymus
   f. Previous treatment courses of at least 12 weeks with one of the following standards of care have been ineffective: methotrexate, azathioprine, cyclophosphamide, cyclosporine, mycophenolate mofetil, or tacrolimus unless all are contraindicated or not tolerated
   g. Patient is currently receiving, and will continue to receive, a stable standard of care regimen
   h. Must not be used with other biologic therapies for myasthenia gravis or immunoglobulin therapy
   i. Trial and failure, intolerance, or a contraindication to the preferred products as specified in the BCBSM/BCN medical utilization management drug list

B. Quantity Limitations, Authorization Period and Renewal Criteria
    a. Quantity Limits: Align with FDA recommended dosing
    b. Authorization Period: One year at a time
    c. Renewal Criteria: Clinical documentation must be provided to confirm that current criteria are met and that the medication is providing clinical benefit

***Note: Coverage and approval duration may differ for Medicare Part B members based on any applicable criteria outlined in Local Coverage Determinations (LCD) or National Coverage Determinations (NCD) as determined by Center for Medicare and Medicaid Services (CMS). See the CMS website at http://www.cms.hhs.gov/. Determination of coverage of Part B drugs is based on medically accepted indications which have supported citations included or approved for inclusion determined by CMS approved compendia.

Background Information:

- 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.

- Myasthenia gravis (MG) is a rare autoimmune disease resulting from an immunologic attack of AChR, MuSK, and/or other receptors found on the postsynaptic neuromuscular junction. It typically presents initially as asymmetric ptosis and diplopia and is known as ocular, or class I, MG of the eyelids and extraocular muscles. As weakness extends beyond the ocular muscles, the disease progresses into gMG with patients experiencing widespread fatigue and muscle weakness most commonly in the head, neck, and extremities. Depending on the severity of muscle weakness, at this point MG is classified as either class II for mild, class III for moderate, and class IV for severe presentation. Those with class V disease require intubation due to profound debilitating muscle weakness and fatigue and difficulty breathing, swallowing, speaking, and walking. Imaavy has only been studied in patients with class II – IV disease. There is no safety and efficacy data to support use in patients with class I or V disease at this time.

- Imaavy is only indicated for use in patients with anti-AChR or anti-MuSK antibodies. An immunologic assay to detect for the presence of anti-AChR and anti-MuSK antibodies is the first step towards a diagnosis of MG. Once it is determined a patient has one of these antibody types, at least one other confirmatory test should be conducted. A positive edrophonium test, history of response to oral cholinesterase inhibitors, repetitive nerve stimulation (RNS), or single-fiber electromyography (SFEMG) all can be used to verify anti-AChR MG. Only a repetitive nerve stimulation (RNS) or single-fiber electromyography (SFEMG) can be used to confirm anti-MuSK antibody positive disease.

- The thymus plays an important role in the pathogenesis of MG. Studies have shown that muscle-like myoid cells in the thymic medulla expressing AChR could be driving the antibody mediated response seen in MG. MuSK antibody positive disease is not typically associated with thymic abnormalities or thymoma. The 2021 international consensus guidance for management of myasthenia gravis state thymectomy can be considered for patients with gMG without thymoma based on class II evidence from a meta-analysis. Benefit from thymectomy is usually delayed and is often only identified several years post-surgery. Also, patients with thymomas, tumors originating from the epithelial cells of the thymus, may develop MG. Guidelines state the presence of thymoma is always a surgical indication, regardless of the severity of MG, followed by chemotherapy and radiation to treat the tumor as appropriate. Imaavy has not been studied in patients who have undergone thymectomy within 6 months, those with thymoma, and those with other tumors of the thymus. There is no safety and efficacy data to support use of Imaavy in these patient populations at this time regardless of antibody status.

- Safety and efficacy of Imaavy were established in the Vivacity-MG3 trial, a multicenter, randomized, double-blind, placebo-controlled study of 153 patients with gMG. Patients had class II – IV disease and were already stable on at least one treatment, which included acetylcholinesterase inhibitors, corticosteroids, or immunosuppressants, for MG

prior to study entry. They also had a myasthenia gravis activities of daily living (MG-ADL) score of at least 6. Patients were randomly assigned 1:1 to receive Imaavy plus standard of care (SOC) or placebo plus SOC. The primary endpoint was the mean change in MG-ADL score from baseline over weeks 22, 23, and 24. The trial met its primary endpoint with reductions in MG-ADL score by 4.70 points in the Imaavy plus SOC group which was significantly more than the 3.25 point improvement from baseline observed in the placebo plus SOC arm (p-value = 0.002).

- Standard therapies recommended by the 2021 international consensus guidance for management of myasthenia gravis include acetylcholinesterase inhibitors, corticosteroids, immunosuppressants, rituximab, Soliris®, IVIG, and PLEX.

    - Acetylcholinesterase inhibitors are used for temporary symptomatic relief of MG symptoms. Their use is limited as an adjunct therapy to immunotherapy in those with residual or refractory MG or for treatment of ocular and mild generalized disease in those who cannot receive immunosuppressants.

    - Corticosteroids are effective in ocular MG and in patients with general MG with unsatisfactory responses to acetylcholinesterase inhibitors. They produce improvement in up 80% of MG patients often beginning within 2 weeks. However, they are associated with significant dose-dependent adverse events and are typically started with an immunosuppressant and then tapered slowly.

    - Azathioprine and mycophenolate mofetil are standard immunosuppressant therapies and act as steroid-sparing agents. Other options include cyclosporin, methotrexate, and tacrolimus. The onset of action is slow and may take up to 9 to 12 months. Guidelines recommend dose adjustments no more frequently than every 3 to 6 months. Once the patient experiences treatment effect, doses should be maintained for six months to two years of therapy and then tapered to the lowest effective dose.

    - Oral methotrexate may be considered as a steroid-sparing agent in patients with gMG who have not tolerated or responded to steroid-sparing agents that are better supported by randomized clinical trial data.

    - Cyclophosphamide is typically used after failure of standard therapy in severe MG. It has several serious potential side effects. Since there are effective agents with less toxicity cyclophosphamide is usually reserved for patients refractory to the other immunosuppressive therapies.

    - PLEX and IVIG provide short-term symptomatic relief during exacerbations for surgical preparation or in patients with septicemia through downregulating autoantibodies and/or inducing antiidiopathic antibodies. IVIG has been shown to be effective in reducing the time of mechanical ventilation in myasthenic crisis, in management of severe gMG, to stabilize MG before surgery, and prior to high-dose corticosteroid therapy to minimize or prevent steroid-induced exacerbations. IVIG may be a maintenance treatment option for patients intolerant to or not responding to an adequate course of non-steroid immunosuppressive therapy. In contrast, the clinical effects of PLEX last only a few weeks unless concomitant immunosuppressants are given. Studies indicate that there is no long-term immunosuppressive effect of PLEX

    - There is good rationale for the use of rituximab in MG as the disease is B-cell mediated and rituximab targets CD20 on the B-cell membrane. Treatment guidelines state rituximab should be considered as an early therapeutic option in patients with MuSK antibody positive MG who have an unsatisfactory response to initial immunotherapy. The efficacy of rituximab in refractory AChR antibody positive MG is uncertain. It is an option if patients fail or do not tolerate other immunosuppressive agents.

    - Soliris should be considered in the treatment of severe, refractory, AChR antibody positive gMG. Until further data become available to allow comparisons of cost and efficacy with other treatments guidelines

state, Soliris should be considered after trials of other immunotherapies have been unsuccessful in meeting treatment goals.

- Imaavy has not been studied in combination with other medications used to treat MG such as Soliris; therefore, there is no data to support combination use of MG treatments.

References:

1. Imaavy [prescribing information]. Horsham, PA: Janssen Biotech, Inc.; April 2025.
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3. Sanders DB, Wolfe GI, Benatar M, et al. International consensus guidance for management of myasthenia gravis: executive summary. Neurology. 2016 Jul 26; 87 (4): 419 - 25.
4. Narayanaswami P, Sanders DB, Wolfe GI, et al. International consensus guidance for management of myasthenia gravis: 2020 update. Neurology. 2021; 96: 114 - 22.
5. Skeie GO, Apostolski S, Evoli A, et al. Guidelines for treatment of autoimmune neuromuscular transmission disorders. European J Neurol. 2010 Jul; 17 (7): 893 - 902.
6. Pasnoor M, Dimachkie MM, Farmakidis C, at al. Diagnosis of myasthenia gravis. Neurol Clinic. 2018 May; 36 (2): 261 – 74.
7. Marx A, Pfister F, Schalke B, et al. The different roles of the thymus in the pathogenesis of the various myasthenia gravis subtypes. Autoimmun Rev. 2013; 12: 875 – 84.
8. Antozzi C, Vu T, Ramchandren S, et al. Efficacy and safety of nipocalimab in adults with generalised myasthenia gravis (Vivacity MG3): a randomised, double-blind, placebo-controlled phase 3 study. Lancet Neuro. 2025 Feb; 24: 105 – 16.

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<tr><th>#</th><th>Date</th><th>Change Description</th></tr>
<tr><td>1.3</td><td>Effective Date: 07/01/2025</td><td>UM medical management system update for MAPPO and BCNA
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<tr><td>1.2</td><td>Effective Date: 06/05/2025</td><td>New policy - this criteria replaces previously approved preliminary criteria</td></tr>
<tr><td>1.1</td><td>Effective Date: 05/08/2025</td><td>UM medical management system update for BCBS and BCN
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02/13/2025</td>
<td>Preliminary Drug Review

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** The prescribing information for a drug is subject to change. To ensure you are reading the most current information it is advised that you reference the most updated prescribing information by visiting the drug or manufacturer website or http://dailymed.nlm.nih.gov/dailymed/index.cfm.*