FcRn Blockers

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➲ Instructions for Use

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Related Commercial Policy
- Provider Administered Drugs – Site of Care

Community Plan Policy
- FcRn Blockers

Coverage Rationale

➲ See Benefit Considerations

This policy refers to the following drug products for administration by a healthcare professional:
- Imaavy™ (nipocalimab-aahu) for intravenous (IV) route
- Rystiggo® (rozanolixizumab-noli) for subcutaneous (SC) route
- Vyvgart® (efgartigimod alfa-fcab) for intravenous (IV) route
- Vyvgart Hytrulo® (efgartigimod alfa and hyaluronidase-qvfc) vial for subcutaneous (SC) route

Vyvgart Hytrulo (efgartigimod alfa and hyaluronidase-qvfc) for self-administered subcutaneous injection is obtained under the pharmacy benefit, unless otherwise specified in the member specific benefit plan document. **Exception**: For members enrolled in UnitedHealthcare of California plans with a delegated provider group conducting the prior authorization review, the self-administered Vyvgart Hytrulo may be obtained under the medical benefit.

Imaavy is proven for the treatment of generalized myasthenia gravis in patients who are anti-acetylcholine receptor (AChR) antibody positive or antimuscle-specific tyrosine kinase (MuSK) antibody positive. Imaavy is medically necessary for the treatment of generalized myasthenia gravis in patients who are anti-AChR antibody positive or anti-MuSK antibody positive when the following criteria are met:
- For **initial therapy, all** of the following:
  - Submission of medical records (e.g., chart notes, laboratory values, etc.) confirming **all** of the following:
    - Patient has not failed a previous course of Imaavy therapy; **and**
    - Diagnosis of generalized myasthenia gravis (gMG); **and**
    - **One** of the following:
      – Positive serologic test for anti-AChR antibodies; **or**
      – Positive serologic test for anti-MuSK antibodies

      and
    - Patient has a Myasthenia Gravis Foundation of America (MGFA) Clinical Classification of class II, III, or IV at initiation of therapy; **and**
    - Patient has a Myasthenia Gravis Activities of Daily Living scale (MG-ADL) total score ≥ 5 at initiation of therapy

    and
  - **One** of the following (*For Medicare reviews, refer to the CMS section.**):
    - If anti-acetylcholine receptor (AChR) antibody positive, **one** of the following:

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        - History of failure of at least **two** immunosuppressive agents over the course of at least 12 months (e.g., azathioprine, corticosteroids, cyclosporine, methotrexate, mycophenolate, etc.); **or**
        - Patient has a history of failure of at least one immunosuppressive therapy and has required four or more courses of plasmapheresis/plasma exchanges and/or immune globulin over the course of at least 12 months without symptom control

      or
    - If anti-muscle-specific tyrosine kinase (MuSK) antibody positive:
        - History of failure of at least one immunosuppressive agent over the course of at least 12 months (e.g., azathioprine, corticosteroids, cyclosporine, methotrexate, mycophenolate, etc.)

    and
  - Patient is **not** receiving Imaavy in combination with any of the following:
    - CD19-directed cytolytic antibody [e.g., Uplizna (inebilizumab)]; **and**
    - Complement inhibitor [e.g., eculizumab, Ultomiris (ravulizumab), Zilbrysq (zilucoplan)]; **and**
    - FcRn blocker [e.g., Rystiggo (rozanolixizumab-noli), Vyvgart (efgartigimod alfa-fcab), Vyvgart Hytrulo (efgartigimod alfa and hyaluronidase-qvfc)]; **and**
    - Immune globulin (e.g., Hizentra, Privigen, Gammagard)

    and
  - Imaavy is dosed according to the U.S. Food and Drug Administration (FDA)–labeled dosing for gMG; **and**
  - Prescribed by, or in consultation with, a neurologist; **and**
  - Initial authorization will be for no more than 12 months

- For **continuation of therapy, all** of the following:
  - Patient has previously been treated with Imaavy; **and**
  - Submission of medical records (e.g., chart notes, laboratory tests) demonstrating **all** of the following:
    - Improvement and/or maintenance of at least a 2 point improvement (reduction in score) in the MG-ADL score from pre-treatment baseline; **and**
    - Reduction in signs and symptoms of myasthenia gravis; **and**
    - Maintenance, reduction, or discontinuation of dose(s) of baseline immunosuppressive therapy (IST) prior to starting Imaavy (**Note**: Add on, dose escalation of IST, or additional rescue therapy from baseline to treat myasthenia gravis or exacerbation of symptoms while on Imaavy therapy will be considered as treatment failure.)

    and
  - Patient is **not** receiving Imaavy in combination with any of the following:
    - CD19-directed cytolytic antibody [e.g., Uplizna (inebilizumab)]; **and**
    - Complement inhibitor [e.g., eculizumab, Ultomiris (ravulizumab), Zilbrysq (zilucoplan)]; **and**
    - FcRn blocker [e.g., Rystiggo (rozanolixizumab-noli), Vyvgart (efgartigimod alfa-fcab), Vyvgart Hytrulo (efgartigimod alfa and hyaluronidase-qvfc)]; **and**
    - Immune globulin (e.g., Hizentra, Privigen, Gammagard)

    and
  - Imaavy is dosed according to the FDA-labeled dosing for gMG; **and**
  - Prescribed by, or in consultation with, a neurologist; **and**
  - Reauthorization will be for no more than 12 months

Rystiggo is proven for the treatment of generalized myasthenia gravis in patients who are anti-acetylcholine receptor (AChR) antibody positive or antimuscle-specific tyrosine kinase (MuSK) antibody positive. Rystiggo is medically necessary for the treatment of generalized myasthenia gravis in patients who are anti-AChR antibody positive or anti-MuSK antibody positive when the following criteria are met:

- For **initial therapy, all** of the following:
  - Submission of medical records (e.g., chart notes, laboratory values, etc.) confirming **all** of the following:
    - Patient has not failed a previous course of Rystiggo therapy; **and**
    - Diagnosis of generalized myasthenia gravis (gMG); **and**
    - **One** of the following:
        - Positive serologic test for anti-AChR antibodies; **or**
        - Positive serologic test for anti-MuSK antibodies

      and
    - Patient has a Myasthenia Gravis Foundation of America (MGFA) Clinical Classification of class II, III, or IV at initiation of therapy; **and**
    - Patient has a Myasthenia Gravis Activities of Daily Living scale (MG-ADL) total score ≥ 5 at initiation of therapy

    and

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- **One** of the following (*For Medicare reviews, refer to the CMS section.***):
  - If anti-acetylcholine receptor (AChR) antibody positive, one of the following:
    - History of failure of at least **two** immunosuppressive agents over the course of at least 12 months (e.g., azathioprine, corticosteroids, cyclosporine, methotrexate, mycophenolate, etc.); **or**
    - Patient has a history of failure of at least one immunosuppressive therapy and has required four or more courses of plasmapheresis/plasma exchanges and/or immune globulin over the course of at least 12 months without symptom control

    or
  - If anti-muscle-specific tyrosine kinase (MuSK) antibody positive:
    - History of failure of at least one immunosuppressive agent over the course of at least 12 months (e.g., azathioprine, corticosteroids, cyclosporine, methotrexate, mycophenolate, etc.)

  and
- Patient is **not** receiving Rystiggo in combination with any of the following:
  - CD19-directed cytolytic antibody [e.g., Uplizna (inebilizumab)]; **and**
  - Complement inhibitor [e.g., eculizumab, Ultomiris (ravulizumab), Zilbrysq (zilucoplan)]; **and**
  - FcRn blocker [e.g., Imaavy (nipocalimab-aahu), Vyvgart (efgartigimod alfa-fcab), Vyvgart Hytrulo (efgartigimod alfa and hyaluronidase-qvfc)]; **and**
  - Immune globulin (e.g., Hizentra, Privigen, Gammagard)

  and
- Patient will be given Rystiggo no sooner than 63 days from the start of the previous treatment cycle; **and**
- Rystiggo is dosed according to the FDA-labeled dosing for gMG; **and**
- Prescribed by, or in consultation with, a neurologist; **and**
- Initial authorization will be for no more than 12 months

- For **continuation of therapy, all** of the following:
  - Patient has previously been treated with Rystiggo; **and**
  - Submission of medical records (e.g., chart notes, laboratory tests) demonstrating **all** of the following:
    - Improvement and/or maintenance of at least a 2 point improvement (reduction in score) in the MG-ADL score from pre-treatment baseline; **and**
    - Reduction in signs and symptoms of myasthenia gravis; **and**
    - Maintenance, reduction, or discontinuation of dose(s) of baseline immunosuppressive therapy (IST) prior to starting Rystiggo (**Note**: Add on, dose escalation of IST, or additional rescue therapy from baseline to treat myasthenia gravis or exacerbation of symptoms while on Rystiggo therapy will be considered as treatment failure.)

    and
  - Patient is **not** receiving Rystiggo in combination with any of the following:
    - CD19-directed cytolytic antibody [e.g., Uplizna (inebilizumab)]; **and**
    - Complement inhibitor [e.g., eculizumab, Ultomiris (ravulizumab), Zilbrysq (zilucoplan)]; **and**
    - FcRn blocker [e.g., Imaavy (nipocalimab-aahu), Vyvgart (efgartigimod alfa-fcab), Vyvgart Hytrulo (efgartigimod alfa and hyaluronidase-qvfc)]; **and**
    - Immune globulin (e.g., Hizentra, Privigen, Gammagard)
  - Patient is not being given Rystiggo sooner than 63 days from the start of the previous treatment cycle; **and**
  - Rystiggo is dosed according to the FDA-labeled dosing for gMG; **and**
  - Prescribed by, or in consultation with, a neurologist; **and**
  - Reauthorization will be for no more than 12 months

Vyvgart and Vyvgart Hytrulo are proven for the treatment of generalized myasthenia gravis. Vyvgart and Vyvgart Hytrulo are medically necessary for the treatment of generalized myasthenia gravis when the following criteria are met:

- For **initial therapy, all** of the following:
  - Submission of medical records (e.g., chart notes, laboratory values, etc.) confirming **all** of the following:
    - Patient has not failed a previous course of Vyvgart therapy; **and**
    - Patient has not failed a previous course of Vyvgart Hytrulo therapy; **and**
    - Diagnosis of generalized myasthenia gravis (gMG); **and**
    - **One** of the following:
      - Positive serologic test for anti-AChR antibodies; **or**
      - Positive serologic test for anti-MuSK antibodies; **or**
      - Positive serologic test for anti-LRP4 antibodies; **or**
      - Negative serologic test for anti-AChR, anti-MuSK, and anti-LRP4 antibodies (triple seronegative)

      and

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- Patient has a Myasthenia Gravis Foundation of America (MGFA) Clinical Classification of class II, III, or IV at initiation of therapy; **and**
- Patient has a Myasthenia Gravis Activities of Daily Living scale (MG-ADL) total score ≥ 5 at initiation of therapy

and

- **One** of the following (*For Medicare reviews, refer to the CMS section*.**):
  - If anti-AChR antibody positive, anti-LRP4 antibody positive, or triple seronegative, **one** of the following:
    - History of failure of at least **two** immunosuppressive agents over the course of at least 12 months (e.g., azathioprine, corticosteroids, cyclosporine, methotrexate, mycophenolate, etc.); **or**
    - Patient has a history of failure of at least one immunosuppressive therapy and has required four or more courses of plasmapheresis/plasma exchanges and/or immune globulin over the course of at least 12 months without symptom control

    or
  - If anti-muscle-specific tyrosine kinase (MuSK) antibody positive:
    - History of failure of at least one immunosuppressive agent over the course of at least 12 months (e.g., azathioprine, corticosteroids, cyclosporine, methotrexate, mycophenolate, etc.)

  and
- Patient is **not** receiving Vyvgart or Vyvgart Hytrulo in combination with any of the following:
  - CD19-directed cytolytic antibody [e.g., Uplizna (inebilizumab)]; **and**
  - Complement inhibitor [e.g., eculizumab, Ultomiris (ravulizumab), Zilbrysq (zilucoplan)]; **and**
  - FcRn blocker [e.g., Imaavy (nipocalimab-aahu), Rystiggo (rozanolixizumab-noli)]; **and**
  - Immune globulin (e.g., Hizentra, Privigen, Gammagard)

  and
- Vyvgart or Vyvgart Hytrulo is dosed according to the FDA-labeled dosing for gMG; **and**
- Prescribed by, or in consultation with, a neurologist; **and**
- Initial authorization will be for no more than 12 months

- For **continuation of therapy, all** of the following:
  - Patient has previously been treated with Vyvgart or Vyvgart Hytrulo; **and**
  - Submission of medical records (e.g., chart notes, laboratory tests) demonstrating **all** of the following:
    - Improvement and/or maintenance of at least a 2 point improvement (reduction in score) in the MG-ADL score from pre-treatment baseline; **and**
    - Reduction in signs and symptoms of myasthenia gravis; **and**
    - Maintenance, reduction, or discontinuation of dose(s) of baseline immunosuppressive therapy (IST) prior to starting Vyvgart or Vyvgart Hytrulo (**Note**: Add on, dose escalation of IST, or additional rescue therapy from baseline to treat myasthenia gravis or exacerbation of symptoms while on Vyvgart or Vyvgart Hytrulo therapy will be considered as treatment failure.)

    and
  - Patient is **not** receiving Vyvgart or Vyvgart Hytrulo in combination with any of the following:
    - A CD19-directed cytolytic antibody [e.g., Uplizna (inebilizumab)]; **and**
    - A complement inhibitor [e.g., eculizumab, Ultomiris (ravulizumab), Zilbrysq (zilucoplan)]; **and**
    - An FcRn blocker [e.g., Imaavy (nipocalimab-aahu), Rystiggo (rozanolixizumab-noli)]; **and**
    - An immune globulin (e.g., Hizentra, Privigen, Gammagard)

    and
  - Vyvgart or Vyvgart Hytrulo is dosed according to the FDA-labeled dosing for gMG; **and**
  - Prescribed by, or in consultation with, a neurologist; **and**
  - Reauthorization will be for no more than 12 months

Vyvgart Hytrulo is proven for the treatment of chronic inflammatory demyelinating polyneuropathy (CIDP).
Vyvgart Hytrulo is medically necessary for the treatment of CIDP when the following criteria are met:

- For **initial therapy, all** of the following:
  - Patient has not failed a previous course of Vyvgart Hytrulo therapy; **and**
  - Diagnosis of chronic inflammatory demyelinating polyneuropathy (CIDP) as confirmed by **all** of the following:
    - Progressive symptoms present for at least 2 months; **and**
    - Symptomatic polyradiculoneuropathy as indicated by progressive or relapsing motor or sensory impairment of more than one limb; **and**
    - Electrodiagnostic findings (consistent with EFNS/PNS guidelines for definite CIDP) indicating the presence of at least **one** of the following:
      - Motor distal latency prolongation in 2 nerves
      - Reduction of motor conduction velocity in 2 nerves

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        - Prolongation of F-wave latency in 2 nerves
        - Absence of F-waves in at least 1 nerve
        - Partial motor conduction block of at least 1 motor nerve
        - Abnormal temporal dispersion in at least 2 nerves
        - Distal CMAP duration increase in at least 1 nerve

    and

    - Trial and failure (after a trial of at least two months), contraindication, or intolerance to corticosteroids (*For Medicare reviews, refer to the CMS section.***); **and**
    - **One** of the following:
        - Trial and failure (after a trial of at least three months) to an immune globulin (i.e., intravenous immunoglobulin or subcutaneous immunoglobulin) (*For Medicare reviews, refer to the CMS section.***); **or**
        - **Both** of the following:
            - Intolerance to all immune globulins (i.e., intravenous immunoglobulin or subcutaneous immunoglobulin); **and**
            - Dose has been adjusted or escalated to the maximally allowable and/or tolerated dose

        or

        - Contraindication to **all** immune globulins (i.e., intravenous immunoglobulin or subcutaneous immunoglobulin)

    and

    - Patient is **not** receiving Vyvgart Hytrulo in combination with an immune globulin; **and**
    - Vyvgart Hytrulo is dosed according to the FDA-labeled dosing for CIDP; **and**
    - Prescribed by, or in consultation with, a neurologist; **and**
    - Initial authorization will be for no more than 12 months

- For **continuation of therapy, all** of the following:
    - Patient has previously been treated with Vyvgart Hytrulo; **and**
    - Documentation of positive clinical response to therapy as measured by an objective scale [e.g., Rankin, Modified Rankin, Medical Research Council (MRC) scale]; **and**
    - Patient is **not** receiving Vyvgart Hytrulo in combination with an immune globulin; **and**
    - Vyvgart Hytrulo is dosed according to the FDA-labeled dosing for CIDP; **and**
    - Prescribed by, or in consultation with, a neurologist; **and**
    - Reauthorization will be for no more than 12 months

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other policies and guidelines may apply.

HCPCS Code	Description
J9256	Injection, nipocalimab-aahu, 3 mg
J9332	Injection, efgartigimod alfa-fcab, 2 mg
J9333	Injection, rozanolixizumab-noli, 1 mg
J9334	Injection, efgartigimod alfa, 2 mg and hyaluronidase-qvfc

Diagnosis Code	Description
G61.81	Chronic inflammatory demyelinating polyneuritis
G70.0	Myasthenia gravis
G70.00	Myasthenia gravis without (acute) exacerbation
G70.01	Myasthenia gravis with (acute) exacerbation

Background

Efgartigimod alfa-fcab is a human IgG1 antibody fragment that binds to the neonatal Fc receptor (FcRn), resulting in the reduction of circulating IgG. The pharmacological effect of efgartigimod alfa-fcab was assessed by measuring the decrease in serum IgG levels and AChR autoantibody levels. In patients testing positive for AChR antibodies and who

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were treated with efgartigimod alfa-fcab, there was a reduction in total IgG levels relative to baseline. Decrease in AChR autoantibody levels followed a similar pattern.

Efgartigimod alfa and hyaluronidase-qvfc is a coformulation of efgartigimod alfa and hyaluronidase. Efgartigimod alfa is a human IgG1 antibody fragment that binds to the neonatal Fc receptor (FcRn), resulting in the reduction of circulating IgG. Hyaluronidase increases permeability of the subcutaneous tissue by depolymerizing hyaluronan. This effect is transient and permeability of the subcutaneous tissue is restored within 24 to 48 hours.

Nipocalimab-aahu is a human IgG1 monoclonal antibody that binds to neonatal Fc receptor (FcRn), resulting in the reduction of circulating IgG levels.

Rozanolixizumab-noli is a humanized IgG4 monoclonal antibody that binds to the neonatal Fc receptor (FcRn), resulting in the reduction of circulating IgG.

Benefit Considerations

Some Certificates of Coverage allow for coverage of experimental/investigational/unproven treatments for life-threatening illnesses when certain conditions are met. The member specific benefit plan document must be consulted to make coverage decisions for this service. Some states mandate benefit coverage for off-label use of medications for some diagnoses or under some circumstances when certain conditions are met. Where such mandates apply, they supersede language in the benefit document or in the medical or drug policy.

Additional Information: Clinical coverage in this policy addresses the drug only. It does not address coverage for drug administration in a hospital outpatient department. Refer to the member specific benefit plan document and the Medical Benefit Drug Policy titled Provider Administered Drugs – Site of Care for more information. The member specific benefit plan document determines coverage.

Clinical Evidence

Generalized Myasthenia Gravis

Efgartigimod alfa-fcab is indicated for the treatment of generalized myasthenia gravis (gMG) in adult patients who are anti-acetylcholine receptor (AChR) antibody positive.

The efficacy of efgartigimod alfa-fcab for the treatment of generalized myasthenia gravis (gMG) in adults who are AChR antibody positive was established in a 26-week, multicenter, randomized, double-blind, placebo-controlled trial (Study 1; NCT03669588).

Study 1 enrolled patients who met the following criteria at screening:

- Myasthenia Gravis Foundation of America (MGFA) clinical classification class II to IV
- MG-Activities of Daily Living (MG-ADL) total score of ≥ 5
- On stable dose of MG therapy prior to screening, that included acetylcholinesterase (AChE) inhibitors, steroids, or non-steroidal immunosuppressive therapies (NSISTs), either in combination or alone
- IgG levels of at least 6 g/L

A total of 167 patients were enrolled in Study 1 and were randomized to receive either efgartigimod alfa-fcab 10mg/kg (1200 mg for those weighing 120 kg or more) (n = 84) or placebo (n = 83). Baseline characteristics were similar between treatment groups. Patients had a median age of 46 years at screening (range: 19 to 81 years) and a median time since diagnosis of 9 years. Seventy-one percent were female, and 84% were White. Median MG-ADL total score was 9, and median Quantitative Myasthenia Gravis (QMG) total score was 16. The majority of patients (n = 65 for efgartigimod alfa-fcab; n = 64 for placebo) were positive for AChR antibodies.

At baseline, over 80% of patients in each group received AChE inhibitors, over 70% in each treatment group received steroids, and approximately 60% in each treatment group received NSISTs, at stable doses.

Patients were treated with efgartigimod alfa-fcab at the recommended dosage regimen.

The efficacy of efgartigimod alfa-fcab was measured using the Myasthenia Gravis-Specific Activities of Daily Living scale (MG-ADL) which assesses the impact of gMG on daily functions of 8 signs or 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

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of ability to perform that function. A total score ranges from 0 to 24, with the higher scores indicating more impairment. In this study, an MGADL responder was defined as a patient with a 2 point or greater reduction in the total MG-ADL score compared to the treatment cycle baseline for at least 4 consecutive weeks, with the first reduction occurring no later than 1 week after the last infusion of the cycle. Studies have used different thresholds of change in MG-ADL score to indicate clinically meaningful change.[6,7] In a validation study that aimed to determine the change in MG-ADL value that would best predict improvement in MG clinical status, results from sensitivity and specificity analyses indicated that a 1-point change in MG-ADL was highly sensitive (96%) but did not have good specificity (71%), and a 3-point change had good specificity (90%) but was not very sensitive (62%). A 2-point change provided a balance between sensitivity (77%) and specificity (82%).

The primary efficacy endpoint was the comparison of the percentage of MG-ADL responders during the first treatment cycle between treatment groups in the AChR-Ab positive population. A statistically significant difference favoring efgartigimod alfa-fcab was observed in the MG-ADL responder rate during the first treatment cycle [67.7% in the efgartigimod alfa-fcab treated group vs 29.7% in the placebo-treated group ($p < 0.0001$)].

The efficacy of efgartigimod alfa-fcab was also measured using the Quantitative Myasthenia Gravis (QMG) total score which is a 13-item categorical 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. In this study, a QMG responder was defined as a patient who had a 3-point or greater reduction in the total QMG score compared to the treatment cycle baseline for at least 4 consecutive weeks, with the first reduction occurring no later than 1 week after last infusion of the cycle.

The secondary endpoint was the comparison of the percentage of QMG responders during the first treatment cycle between both treatment groups in the AChR-Ab positive patients. A statistically significant difference favoring Vyvgart was observed in the QMG responder rate during the first treatment cycle [63.1% in the efgartigimod alfa-fcab -treated group vs 14.1% in the placebo-treated group ($p < 0.0001$)].

Efgartigimod alfa and hyaluronidase-qvfc is indicated for the treatment of gMG in adult patients who are anti-acetylcholine receptor (AChR) antibody positive. Study 1 (described above) which established the effectiveness of efgartigimod alfa-fcab for the treatment of gMG in adults who are AChR antibody positive was conducted with efgartigimod alfa-fcab intravenous formulation. In Study 2, efgartigimod alfa and hyaluronidase-qvfc demonstrated a comparable pharmacodynamic effect on AChR antibody reduction as compared to the efgartigimod alfa-fcab intravenous formulation, which established the efficacy of efgartigimod alfa and hyaluronidase-qvfc. In Study 2, the pharmacological effect of efgartigimod alfa and hyaluronidase-qvfc administered subcutaneously (SC) at 1,008 mg / 11,200 Units was compared to efgartigimod alfa-fcab administered intravenously at 10 mg/kg (EFG IV) in gMG patients. The maximum mean reduction in AChR-Ab level was observed at week 4, with a mean reduction of 62.2% and 59.7% in the efgartigimod alfa and hyaluronidase-qvfc SC and efgartigimod alfa-fcab IV arm, respectively. The decrease in total IgG levels followed a similar pattern. The 90% confidence intervals for the geometric mean ratios of AChR-Ab reduction at day 29 and $AUEC_{0\text{-}4w}$ (area under the effect-time curve from time 0 to 4 weeks post dose) were within the range of 80% to 125%, indicating no clinically significant difference between the two formulations.

The efficacy of intravenous efgartigimod alfa (EFG IV) in adult patients with generalized myasthenia gravis (gMG) who are anti–acetylcholine receptor (AChR) antibody negative was evaluated in an 8-week, randomized, double-blind, placebo-controlled study (NCT06298552).

In Part A of the study, patients received EFG IV according to the recommended intravenous dosing regimen. In Part B (open-label), patients received two additional treatment cycles using the same regimen, followed by further cycles administered with variable intervals of at least 7 days between treatments, for up to two years. Study 2 included patients with gMG who met the following criteria at screening: Myasthenia Gravis Foundation of America (MGFA) Class II to IV, MG Activities of Daily Living (MG-ADL) total score ≥ 5, stable doses of standard gMG therapies [e.g., acetylcholinesterase (AChE) inhibitors, corticosteroids, and/or nonsteroidal immunosuppressive therapies (NSISTs)], and IgG levels ≥ 4 g/L. A total of 119 patients were randomized 1:1 to receive: EFG IV (10 mg/kg; 1,200 mg for patients ≥ 120 kg; n = 58), or placebo (n = 61). Treatments were given as once-weekly infusions for 4 weeks. Baseline characteristics were generally similar between groups. The median time since diagnosis was 4 years, 76% of the population was female, 80% were white, 14% were asian, and 3% were black or African American. At baseline the median MG-ADL score was 9, the Median Quantitative Myasthenia Gravis (QMG) score was 14, 75% of patients were receiving AChE inhibitors, 60% were receiving corticosteroids. NSIST use was more common in the EFG IV group (53%) than in the placebo group (36%), and a breakout of the gMG type was as follows: 61% (n = 73) were triple seronegative (negative for anti-AChR, anti-MuSK, and anti-LRP4 antibodies), 34% (n = 40) were anti-MuSK positive, and 5% (n = 6) were anti-LRP4 positive. The primary endpoint was the difference between treatment groups in mean change from baseline in MG-ADL total score at Week 4. A

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statistically significant improvement was observed with EFG IV compared with placebo with a least squares (LS) mean difference (95% CI) = -1.46 (- 2.50 to -0.41); p-value = 0.0068.

The efficacy of rozanolixizumab-noli for the treatment of gMG in adults who are anti-AChR antibody positive or anti-MuSK antibody positive was established in a multicenter, randomized, double-blind, placebo-controlled study (Study 1; NCT03971422). The study included a 4-week screening period and a 6-week treatment period followed by 8 weeks of observation. During the treatment period, rozanolixizumab-noli or placebo were administered subcutaneously once a week for six weeks.
Study 1 enrolled patients who met the following criteria:

- Presence of autoantibodies against AChR or MuSK
- Myasthenia Gravis Foundation of America (MGFA) Clinical Classification Class II to IVa
- Myasthenia Gravis-Activities of Daily Living (MG-ADL) total score of at least 3 (with at least 3 points from non-ocular symptoms)
- On stable dose of MG therapy prior to screening that included acetylcholinesterase (AChE) inhibitors, steroids, or non-steroidal immunosuppressive therapies (NSISTs), either in combination or alone
- Serum IgG levels of at least 5.5 g/L

In Study 1, a total of 200 patients were randomized 1:1:1 to receive weight-tiered doses of rozanolixizumab-noli (n = 133), equivalent to = 7 mg/kg (n = 66) or ≈10 mg/kg (n = 67), or placebo (n = 67). Baseline characteristics were similar between treatment groups. Patients had a median age of 52 years at baseline (range: 18 to 89 years) and a median time since diagnosis of 6 years. Sixty-one percent of patients were female, 68% were White, 11% were Asian, 3% were Black or African American, 1% were American Indian or Alaska Native, and 7% were of Hispanic or Latino ethnicity. Median MG-ADL total score was 8, and the median Quantitative Myasthenia Gravis (QMG) total score was 15. The majority of patients, 89.5% (n = 179) were positive for AChR antibodies and 10.5% (n = 21) were positive for MuSK antibodies. At baseline in each group, over 83% of patients received AChE inhibitors, over 56% of patients received steroids, and approximately 50% received NSISTs, at stable doses. Patients were treated with Rystiggo via subcutaneous infusion once per week for a period of 6 weeks, followed by an observation period of up to 8 weeks. The efficacy of rozanolixizumab-noli was measured using the MG-ADL scale. The primary efficacy endpoint was the comparison of the change from baseline between treatment groups in the MG-ADL total score at day 43. A statistically significant difference favoring rozanolixizumab-noli was observed in the MG-ADL total score change from baseline [-3.4 points in rozanolixizumab-noli -treated group at either dose vs -0.8 points in the placebo-treated group ($p < 0.001$)]. Reductions from baseline to day 43 in MG-ADL scores were observed in patients with AChR autoantibodypositive generalized myasthenia gravis [rozanolixizumab 7 mg/kg least-squares mean –3·03 (SE 0·89); rozanolixizumab 10 mg/kg –3·36 (0·87); placebo –1·10 (0·87); least-squares mean difference from placebo −1·94 (97·5% CI −3·06 to −0·81) and −2·26 (−3·39 to −1·13) in the rozanolixizumab 7 mg/kg and 10 mg/kg groups, respectively]. For patients with MuSK autoantibodypositive gMG, least-squares mean reductions were –7·28 (SE 1·94) in the rozanolixizumab 7 mg/kg group, –4·16 (1·78) in the rozanolixizumab 10 mg/kg group, and 2·28 (1·95) in the placebo group [least-squares mean difference from placebo for rozanolixizumab 7 mg/kg −9·56 (97·5% CI −15·25 to −3·87); −6·45 (−11·03 to –1·86) for the rozanolixizumab 10 mg/kg group].

Nipocalimab is 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.

The efficacy of nipocalimab was established in a 24-week, multicenter, randomized, double-blind, placebo-controlled study where patients were treated with nipocalimab or placebo. Inclusion criteria consisted of enrolled patients with gMG who had a 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 and were on stable dose of standard of care prior to baseline. The MG-ADL is a 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. In the first study, a total of 196 patients were randomized 1:1 to receive nipocalimab (n = 98) or placebo (n = 98). For the primary efficacy analysis population, 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. The efficacy of nipocalimab was measured using the MG-ADL and 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 nipocalimab was observed in MG-ADL total score change from baseline -4.7 (0.33) for nipocalimab

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compared to -3.3 (0.34) for placebo, resulting in a relative change of -1.5 (-2.4, -0.5) between nipocalimab and placebo (p = 0.002). Said differently, patients taking nipocalimab and standard of care therapy (SOC) experienced a 4.7-point mean improvement in total MG-ADL score to Weeks 22, 23, and 24 while patients taking placebo + SOC therapy saw a 3.3-point mean improvement. The efficacy of nipocalimab 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). In a subgroup analysis based on patients with anti-AChR and anti-MuSK antibody-positive gMG, patients taking nipocalimab showed reduction in MG-ADL consistent with the overall study population. Those with anti-AChR antibody-positive gMG taking nipocalimab experienced a 5.06-point mean improvement from baseline in MG-ADL total score to Weeks 22, 23, and 24, while patients taking placebo (n = 70) had a 3.44-point mean improvement from baseline. The between-group difference was -1.62 (95% CI: -2.62 to -0.62). Patients with anti-MuSK antibody-positive gMG taking nipocalimab experienced a 3.79-point mean improvement from baseline in MG-ADL total score to Weeks 22, 23, and 24, while patients taking placebo had a 0.25-point mean improvement from baseline. The between-group difference was -3.54 (95% CI: -6.78 to -0.30).

Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)

The efficacy of efgartigimod alfa and hyaluronidase-qvfc for CIDP was based on a two-stage study that included an open-label period to identify efgartigimod alfa and hyaluronidase-qvfc responders (stage A), who then entered a randomized, double-blind, placebo-controlled, withdrawal period (stage B). In stage B, a total of 221 patients were randomized to receive efgartigimod alfa and hyaluronidase-qvfc or placebo. The study enrolled male and female patients age 18 years and older, who at the time of screening, had a documented diagnosis of definite or probable CIDP using the European Federation of Neurological Societies/Peripheral Nerve Society (EFNS/PNS; 2010) criteria for progressing or relapsing forms. The primary endpoint was the time to clinical deterioration defined as a 1-point increase in adjusted Inflammatory Neuropathy Cause and Treatment (aINCAT) at two consecutive visits or a > 1-point increase in aINCAT at one visit. Patients who received efgartigimod alfa and hyaluronidase-qvfc experienced a longer time to clinical deterioration compared to patients who received placebo (hazard ratio 0.394, 95% CI: 0.253, 0.614; p < 0.0001).

Professional Societies

Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)

The European Academy of Neurology and Peripheral Nerve Society published in 2021 a second revision of a guideline on diagnosis and treatment of chronic inflammatory demyelinating polyradiculoneuropathy (CIDP).[12] The task force refined the clinical criteria for defining CIDP into “typical CIDP” and “CIDP variants”. The task force also reduced the levels of electrodiagnostic certainty, as used in the 2010 EFNS/PNS guideline from three (definite, probable, possible CIDP) to only two (CIDP and possible CIDP), because of empirical evidence showing that the sensitivity and specificity of electrodiagnostic criteria for probable and definite CIDP do not significantly differ. In regard to the diagnosis of definite or probable CIDP, the task force concluded:

- **Clinical diagnostic criteria**:
  - Typical CIDP
    - All the following:
      - Progressive or relapsing, symmetric, proximal, and distal muscle weakness of upper and lower limbs, and sensory involvement of at least two limbs
      - Developing over at least 8 weeks
      - Absent or reduced tendon reflexes in all limbs
  - CIDP variants
    - One of the following, but otherwise as in typical CIDP (tendon reflexes may be normal in unaffected limbs):
      - Distal CIDP: distal sensory loss and muscle weakness predominantly in lower limbs
      - Multifocal CIDP: sensory loss and muscle weakness in a multifocal pattern, usually asymmetric, upper limb predominant, in more than one limb
      - Focal CIDP: sensory loss and muscle weakness in only one limb
      - Motor CIDP: motor symptoms and signs without sensory involvement
      - Sensory CIDP: sensory symptoms and signs without motor involvement
- **Electrodiagnostic criteria**:
  1. Strongly supportive of demyelination: At least one of the following:
     a. Motor distal latency prolongation ≥ 50% above ULN in two nerves (excluding median neuropathy at the wrist from carpal tunnel syndrome); or
     b. Reduction of motor conduction velocity ≥ 30% below LLN in two nerves; or

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c. Prolongation of F-wave latency ≥ 20% above ULN in two nerves (≥ 50% if amplitude of distal negative peak CMAp < 80% of LLN); or
d. Absence of F-waves in two nerves (if these nerves have distal negative peak CMAP amplitudes ≥ 20% of LLN) + ≥ 1 other demyelinating parameter* in ≥ 1 other nerve; or
e. Motor conduction block: ≥ 30% reduction of the proximal relative to distal negative peak CMAP amplitude, excluding the tibial nerve, and distal negative peak CMAP amplitude ≥ 20% of LLN in two nerves; or in one nerve + ≥ 1 other demyelinating parameter* except absence of F-waves in ≥ 1 other nerve; or
f. Abnormal temporal dispersion: > 30% duration increase between the proximal and distal negative peak CMAP (at least 100% in the tibial nerve) in ≥ 2 nerves; or
g. Distal CMAP duration (interval between onset of the first negative peak and return to baseline of the last negative peak) prolongation in ≥ 1 nerve[13] + ≥ 1 other demyelinating parameter* in ≥ 1 other nerve
    - (LFF 2 Hz) median > 8.4 ms, ulnar > 9.6 ms, peroneal > 8.8 ms, tibial > 9.2 ms
    - (LFF 5 Hz) median > 8.0 ms, ulnar > 8.6 ms, peroneal > 8.5 ms, tibial > 8.3 ms
    - (LFF 10 Hz) median > 7.8 ms, ulnar > 8.5 ms, peroneal > 8.3 ms, tibial > 8.2 ms
    - (LFF 20 Hz) median > 7.4 ms, ulnar > 7.8 ms, peroneal > 8.1 ms, tibial > 8.0 ms

2. Weakly supportive of demyelination: As in (1) but in only one nerve

*Any nerve meeting any of the criteria (a-g)

U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

Vyvgart is a neonatal Fc receptor blocker indicated for the treatment of generalized myasthenia gravis (gMG).

Vyvgart Hytrulo is a combination of efgartigimod alfa, a neonatal Fc receptor blocker, and hyaluronidase, an endoglycosidase, indicated for the treatment of generalized myasthenia gravis (gMG). Vygart Hytrulo is also indicated for the treatment of adult patients with chronic inflammatory demyelinating polyneuropathy (CIDP).

Rystiggo is a neonatal Fc receptor blocker indicated for the treatment of generalized myasthenia gravis (gMG) in adult patients who are anti-acetylcholine receptor (AChR) or anti muscle-specific tyrosine kinase (MuSK) antibody positive.

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.

Centers for Medicare and Medicaid Services (CMS)

Medicare does not have a National Coverage Determination (NCD) for Vyvgart (efgartigimod alfa-fcab), Vyvgart Hytrulo (efgartigimod alfa and hyaluronidase-qvfc), Rystiggo (rozanolixizumab-noli), and Imaavy (nipocalimab-aahu). Local Coverage Determinations/Articles (LCDs/LCAs) do not exist.

In general, Medicare covers outpatient (Part B) drugs that are furnished "incident to" a physician's service provided that the drugs are not usually self-administered by the patients who take them. Refer to the Medicare Benefit Policy Manual, Chapter 15, §50 - Drugs and Biologicals. (Accessed January 13, 2026).

**Preferred therapy criteria is not applicable for Medicare Advantage members.

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Policy History/Revision Information

Date	Summary of Changes
10/01/2026	**Coverage Rationale** ***Generalized Myasthenia Gravis*** • Replaced criterion requiring: ○ "Positive serologic test for anti-AChR antibodies" with "*One of the following:* positive serologic test for anti-AChR antibodies, *positive serologic test for anti-MuSK antibodies, positive serologic test for anti-LRP4 antibodies, or negative serologic test for anti-AChR, anti-MuSK, and anti-LRP4 antibodies (triple seronegative)*" ○ "One of the following: the patient has a history of failure of at least two immunosuppressive agents over the course of at least 12 months (e.g., azathioprine, corticosteroids, cyclosporine, methotrexate, mycophenolate, etc.), or the patient has a history of failure of at least one immunosuppressive therapy and has required four or more courses of plasmapheresis/plasma exchanges and/or immune globulin over the course of at least 12 months without symptom control" with "*if anti-AChR antibody positive, anti-LRP4 antibody positive, or triple seronegative,* one of the following: the patient has a history of failure of at least two immunosuppressive agents over the course of at least 12 months (e.g., azathioprine, corticosteroids, cyclosporine, methotrexate, mycophenolate, etc.), or the patient has a history of failure of at least one immunosuppressive therapy and has required four or more courses of plasmapheresis/plasma exchanges and/or immune globulin over the course of at least 12 months without symptom control • Added criterion requiring the patient has a history of failure of at least one immunosuppressive agent over the course of at least 12 months (e.g., azathioprine, corticosteroids, cyclosporine, methotrexate, mycophenolate, etc.) if anti-muscle-specific tyrosine kinase (MuSK) antibody positive **Applicable Codes** • Added ICD-10 diagnosis code G70.0 **Supporting Information** • Updated *Clinical Evidence*, *FDA*, and *References* sections to reflect the most current information • Archived previous policy version 2026D0111O

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Instructions for Use

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