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Efgartigimod alfa-fcab or Efgartigimod alfa and hyaluronidase-qvfc

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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 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, New England Journal of Medicine, 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

NOTE 1: Efgartigimod alfa and hyaluronidase-qvfc (Vyvgart® Hytrulo) may be self-administered. For self-administered medications, please refer to the applicable pharmacy benefit plan.

Chronic Inflammatory Demyelinating Polyneuropathy

Efgartigimod alfa and hyaluronidase-qvfc (Vyvgart Hytrulo) **may be considered medically necessary** to treat individuals 18 years of age or older with chronic inflammatory demyelinating polyneuropathy following previous failure of or contraindication to immunoglobulin and corticosteroids.

Myasthenia Gravis

Efgartigimod alfa-fcab (Vyvgart®) or efgartigimod alfa and hyaluronidase-qvfc (Vyvgart Hytrulo) **may be considered medically necessary** to treat individuals 18 years of age or older with generalized myasthenia gravis meet ALL the following criteria:

- Positive serologic test for anti-acetylcholine receptor;
- Myasthenia Gravis Foundation of America Clinical Classification II to IV;
- Myasthenia Gravis Activities of Daily Living total score of ≥ 5 ; and

- Inadequate treatment response, intolerance, or contraindication to an acetylcholinesterase inhibitor (e.g., pyridostigmine, neostigmine) and at least ONE immunosuppressive therapy (e.g., azathioprine, cyclosporine, mycophenolate mofetil, tacrolimus, methotrexate, cyclophosphamide) either in combination or as monotherapy.

Efgartigimod alfa-fcab (Vyvgart) or Efgartigimod alfa and hyaluronidase-qvfc (Vyvgart Hytrulo) **are 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

Efgartigimod alfa-fcab

Efgartigimod is supplied in a 400 mg/20 mL single-dose vial. The recommended dose of efgartigimod for adults with gMG who are anti-AChR antibody positive is 10 mg/kg given as an IV infusion over 1 hour once weekly for 4 weeks. In individuals weighing ≥ 120 kg, the recommended dose is 1200 mg per infusion. Providers should avoid administration of efgartigimod alfa-fcab to individuals with an active infection. Subsequent treatment cycles should be administered based on clinical evaluation. The safety of initiating subsequent cycles sooner than 50 days from the start of the previous treatment cycle has not been established. If a scheduled infusion is missed, the drug may be given up to 3 days after the scheduled time point. Thereafter, the original dosing schedule can resume until the treatment cycle is completed. Individuals should be monitored during administration and for 1 hour thereafter for clinical signs and symptoms of hypersensitivity reactions. If such a reaction occurs, therapy should be discontinued and appropriate supportive measures instituted. Providers should evaluate the need to administer age-appropriate vaccines according to immunization guidelines before initiation of a new treatment cycle with efgartigimod alfa-fcab.

Efgartigimod alfa and hyaluronidase-gvfc

Efgartigimod alfa and hyaluronidase-gvfc is supplied as a single-dose vial containing 1008 mg efgartigimod alfa and 11,200 units hyaluronidase per 5.6 mL. Efgartigimod alfa and hyaluronidase-gvfc is intended for subcutaneous administration every 4 weeks by a healthcare professional. Subsequent treatment cycles should be administered based on clinical evaluation. The safety of initiating subsequent cycles sooner than 50 days from the start of the previous treatment cycle has not been established. If a scheduled infusion is missed, the drug may be given up to 3 days after the scheduled time point. Thereafter, the original dosing schedule may resume until the treatment cycle is completed. Individuals should be monitored during administration and for 30 minutes thereafter for clinical signs and symptoms of hypersensitivity reactions. If such a reaction occurs, therapy should be discontinued and appropriate supportive measures instituted. Prescribers should evaluate

the need to administer age-appropriate vaccines according to immunization guidelines before initiation of a new treatment cycle with efgartigimod alfa and hyaluronidase-gvfc.

Myasthenia Gravis Foundation of America Clinical Classification

In 1997, the Medical Scientific Advisory Board of the Myasthenia Gravis Foundation of America formed a task force to address the need for universally accepted classifications, grading systems, and analytic methods for 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 into 5 main classes and several subclasses, as follows:

- **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.

The Myasthenia Gravis Activities of Daily Living Scale

The Myasthenia Gravis Activities of Daily Living scale was developed in the late 1990s to assess the status of symptoms and activities in MG. It is an 8-item, patient reported questionnaire that can be completed in 2–3 minutes with no need for specialized equipment or training. See Table 1.

Table 1. Myasthenia Gravis Activities of Daily Living Scale

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

Chronic Inflammatory Demyelinating Polyneuropathy

Chronic inflammatory demyelinating polyneuropathy (also known as chronic inflammatory demyelinating polyradiculoneuropathy) is an acquired, immune mediated neuropathy affecting peripheral nerves and nerve roots, typically characterized by a relapsing remitting or progressive course of symmetric weakness of proximal and distal muscles. CIDP is identified by electrodiagnostic and/or pathologic features of demyelination and responsiveness to immunomodulatory treatments. (3)

Patients with CIDP should have an established diagnosis based on criteria like those established by the American Academy of Neurology in 1991, (4) or those described in guidelines from the European Academy of Neurology/Peripheral Nerve Society guidelines,

revised in 2021. The 2021 EAN/PNS guidelines are the 2nd revision of the European Federation of Neurological Societies/PNS guidelines. (5) There is currently no criterion standard set of clinical or electrophysiologic criteria for the diagnosis of CIDP and its variants.

Diagnostic Criteria for CIDP

Table 2. European Academy of Neurology (EAN)/Peripheral Nerve Society guidelines: Diagnostic Criteria for CIDP (5)

Clinical Criteria for CIDP	
Typical CIDP	CIDP Variants
<p>All of the following:</p> <ul style="list-style-type: none"> • 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. 	<p>One of the following, but otherwise as in typical CIDP (tendon reflexes may be normal in unaffected limbs):</p> <ul style="list-style-type: none"> • 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.
Motor nerve conduction criteria	
<p>1) Strongly supportive of demyelination: At least one of the following: (a) Motor distal latency prolongation $\geq 50\%$ above ULN in two nerves (excluding median neuropathy at the wrist from carpal tunnel syndrome), or (b) Reduction of motor conduction velocity $\geq 30\%$ below LLN in two nerves, or (c) Prolongation of F-wave latency $\geq 20\%$ above ULN in two nerves ($\geq 50\%$ 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 $\geq 20\%$ of LLN) + ≥ 1 other demyelinating parameters^a in ≥ 1 other nerve, or (e) Motor conduction block: $\geq 30\%$ reduction of the proximal relative to distal negative peak CMAP amplitude, excluding the tibial nerve, and distal negative peak CMAP amplitude $\geq 20\%$ of LLN in two nerves; or in one nerve + ≥ 1 other demyelinating parameters^a 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</p>	

(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^b + ≥ 1 other demyelinating parameter^a 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.

Note 1. These criteria have been established by using a frequency filter bandpass of 2 Hz to 10 kHz for all parameters, except for distal CMAP duration prolongation where separate criteria were defined for four different LFFs of 2, 5, 10, and 20 Hz. Skin temperature should be maintained to at least 33°C at the palm and 30°C at the external malleolus.

Note 2. Extensiveness of motor nerve conduction studies (number of nerves to be studied and proximal studies):

- To apply motor nerve conduction criteria, the median, ulnar (stimulated below the elbow), peroneal (stimulated below the fibular head), and tibial nerves on one side are tested.
- If criteria are not fulfilled, the same nerves are tested at the other side, and/or the ulnar and median nerves are stimulated at the axilla and at Erb's point.
- Motor conduction block or slowing is not considered in the ulnar nerve across the elbow or the peroneal nerve across the knee.
- Between Erb's point and the wrist, at least 50% CMAP amplitude reduction is required for conduction block in the ulnar and median nerves. Proximal studies of the median nerve may require collision techniques to avoid ulnar nerve components in the median nerve CMAP when recorded from the abductor pollicis brevis muscle (but not when recorded from the flexor carpi radialis muscle).
- For ulnar motor conduction block in the forearm, a Martin-Gruber anastomosis should be ruled out with stimulation of the median nerve at the elbow recording over the abductor digiti minimi muscle.
- For median motor conduction block in the forearm, co-stimulation of the ulnar nerve at the wrist must be ruled out. Stimulation of the median nerve at the wrist while simultaneously recording over the abductor pollicis brevis muscle and the abductor digiti minimi muscle can detect ulnar nerve co-stimulation; stimulation should be adapted so that no CMAP is recorded from the ulnar nerve-innervated abductor digiti minimi muscle.
- If distal CMAP amplitudes are severely reduced (<1 mV), recording from more proximal muscles innervated by the peroneal, median, ulnar or radial nerve may be attempted to demonstrate motor nerve conduction abnormalities meeting electrodiagnostic criteria.

Sensory nerve conduction criteria

1) CIDP

- Sensory conduction abnormalities (prolonged distal latency, or reduced SNAP amplitude, or slowed conduction velocity outside of normal limits) in two nerves.

2) Possible CIDP

- As in (1).
- Sensory CIDP with normal motor nerve conduction studies needs to fulfil a. or b.
 - a) sensory nerve conduction velocity <80% of LLN (for SNAP amplitude >80% of LLN) or <70% of LLN (for SNAP amplitude <80% of LLN) in at least two nerves (median, ulnar, radial, sural nerve), or
 - b) sural sparing pattern (abnormal median or radial sensory nerve action potential [SNAP amplitude] with normal sural nerve SNAP amplitude) (excluding carpal tunnel syndrome).

Note 1. Skin temperature should be maintained to at least 33°C at the palm and 30°C at the external malleolus. 1. Since these criteria do not permit to identify normal reference values compatible with sensory nerve demyelination, sensory CIDP cannot be more than a possible diagnosis as based on clinical and electrophysiological criteria.

Note 2. Decline in sural nerve action potential amplitude occurs with age and use of age-dependent reference values after age 60 is advised.

CIDP: chronic inflammatory demyelinating polyneuropathy; LLN: lower limit of normal value; SNAP: sensory nerve action potential; ULN: upper limit of normal value; CMAP: compound muscle action potential; LFF: low frequency filter.

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

^b Mitsuma et al.

Myasthenia Gravis

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 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. (6) 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. (7) In contrast with AChR antibody-positive myasthenia gravis, in which complement-fixing immunoglobulin G1 (IgG1) and G3 (IgG3) subclasses predominate (8), muscle-specific kinase antibodies are mainly IgG4, (9) 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 (10) and is summarized in the section of "Policy Guidelines". 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. (11) 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. (12, 13) 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. (14)

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.

Regulatory Status

Efgartigimod alfa-fcab (Vyvgart) was approved by U.S. Food and Drug Administration on Dec. 17, 2021, for the treatment of generalized myasthenia gravis in adult patients who are anti-acetylcholine receptor antibody positive. On June 20, 2023, the FDA approved efgartigimod alfa and hyaluronidase-qvfc (Vyvgart Hytrulo) for the same indication.

On June 21, 2024, the FDA approved efgartigimod alfa and hyaluronidase-qvfc (Vyvgart Hytrulo) for the treatment of adult patients with chronic inflammatory demyelinating polyneuropathy. (2)

Rationale

This policy is based on the U.S. Food and Drug Administration labeled indications for efgartigimod alfa-fcab (Vyvgart) and efgartigimod alfa and hyaluronidase-qvfc (Vyvgart Hytrulo).

Efgartigimod alfa-fcab (Vyvgart) (1)

The efficacy of Vyvgart for the treatment of generalized myasthenia gravis 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 clinical classification class II to IV;
- MG-Activities of Daily Living total score of ≥ 5 ;
- On stable dose of MG therapy prior to screening, that included acetylcholinesterase (AChE) inhibitors, steroids, or non-steroidal immunosuppressive therapies, 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 Vyvgart 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 7 years. Seventy-one percent were female, and 84% were White. Median MG-ADL total score was 9, and median Quantitative Myasthenia Gravis total score was 16. The majority of patients (n=65 for Vyvgart; 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 Vyvgart at the recommended dosage regimen. Subsequent treatment cycles were administered based on clinical evaluation, but no sooner than 28 days from the last administration of the previous treatment cycle.

The efficacy of Vyvgart was measured using the Myasthenia Gravis-Specific Activities of Daily Living scale 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 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.

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 Vyvgart was observed in the MG-ADL responder rate during the first treatment cycle [67.7% in the Vyvgart-treated group vs 29.7% in the placebo-treated group (p<0.0001)].

The efficacy of Vyvgart was also measured using the Quantitative Myasthenia Gravis 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 Vyvgart-treated group vs 14.1% in the placebo-treated group (p<0.0001)].

The results are presented in Table 3.

Table 3. MG-ADL and QMG Responders During Cycle 1 in AChR-Ab Positive Patients (mITT Analysis Set)

	Vyvgart n=65	Placebo n=64	P-value	Odds Ratio (95% CI)
MG-ADL Responders	67.7	29.7	<0.0001	4.951 (2.213, 11.528)
QMG Responders	63.1	14.1	<0.0001	10.842 (4.179, 31.200)

CI: confidence interval; MG-ADL: Myasthenia Gravis Activities of Daily Living; mITT: modified intent-to-treat; n:number of patients for whom the observation was reported; QMG: Quantitative Myasthenia Gravis.

Logistic regression stratified for AChR-Ab status (if applicable), Japanese/Non-Japanese and standard of care, with baseline MG-ADL as covariate/QMG as covariates.

Two-sided exact p-value.

Figure 1 shows the mean change from baseline on the MG-ADL during cycle 1.

Figure 1. Mean Change in Total MG-ADL From Cycle 1 Baseline Over Time in AChR-Ab Positive Patients (mITT Analysis Set)

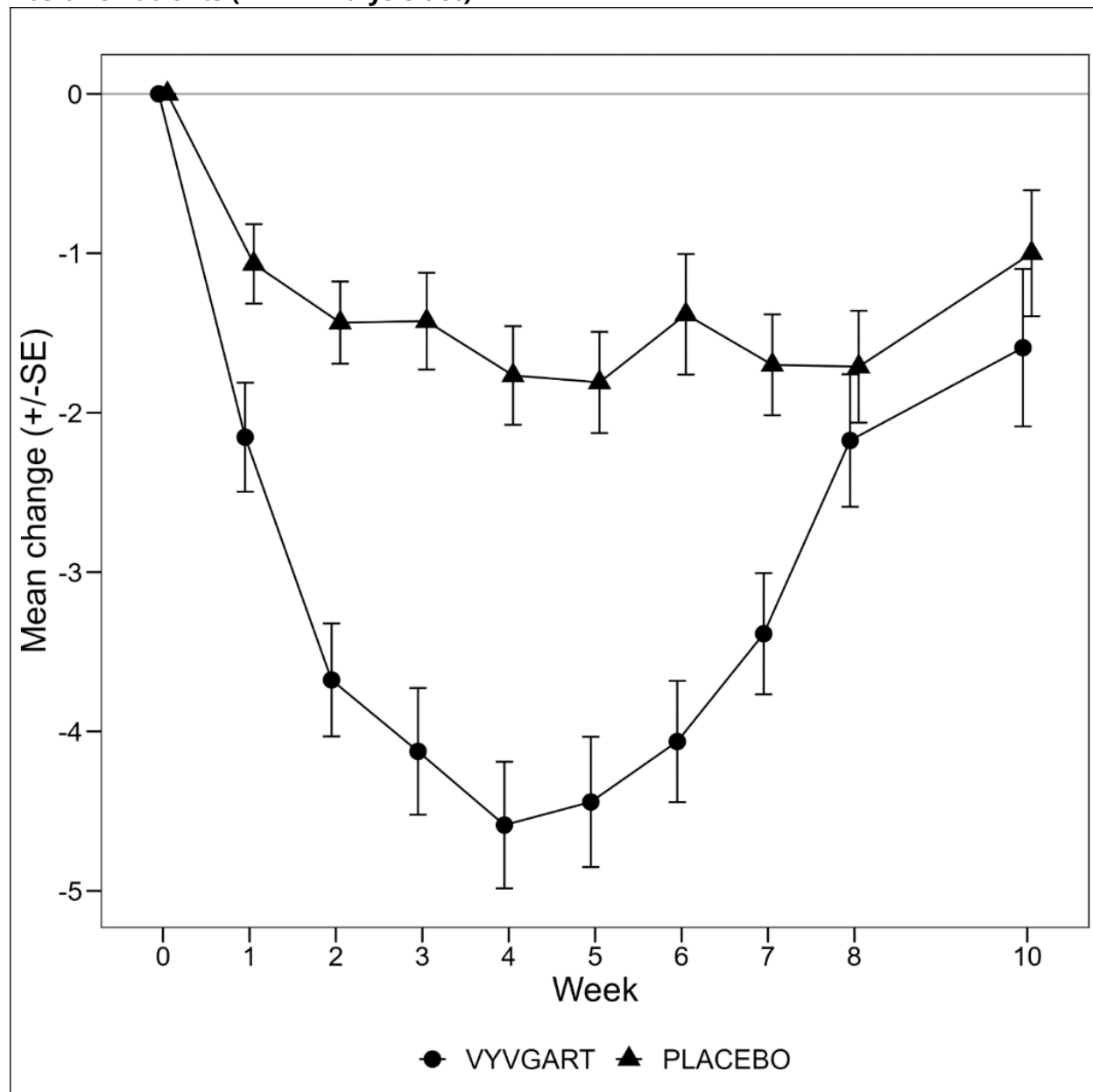
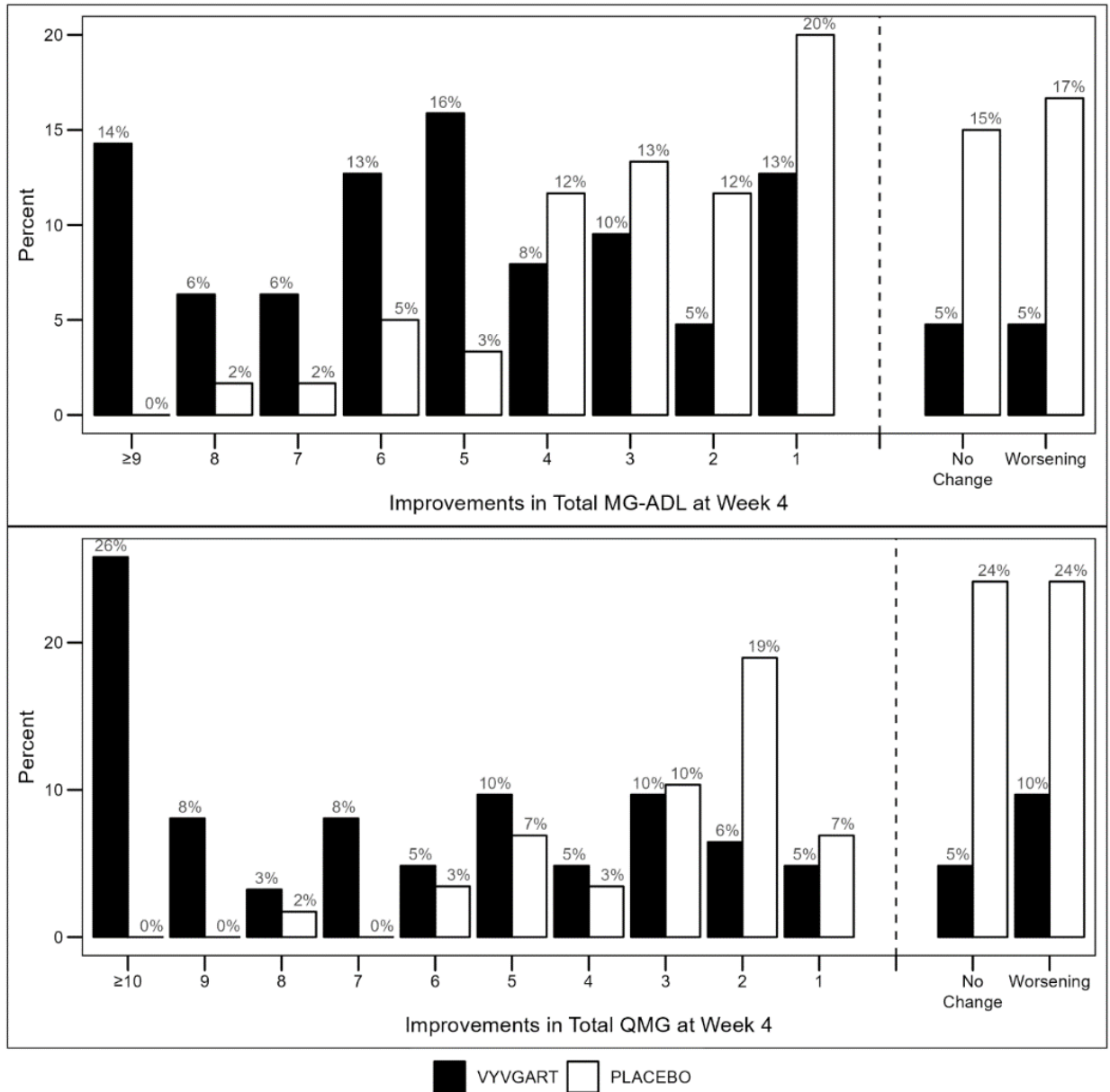


Figure 2 shows the distribution of response on the MG-ADL and QMG during cycle 1, four weeks after the first infusion of Vyvgart.

Figure 2: Percentage of Patients with MG-ADL and QMG Total Score Change 4 Weeks Post Initial Infusion of the First Cycle in AChR-Ab Positive Population



Efgartigimod alfa and hyaluronidase-qvfc (Vyvgart Hytrulo) (2)

Generalized Myasthenia Gravis

Study 1 (described below) which established the effectiveness of efgartigimod alfa-fcab for the treatment of generalized myasthenia gravis in adults who are AChR antibody positive was conducted with efgartigimod alfa-fcab intravenous formulation. In Study 2, Vyvgart Hytrulo demonstrated a comparable pharmacodynamic effect on AChR antibody reduction as compared to the efgartigimod alfa-fcab intravenous formulation, which established the efficacy of Vyvgart Hytrulo.

Study 1 (Efgartigimod Alfa-fcab Intravenous)

The efficacy of efgartigimod alfa-fcab intravenous for the treatment of generalized myasthenia gravis 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 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 EFG IV 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 7 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 EFG IV; 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 10 mg/kg EFG IV administered as an intravenous infusion over one hour once weekly for 4 weeks. In patients weighing 120 kg or more, EFG IV was administered as 1200 mg per infusion. Subsequent treatment cycles were administered based on clinical evaluation, but no sooner than 28 days from the last administration of the previous treatment cycle.

The efficacy of EFG IV was measured using the Myasthenia Gravis-Specific Activities of Daily Living scale 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 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 MG-ADL 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.

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 EFG IV was observed in the

MG-ADL responder rate during the first treatment cycle [67.7% in the EFG IV-treated group vs 29.7% in the placebo-treated group ($p < 0.0001$)].

The efficacy of EFG IV was also measured using the Quantitative Myasthenia Gravis 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 EFG IV was observed in the QMG responder rate during the first treatment cycle [63.1% in the EFG IV-treated group vs 14.1% in the placebo-treated group ($p < 0.0001$)].

Chronic Inflammatory Demyelinating Polyneuropathy

The efficacy of Vyvgart Hytrulo for the treatment of adults with chronic inflammatory demyelinating polyneuropathy was established in a two stage, multicenter study (Study 3; NCT04281472). Study 3 included an open-label period to identify Vyvgart Hytrulo responders (stage A) who then entered a randomized, double-blind, placebo-controlled, withdrawal period (stage B).

Study 3 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 Inflammatory Neuropathy Cause and Treatment disability score is a scale used to assess the impact of CIDP on daily upper and lower limb function, and is composed of the arm score and leg score (0 to 5 points for each). A total score on the INCAT ranges from 0 to 10 points with a higher number representing more disability. The adjusted INCAT disability score, identical to the INCAT disability score but with changes in the upper limb function from 0 (normal) to 1 (minor symptoms) excluded, was used to assess efficacy for Vyvgart Hytrulo for the treatment of CIDP.

Stage A

In stage A, a total of 322 patients received up to 12 once weekly subcutaneous injections of Vyvgart Hytrulo 1008 mg / 11,200 units until evidence of improvement occurred at two consecutive study visits. Improvement was defined as aINCAT improvement ≥ 1 point, I-RODS improvement ≥ 4 points, or mean grip strength improvement ≥ 8 kPa. Stage A

included 228 patients currently receiving standard-of-care therapy and 94 patients who had either not received prior treatment for CIDP or were not treated with standard-of-care therapy for at least 6 months before study entry. Sixty-nine percent of patients (n=221) who had documented improvement at two consecutive visits during Stage A then entered Stage B.

Stage B

In stage B, a total of 221 patients were randomized to receive once weekly subcutaneous injections of Vyvgart Hytrulo 1008 mg / 11,200 units (n=111) or placebo (n=110).

Baseline characteristics of patients in stage B were similar between treatment groups. Patients had a median age of 55 years (range: 20 to 82 years), a median time since CIDP diagnosis of 2.2 years, and median INCAT score of 3.0. Sixty-four percent were male and 65% were White, 30% Asian, and 1% African American.

Stage B included 146 patients currently receiving standard-of-care therapy and 75 patients who had either not received prior treatment for CIDP or were not treated with standard-of-care therapy for at least 6 months before study entry.

The primary endpoint was the time to clinical deterioration defined as a 1-point increase in aINCAT at two consecutive visits or a >1-point increase in aINCAT at one visit. Patients who had clinical deterioration or completed week 48 in Stage B without clinical deterioration were withdrawn from the placebo-controlled portion of the study. The study stopped when 88 events of clinical deterioration occurred for the primary endpoint analysis.

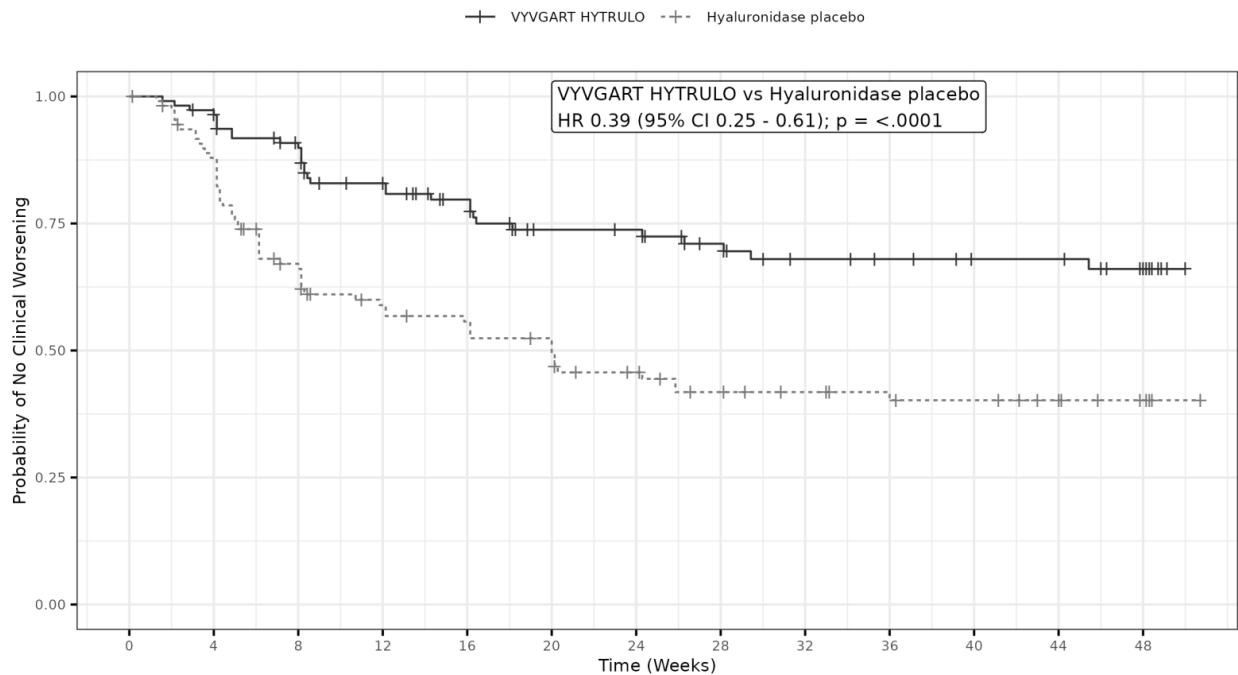
Patients who received Vyvgart Hytrulo experienced a longer time to clinical deterioration (i.e., increase of ≥1 point in aINCAT score) compared to patients who received placebo, which was statistically significant, as demonstrated by a hazard ratio of 0.394 [95% CI (0.253; 0.614) p<0.0001]. The results are presented in Table 4 and Figure 3.

Table 4: Time to First Increase of ≥1 Point in aINCAT Score In Patients With CIDP In Study 3 Stage B

	Stage B	
	Vyvgart Hytrulo (N=111)	Placebo (N=110)
Time to 1st aINCAT increase (clinical deterioration) in days Hazard ratio (95% CI)	0.394 (0.253; 0.614) p-value <0.0001	

aINCAT: adjusted Inflammatory Neuropathy Cause and Treatment; CI: confidence interval; CIDP: chronic inflammatory demyelinating neuropathy; N: number of patients in the analysis set; %: percentage.

Figure 3: Time To The First aINCAT Increase (Kaplan-Meier Curve) In Patients With CIDP In Study 3 Stage B



	Number of participants at risk												
VYVGART HYTRULO	111	107	93	80	68	56	55	48	42	40	36	36	28
Hyaluronidase placebo	110	94	67	55	51	47	38	31	28	26	24	21	16

Note: The time to clinical deterioration is defined as the time in days from the first Vyvgart Hytrulo or placebo administration in Stage B to the first occurrence of either: an increase in aINCAT score of 1 point compared with Stage B baseline if confirmed at the next visit or an increase in aINCAT score of >1 point compared with Stage B baseline.

Practice Guidelines and Position Statements

European Academy of Neurology/Peripheral Nerve Society

A 2021 guideline from the European Academy of Neurology/Peripheral Nerve Society on the diagnosis and treatment of chronic inflammatory demyelinating polyradiculoneuropathy offered the following principal treatment recommendation: “intravenous immunoglobulin or corticosteroids are strongly recommended as initial treatment in typical CIDP [chronic inflammatory demyelinating polyradiculoneuropathy] and CIDP variants.” (5)

Ongoing and Unpublished Clinical Trials

Some currently unpublished trials that might influence this review are listed in Table 5.

Table 5. Summary of Key Trials

NCT Number	Trial Name	Planned Enrollment	Completion Date
NCT04833894 ^a	Evaluating the Pharmacokinetics, Pharmacodynamics, and Safety of Efgartigimod Administered Intravenously in Children with Generalized Myasthenia Gravis (ADAPT Jr)	12	Mar 2027
NCT04980495 ^a	A Phase 3b, Randomized, Open-Label, Parallel-Group Study to Evaluate Different Dosing Regimens of Intravenous Efgartigimod to Maximize and Maintain Clinical Benefit in Patients With Generalized Myasthenia Gravis	69	May 2026
NCT05374590	A Long-term, Single-Arm, Open-label, Multicenter, Follow-on Trial of ARGX-113-2006 to Evaluate Safety of Efgartigimod Administered Intravenously in Children With Generalized Myasthenia Gravis	12	Sep 2028

NCT: national clinical trial.

^a Denotes industry-sponsored or cosponsored trial.

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 for defined coverage vs. non-coverage, benefit exclusions, and benefit limitations such as dollar or duration caps.

CPT Codes	None
HCPCS Codes	J9332, J9334

References

U.S. Food and Drug Administration Label:

1. U.S. Food and Drug Administration. Drugs@FDA. Highlights of Prescribing Information. Vyvgart. (September 2025). Available at accessdata.fda.gov (accessed Feb. 24, 2026).
2. Prescribing Label: Vyvgart Hytrulo (efgartigimod alfa and hyaluronidase-qvfc) injection, for subcutaneous use. (September 2025). Available at argenx.com (accessed on February 24, 2026).

Other:

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Centers for Medicare & Medicaid Services

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 & Medicaid Services 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 [cms.hhs.gov](https://www.cms.hhs.gov).

Policy History/Revision

Date	Description of Change
5/7/26	New medical document. Efgartigimod alfa-fcab (Vyvgart) or efgartigimod alfa and hyaluronidase-qvfc (Vyvgart Hytrulo) may be considered medically necessary to treat individuals 18 years of age or older with generalized myasthenia gravis when criteria in Coverage are met. Efgartigimod alfa and hyaluronidase-qvfc (Vyvgart Hytrulo) may be considered medically necessary to treat individuals 18 years of age or older with chronic inflammatory demyelinating polyneuropathy following previous failure of or contraindication to immunoglobulin and corticosteroids. Efgartigimod alfa-fcab (Vyvgart) or Efgartigimod alfa and hyaluronidase-qvfc (Vyvgart Hytrulo) are considered experimental, investigational and/or unproven for all other non-Food and Drug Administration approved indications, and when the above criteria are not met.