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Coverage Policy Number IP0376

Efgartigimod Intravenous

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Related Coverage Resources

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Overview

This policy supports medical necessity review for efgartigimod alfa-fcab intravenous infusion (**Vyvgart**™).

Receipt of sample product does not satisfy any criteria requirements for coverage.

Medical Necessity Criteria

Efgartigimod alfa-fcab (Vyvgart) is considered medically necessary when the following are met:

Generalized Myasthenia Gravis. Individual meets **ALL** of the following criteria:
A. Age 18 years or older
B. Documentation that the individual has confirmed anti-acetylcholine receptor antibody positive generalized myasthenia gravis

C. Has a Myasthenia Gravis Foundation of America (MGFA) clinical classification of II-IV (prior to starting therapy with Vyvgart or Vyvgart Hytrulo) [See APPENDIX 1]
D. Has a MG-Activities of Daily Living (MG-ADL) score of 5 or higher (prior to starting therapy with Vyvgart or Vyvgart Hytrulo) [See APPENDIX 2]
E. Has objective evidence of unresolved symptoms of generalized myasthenia gravis, such as difficulty swallowing, difficulty breathing, or a functional disability resulting in the discontinuation of physical activity (for example, double vision, talking, impairment of mobility)
F. Documentation of **ONE** of the following:
    i. Is currently receiving pyridostigmine
    ii. Failure, contraindication or intolerance to pyridostigmine
G. Medication is prescribed by or in consultation with a neurologist

Dosing. **ONE** of the following dosing regimens:
1. Individual is less than 120 kg. The dose is 10 mg/kg administered by intravenous infusion once weekly for 4 weeks. Additional treatment cycles are initiated no sooner than every 50 days from the start of the previous treatment cycle.
2. Individual is 120 kg or more. The dose is 1200 mg administered by intravenous infusion once weekly for 4 weeks. Additional treatment cycles are initiated no sooner than 50 days from the start of the previous treatment cycle.

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Reauthorization Criteria

Continuation of efgartigimod alfa-fcab intravenous infusion (Vyvgart) is considered medically necessary for generalized myasthenia gravis when **BOTH** of the following are met:

1. The above medical necessity criteria have been met prior to the start of Vyvgart therapy (or Vyvgart Hytrulo)
2. There is documentation of beneficial response (for example, reductions in exacerbations of myasthenia gravis; improvements in speech, swallowing, mobility, respiratory function, improvement in MG-ADL or QMG scores)

Authorization Duration

Initial approval duration: up to 6 months
Reauthorization approval duration: up to 12 months

Conditions Not Covered

Any other use is considered experimental, investigational or unproven, including the following (this list may not be all inclusive):

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

Coding Information

Note: 1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

HCPCS Codes	Description
J9332	Injection, efgartigimod alfa-fcab, 2 mg

Background

OVERVIEW
Vyvgart Intravenous, a neonatal Fc receptor blocker, is indicated for the treatment of **generalized myasthenia gravis** in adults who are anti-acetylcholine receptor antibody positive.[1]

Disease Overview
Myasthenia gravis is a chronic autoimmune neuromuscular disease that causes weakness in the skeletal muscles, which are responsible for breathing and moving parts of the body, including the arms and legs.[2] The hallmark of myasthenia gravis is muscle weakness that worsens after periods of activity and improves after periods of rest. Certain muscles such as those that control eye and eyelid movement, facial expression, chewing, talking, and swallowing are often involved in the disorder; however, the muscles that control breathing, and neck and limb movements may also be affected. Acquired myasthenia gravis results from the binding of autoantibodies to components of the neuromuscular junction, most commonly the acetylcholine receptor.[3]

Clinical Efficacy
The efficacy of Vyvgart Intravenous was evaluated in a 26-week, multicenter, randomized, double-blind, placebo-controlled trial in adults with myasthenia gravis (n = 167).[5] Among other criteria, patients were on stable doses of myasthenia gravis therapy prior to screening (e.g., acetylcholinesterase inhibitors, steroids, or non-steroidal immunosuppressive therapies), either in combination or alone. In addition, patients had a Myasthenia Gravis Foundation of America (MGFA) clinical classification class II to IV and a Myasthenia Gravis Activities of Daily Living (MG-ADL) total score of ≥ 5. MG-ADL assesses the impact of generalized myasthenia gravis on daily functions of eight signs or symptoms that are typically impacted by this disease. Each sign or symptom is assessed on a 4-point scale; a higher score indicates greater impairment. Patients were randomized to receive Vyvgart Intravenous or placebo. At baseline, most patients had stable doses of acetylcholinesterase inhibitors (> 80%), steroids (> 70%), and/or non-steroidal immunosuppressive therapies (about 60%). The primary efficacy endpoint was comparison of the percentage of MG-ADL responders during the first treatment cycle between treatment groups in the anti-acetylcholine receptor antibody-positive population. 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. Overall, 67.7% of patients who received Vyvgart Intravenous compared with 29.7% of patients who received placebo were considered MG-ADL responders (P < 0.0001).

Non-inferiority of Vyvgart® Hytrulo (efgartigimod alfa and hyaluronidase-qvfc subcutaneous injection) to Vyvgart Intravenous was demonstrated in the ADAPT-SC study, where patients were randomized to either Vyvgart Hytrulo or Vyvgart Intravenous (n = 110).[4]

Dosing Information
For patients weighing < 120 kg, the recommended dose is 10 mg/kg administered as an intravenous infusion over one hour once weekly for 4 weeks.[1] For patients weighing ≥ 120 kg, the recommended dose is 1200 mg per infusion. Administer subsequent treatment cycles 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.

Guidelines
An international consensus guidance for the management of myasthenia gravis was published in 2016.[3] The guidelines recommend pyridostigmine for the initial treatment in most patients with myasthenia gravis. The ability to discontinue pyridostigmine can indicate that the patient has met treatment goals and may guide the tapering of other therapies. Corticosteroids or immunosuppressant therapy should be used in all patients with myasthenia gravis who have not met treatment goals after an adequate trial of pyridostigmine. Nonsteroidal immunosuppressant agents include azathioprine, cyclosporine, mycophenolate mofetil, methotrexate, and tacrolimus. It is usually necessary to maintain some immunosuppression for many years, sometimes for life. Plasma exchange and intravenous immunoglobulin can be used as short-term treatments in certain patients. A 2020 update to these guidelines provides new recommendations for methotrexate, rituximab, and Soliris® (eculizumab intravenous infusion).[5] All recommendations should be considered extensions or additions to recommendations made in the initial international consensus guidance. Oral methotrexate may be considered as a steroid-sparing agent in patients with generalized myasthenia gravis who have not tolerated or responded to steroid-sparing agents. Rituximab should be considered as an early therapeutic option in patients with anti-muscle specific tyrosine kinase antibody-positive myasthenia gravis who have an unsatisfactory response to initial immunotherapy. Soliris should be considered in the treatment of severe, refractory, anti-acetylcholine receptor antibody-positive generalized myasthenia gravis.

APPENDIX 1
[Myasthenia Gravis Foundation of America (MGFA) classification]
The Myasthenia Gravis Foundation of America (MGFA) classification is aimed at separating patients in groups based on disease severity and the localization of the symptoms, and does not have an evaluative purpose. The MGFA classes are pure ocular (class I), mild generalized (class II), moderate generalized (class III), severe generalized (class IV), and intubation/myasthenic crisis (class V). Within the generalized categories II, III, and IV, patients are subclassified as class A if their symptoms are predominantly generalized or class B if their symptoms are predominantly bulbar.[5] The MGFA also has a system to classify patients based on postintervention outcomes and includes remission, defined as 1 year or longer without signs or symptoms and without any symptomatic (pyridostigmine) treatment, and which can be divided in complete (no pharmacologic treatment at all) or pharmacologic remission. Minimal manifestation status is defined as minimal signs or symptoms (no specific time-frame was defined) and pyridostigmine use may be accepted. Additionally, patients can be improved, unchanged, worse, experiencing an MG exacerbation, or have died of MG.[5] Because the original MGFA severity classification does not take into account those patients who are asymptomatic, many MG studies use a hybrid, whereby symptomatic patients are classified based on the I to V class system, and asymptomatic or oligosymptomatic patients are classified as remission or minimal manifestation status.[6]

APPENDIX 2
[Myasthenia Gravis Activities of Daily Living (MG-ADL)]
The Myasthenia Gravis Activities of Daily Living (MG-ADL) is a patient-reported outcome that combines 2 items on daily life activities—ability to brush teeth or comb hair, and limitations in the ability to rise from a chair—with 6 items reflecting other MG symptoms: diplopia, ptosis, chewing, swallowing, voice/speech problems, and respiratory symptoms. Each item is scored between 0 and 3 and total scores range from 0 to 24, where higher scores indicate more disease severity. The main advantages of the MG-ADL are that it is very easy to use, and it is completely patient reported. A drawback is that it does not have a specific recall time frame (e.g., 2 or 4 weeks) because it relies on comparing with the last visit, and that it is prone to floor effects.[7]

References

1. Vyvgart® intravenous infusion [prescribing information]. Boston, MA: Argenx; May 2022.
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3. Sanders DB, Wolfe GI, Benatar M, et al. International consensus guidance for management of myasthenia gravis. *Neurology*. 2016;87:419–425.
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5. Narayanaswami P, Sanders DB, Wolfe G, et al. International Consensus Guidance for Management of Myasthenia Gravis: 2020 Update. *Neurology*. 2021 Jan 19;96(3):114-122.

Supplemental References

6. Baggi F, Mantegazza R, Antozzi C, et al. Patient registries: useful tools for clinical research in myasthenia gravis. Ann N Y Acad Sci 2012;1274(1):107–13. [PubMed: 23252904]
7. Wolfe GI, Herbelin L, Nations SP, et al. Myasthenia gravis activities of daily living profile. Neurology 1999; 52(7):1487–9. [PubMed: 10227640]