VENTURA COUNTY
HEALTH CARE PLAN

UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Neurology – Vyvgart Intravenous Utilization Management Medical Policy
- Vyvgart® (efgartigimod alfa-fcab intravenous infusion – Argenx)

REVIEW DATE: 07/05/2023; selected revision 10/18/2023, 02/28/2024

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.

POLICY STATEMENT

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

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

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

FDA-Approved Indication

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1. **Generalized Myasthenia Gravis.** Approve if the patient meets ONE of the following (A or B):
   - **A)** Initial Therapy. Approve for 6 months if the patient meets ALL of the following (i, ii, iii, iv, v, vi, and vii):
     - **i.** Patient is ≥ 18 years of age; AND
     - **ii.** Patient has confirmed anti-acetylcholine receptor antibody positive generalized myasthenia gravis; AND
     - **iii.** Patient meets BOTH of the following (a and b):
       - **a)** Myasthenia Gravis Foundation of America classification of II to IV; AND
       - **b)** Myasthenia Gravis Activities of Daily Living (MG-ADL) score of ≥ 5; AND

iv. Patient meets ONE of the following (a or b):
  a) Patient received or is currently receiving pyridostigmine; OR
  b) Patient has had inadequate efficacy, a contraindication, or significant intolerance to pyridostigmine; AND
v. Patient has evidence of unresolved symptoms of generalized myasthenia gravis; AND
  Note: Examples of unresolved symptoms include difficulty swallowing, difficulty breathing, or a functional disability resulting in the discontinuation of physical activity (e.g., double vision, talking, impairment of mobility); AND
vi. Treatment cycles are no more frequent than every 50 days from the start of the previous treatment cycle; AND
vii. The medication is being prescribed by or in consultation with a neurologist.

B) Patient is Currently Receiving Vyvgart Intravenous (or Vyvgart Hytrulo [efgartigimod alfa and hyaluronidase-qvfc subcutaneous injection]). Approve for 1 year if the patient meets ALL of the following (i, ii, iii, and iv):
i. Patient is ≥ 18 years of age; AND
ii. Patient is continuing to derive benefit from Vyvgart Intravenous (or Vyvgart Hytrulo), according to the prescriber; AND
  Note: Examples of derived benefit include reductions in exacerbations of myasthenia gravis; improvements in speech, swallowing, mobility, and respiratory function.
iii. Treatment cycles are no more frequent than every 50 days from the start of the previous treatment cycle; AND
iv. The medication is being prescribed by or in consultation with a neurologist.

Dosing. Approve if the patient meets BOTH of the following dosing regimens (A and B):
A) Patient meets ONE of the following (i or ii):
i. Patient < 120 kg: The dose is 10 mg/kg administered by intravenous infusion once weekly for 4 weeks; OR
ii. Patient ≥ 120 kg: The dose is 1,200 mg administered by intravenous infusion once weekly for 4 weeks; AND.
B) Treatment cycles are no more frequent than every 50 days from the start of the previous treatment cycle.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Vyvgart Intravenous is not recommended in the following situations:

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

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

REFERENCES

1. Vyvgart® intravenous infusion [prescribing information]. Boston, MA: Argenx; May 2022.
2. National Institute of Neurological Disorders and Stroke (NINDS). Myasthenia Gravis Fact Sheet. National Institutes of Health (NIH) Publication No. 17-768. Publication last updated: March 2020. Available at: https://www.ninds.nih.gov/sites/default/files/migrate-documents/myasthenia_gravis_e_march_2020_508c.pdf. Accessed on June 12, 2023.
3. Sanders DB, Wolfe GI, Benatar M, et al. International consensus guidance for management of myasthenia gravis. *Neurology*. 2016;87:419–425.
4. Vyvgart® Hytrulo subcutaneous injection. Boston, MA and San Diego, CA: Argenx and Halozyme; June 2023.
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.

HISTORY

Type of Revision	Summary of Changes	Review Date
Early Annual Revision	**Generalized Myasthenia Gravis:** A requirement for treatment cycles to be no more frequent than every 50 days from the start of the previous cycle was added to criteria. The frequency for cycles was removed from the dosing section.	11/16/2022
Early Annual Revision	**Generalized Myasthenia Gravis,** Criteria for "Patient is Currently Receiving Vyvgart": Added Vyvgart Hytrulo to the criterion as the criteria will apply to a patient who is currently receiving Vyvgart or Vyvgart Hytrulo. Criterion "Patient is continuing to derive benefit from Vyvgart, according to the prescriber": Added Vyvgart Hytrulo. Criterion regarding evidence of unresolved symptoms of generalized myasthenia gravis: examples are moved to a Note. Policy renamed from Neurology – Vyvgart to Neurology – Vyvgart Intravenous.	07/05/2023
Selected Revision	**Conditions Not Recommended for Approval:** Added "Concomitant Use with Another Neonatal Fc Receptor Blocker, a Complement Inhibitor, or a Rituximab Product". Examples of Neonatal Fc Receptor Blockers and Complement Inhibitors are listed as Notes.	10/18/2023
Selected Revision	**Generalized Myasthenia Gravis:** "Treatment cycles are no more frequent than every 50 days from the start of the previous treatment cycle" was added to the Dosing section.	02/28/2024