UTILIZATION MANAGEMENT MEDICAL POLICY

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

REVIEW DATE: 11/16/2022

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

Disease Overview
MG 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 MG 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 MG results from the binding of autoantibodies to components of the neuromuscular junction, most commonly the acetylcholine receptor.[3]

Clinical Efficacy
The efficacy of Vyvgart was evaluated in a 26-week, multicenter, randomized, double-blind, placebo-controlled trial in adult patients with MG.[1] Among other criteria, patients enrolled (n = 167) were on stable doses of MG therapy prior to screening (e.g., acetylcholinesterase inhibitors, steroids, or non-steroidal immunosuppressive therapies), either in combination or alone. Patients were randomized to receive Vyvgart or placebo. At baseline, most patients had stable doses of acetylcholinesterase inhibitors (> 80%), steroids (> 70%), and/or non-steroidal immunosuppressive therapies (about 60%). The efficacy of Vyvgart was assessed using the Myasthenia Gravis-Specific Activities of Daily Living scale (MG-ADL) which evaluates the impact of generalized MG on daily functions of 8 signs or symptoms that are typically affected. The primary efficacy endpoint was the proportion of patients who were considered MG-ADL responders during the first treatment cycle. Overall, 67.7% patients who received Vyvgart compared with 29.7% of patients who received placebo were considered MG-ADL responders ($p < 0.0001$).

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 MG was published in 2016.[3] The guidelines recommend pyridostigmine for the initial treatment in most patients with MG. 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 MG 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).[4] 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 MG who have not tolerated or responded to steroid-sparing agents. Rituximab should be considered as an early therapeutic option in patients with muscle specific kinase antibody positive MG who have an unsatisfactory response to initial immunotherapy. Soliris should be considered in the treatment of severe, refractory, anti-acetylcholine receptor antibody positive generalized MG.

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of Vyvgart. 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 as well as the monitoring required for adverse events and long-term efficacy, approval requires Vyvgart 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 is recommended in those who meet the following criteria:

FDA-Approved Indication

1. **Generalized Myasthenia Gravis.** Approve if the patient meets ONE of the following criteria (A or B):
   - **A)** Initial Therapy. Approve for 6 months if the patient meets the following criteria (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.** Treatment cycles are no more frequent than every 50 days from the start of the previous treatment cycle; AND
     - **iv.** 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
     - **v.** 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
     - **vi.** Patient has 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 (e.g., double vision, talking, impairment of mobility); AND
     - **vii.** The medication is being prescribed by or in consultation with a neurologist.

B) Patient is Currently Receiving Vyvgart. Approve for 1 year if the patient meets the following (i, ii, iii, and iv):
- **i.** Patient is ≥ 18 years of age; AND
- **ii.** Treatment cycles are no more frequent than every 50 days from the start of the previous treatment cycle; AND
- **iii.** Patient is continuing to derive benefit from Vyvgart, 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.
- **iv.** The medication is being prescribed by or in consultation with a neurologist.

Dosing. Approve the following dosing regimens (A or B):

A) Patient < 120 kg. The dose is 10 mg/kg administered by intravenous infusion once weekly for 4 weeks; OR

B) Patient ≥ 120 kg. The dose is 1200 mg administered by intravenous infusion once weekly for 4 weeks.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Vyvgart is not recommended in the following situations:

1. 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: July 25, 2022. Available at: https://www.ninds.nih.gov/Disorders/Patient-Caregiver-Education/Fact-Sheets/Myasthenia-Gravis-Fact-Sheet. Accessed on November 11, 2022.
3. Sanders DB, Wolfe GI, Benatar M, et al. International consensus guidance for management of myasthenia gravis. *Neurology*. 2016;87:419–425.
4. 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
New Policy	--	12/22/2021
Selected Revision	**Generalized Myasthenia Gravis:** The requirement for a patient to have tried an immunosuppressant therapy was removed from criteria.	01/11/2022
Selected Revision	**Generalized Myasthenia Gravis:** Requirements for Myasthenia Gravis Foundation of America classification of II to IV and Myasthenia Gravis Activities of Daily Living (MG-ADL) score of ≥ 5 were added to criteria.	05/04/2022
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