Original Effective Date: 04/27/2022
Current Effective Date: 10/09/2024
Last P&T Approval/Version: 07/31/2024
Next Review Due By: 10/2024
Policy Number: C23127-A

Vyvgart (efgartigimod)

PRODUCTS AFFECTED

Vyvgart (efgartigimod), Vyvgart Hytrulo (efgartigimod alfa-hyaluronidase-qvfc)

COVERAGE POLICY

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any. This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational, or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DIAGNOSIS:
Generalized myasthenia gravis (gMG), Chronic inflammatory demyelinating polyneuropathy (CIDP)

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review. When the requested drug product for coverage is dosed by weight, body surface area or other member specific measurement, this data element is required as part of the medical necessity review. The Pharmacy and Therapeutics Committee has determined that the drug benefit shall be a mandatory generic and that generic drugs will be dispensed whenever available.

A. GENERALIZED MYASTHENIA GRAVIS:
1. Documentation of a diagnosis of generalized myasthenia gravis
   AND
2. Documentation of a positive serological test for anti-AChR antibodies
   AND

3. Documentation member is currently on a stable dose of at least 1 treatment for generalized myasthenia gravis (acetylcholinesterase (AChE) inhibitors [pyridostigmine], steroids, immunosuppressive therapy)
   AND
4. Documentation of member's Myasthenia Gravis-Specific Activities of Daily Living (MG-ADL) total score (or other means for treatment plan efficacy monitoring)
   AND
5. Documentation of inadequate response, serious side effects, or labeled contraindication to ONE or more immunosuppressive drugs used alone or in combination for at least 12 months [i.e., azathioprine, mycophenolate mofetil, cyclosporine, cyclophosphamide, methotrexate, tacrolimus, steroids]
   AND
6. Prescriber attests efgartigimod will not be used concurrently with Rystiggo (rozanolixizumab), Soliris (eculizumab), or Ultomiris (ravulizumab)

B. CHRONIC INFLAMMATORY DEMYELINATING POLYNEUROPATHY (CIDP) (VYVGART HYTRULO ONLY):
1. Documented diagnosis of CIDP with symmetric or focal neurologic deficits with slowly progressive or relapsing course over 8 weeks or longer with neurophysiological abnormalities
   AND
2. Documentation of member's baseline strength and weakness using an objective clinical measuring tool (e.g., INCAT, MRC, 6- minute timed walking test, Rankin, Modified Rankin), which will be used to monitor member's response to therapy for reauthorization. [DOCUMENTATION REQUIRED]
   AND
3. Documentation that member has met one of the following clinical/electro-diagnostic criteria [DOCUMENTATION REQUIRED]:
   i. Electrodiagnostic evidence of demyelinating neuropathy in at least two limbs, resulting in muscle weakness or sensory dysfunction confirmed by nerve conduction studies (NCS)
      OR
   ii. Results of diagnostic testing meet a recognized set of diagnostic criteria as established by the American Academy of Neurology (AAN), Inflammatory Neuropathy Cause and Treatment (INCAT), or EFNS/PNS guideline

   AND
4. Documentation of trial (3 months) and failure, serious side effects, or contraindication to ONE first line agent: IVIG, plasma exchange, or glucocorticoids (EFNS/PNS, 2021)

CONTINUATION OF THERAPY:

A. GENERALIZED MYASTHENIA GRAVIS:
1. Adherence to therapy at least 85% of the time as verified by the prescriber or member medication fill history OR adherence less than 85% of the time due to the need for surgery or treatment of an infection, causing temporary discontinuation
   AND
2. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity
   AND
3. Documentation of positive clinical response as demonstrated by low disease activity and/or improvements in the condition's signs and symptoms as evidenced by ONE of the following:
   (a) Improvement of at least 3 points (reduction in score) from pre-treatment baseline on the Myasthenia Gravis-Specific Activities of Daily Living (MG-ADL) assessment OR
   (b) Reduction in signs and symptoms of myasthenia gravis OR
   (c) Stabilization, reduction, discontinuation of dose(s) of baseline immunosuppressive therapy (IST) prior to starting Vyvgart.

B. CHRONIC INFLAMMATORY DEMYELINATING POLYNEUROPATHY (CIDP):
1. Documentation of a positive response to therapy as measured by an objective clinical measuring tool, compared to baseline: INCAT, MRC, 6-minute timed walking test, Rankin, or Modified Rankin [DOCUMENTATION REQUIRED]
   AND
2. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity

DURATION OF APPROVAL:
Initial authorization: 6 months, Continuation of Therapy: 12 months

PRESCRIBER REQUIREMENTS:
Prescribed by or in consultation with a board-certified immunologist, neurologist, or rheumatologist [If prescribed in consultation, consultation notes must be submitted with initial request and reauthorization requests]

AGE RESTRICTIONS:
18 years of age and older

QUANTITY:
Vyvgart:
10 mg/kg once weekly for 4 weeks; patients weighing 120 kg or more, the recommended dose is 1200 mg per infusion; Subsequent cycles to be administered no sooner than 50 days from the start of the previous treatment cycle.

Vyvgart Hytrulo:
gMG: 1,008 mg/11,200 units once weekly for 4 weeks; subsequent cycles to be administered no sooner than 50 days from the start of the previous treatment cycle
CIDP: 1,008 mg/11,200 units once weekly

PLACE OF ADMINISTRATION:
The recommendation is that injectable medications in this policy will be for pharmacy or medical benefit coverage and the subcutaneous injectable products administered in a place of service that is a non-hospital facility-based location.

The recommendation is that infused medications in this policy will be for pharmacy or medical benefit coverage administered in a place of service that is a non-hospital facility-based location as per the Molina Health Care Site of Care program.

Note: Site of Care Utilization Management Policy applies for Vyvgart (efgartigimod). For information on site of care, see Specialty Medication Administration Site of Care Coverage Criteria (molinamarketplace.com)

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Intravenous infusion, Subcutaneous

DRUG CLASS:
Neonatal Fc Receptor (FcRn) Antagonists

FDA-APPROVED USES:
Indicated for the treatment of adult patients with generalized myasthenia gravis (gMG) who are anti-

acetylcholine receptor (AChR) antibody positive or chronic inflammatory demyelinating polyneuropathy (CIDP).

COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

APPENDIX:
Reserved for State specific information. *Information includes, but is not limited to, State contract language, Medicaid criteria and other mandated criteria.*

State Specific Information
State Marketplace
Texas (Source: Texas Statutes, Insurance Code)
"Sec. 1369.654. PROHIBITION ON MULTIPLE PRIOR AUTHORIZATIONS.
(a) A health benefit plan issuer that provides prescription drug benefits *may not require an enrollee to receive more than one prior authorization annually* of the prescription drug benefit for *a prescription drug prescribed to treat an autoimmune disease, hemophilia, or Von Willebrand disease*.
(b) This section does not apply to:
(1) opioids, benzodiazepines, barbiturates, or carisoprodol;
(2) prescription drugs that have a typical treatment period of less than 12 months;
(3) drugs that:
(A) have a boxed warning assigned by the United States Food and Drug Administration for use; and
(B) must have specific provider assessment; or
(4) the use of a drug approved for use by the United States Food and Drug Administration in a manner other than the approved use."

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:
Myasthenia gravis is a chronic autoimmune, neuromuscular disease that causes weakness in the skeletal muscles (also called voluntary muscles) that worsens after periods of activity and improves after periods of rest. Myasthenia gravis affects voluntary muscles, especially those that are responsible for controlling the eyes, face, mouth, throat, and limbs. In myasthenia gravis, the immune system produces AChR antibodies that interfere with communication between nerves and muscles, resulting in weakness. Severe attacks of weakness can cause breathing and swallowing problems that can be life-threatening.

Vyvgart is the first approval of a new class of medication. It is an antibody fragment that binds to the neonatal Fc receptor (FcRn), preventing FcRn from recycling immunoglobulin G (IgG) back into the blood. The medication causes a reduction in overall levels of IgG, including the abnormal AChR antibodies that are present in myasthenia gravis.

The application is supported by data from the multicenter, randomized, double-blind phase 3 ADAPT trial (ClinicalTrials.gov: NCT03669588) that evaluated the efficacy and safety of efgartigimod in 167 adults with gMG. In the 26-week study 167 Patients were randomly assigned 1:1 to receive efgartigimod 10mg/kg via intravenous infusion or placebo.

The primary endpoint was the percentage of responders on the Myasthenia Gravis Activities of Daily Living (MG-ADL) score among acetylcholine receptor-antibody positive (AChR-Ab+) generalized myasthenia gravis patients. Responders were defined as having at least a 2-point improvement on the MG-ADL score for at least 4 consecutive weeks.

Findings showed that a significantly greater proportion of AChR-Ab+ patients treated with efgartigimod met the primary end point compared with placebo (67.7% vs 29.7%, respectively; P <.0001). Additionally, a greater proportion of efgartigimod-treated AChR-Ab+ patients responded on the Quantitative Myasthenia Gravis (QMG) score compared with placebo (63.1% vs 14.1%, respectively; P <.0001); a responder was defined as having at least a 3-point improvement for at least 4 consecutive weeks.

The most common adverse reactions reported with efgartigimod were respiratory tract infections, headache, and urinary tract infection. As Vyvgart causes a reduction in IgG levels, the risk of infections may increase. Hypersensitivity reactions such as eyelid swelling, shortness of breath, and rash have occurred. If a hypersensitivity reaction occurs, discontinue the infusion and institute appropriate therapy. Patients using Vyvgart should monitor for signs and symptoms of infections during treatment.

Vyvgart Hytrulo is the first FcRn blocker administered as a subcutaneous injection that is FDA-approved for the treatment of gMG. Vyvgart Hytrulo was approved based on the results of the Phase 3 ADAPTsc trial (NCT04735432), a multicenter, randomized, open-label, parallel-group bridging study to the Phase 3 ADAPT study (NCT03669588), which resulted in the approval of Vyvgart in December 2021. In ADAPTsc, 110 patients were randomized in a 1:1 ratio to receive Vyvgart Hytrulo or Vyvgart for one treatment cycle (one treatment cycle consisted of four doses at once-weekly intervals). The primary endpoint of noninferiority was met, and Vyvgart Hytrulo demonstrated a mean total IgG reduction of 66.4% from baseline at Day 29, compared to 62.2% with Vyvgart (P < 0.0001). Of note, the efficacy and safety of Vyvgart Hytrulo were also established through the ADAPT trial. Myasthenia Gravis Activities of Daily Living (MG-ADL) and Quantitative Myasthenia Gravis (QMG) measures showed consistent responses between Vyvgart and Vyvgart Hytrulo-treated groups. Vyvgart Hytrulo's safety profile is consistent with Vyvgart's, with the exception of injection site reactions (ISRs), which were higher with Vyvgart Hytrulo in clinical trials, but these were mild to moderate in severity and resolved over time.

Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) or Polyradiculoneuropathy is a neurological disorder characterized by progressive weakness and impaired sensory function in the legs and arms. Chronic Inflammatory Demyelinating Polyneuropathy (CIPD) is an immune mediated disorder which affects the peripheral nervous system. The classical presentation has symmetric proximal and distal sensory and motor involvement which develops over 8 weeks. This 8 week development time and persistence greater than 8 weeks helps to distinguish CIPD from Guillain-Barre, also referred to as Acute Inflammatory Demyelinating Polyneuropathy (AIDP). First line treatment options according to the European Academy of Neurology/Peripheral Nerve Society guideline 2021 are intravenous immunoglobulin (IVIg), corticosteroids, or plasma exchange.

The efficacy of Vyvgart Hytrulo for the treatment of adults with chronic inflammatory demyelinating polyneuropathy (CIDP) 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). Patients 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 of CIDP. Change in Inflammatory Neuropathy Cause and Treatment disability score (INCAT) was used to determine efficacy. 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 safety of Vyvgart Hytrulo in patients with CIDP was determined by the patients in Stage B of Study 3. The mean duration of treatment with Vyvgart Hytrulo in stage B was 25 weeks. The overall safety profile observed in patients with CIDP treated with Vyvgart Hytrulo was consistent with the known safety

profile of Vyvgart Hytrulo and of efgartigimod alfa-fcab administered intravenously. In Study 3, injection site reactions occurred in 15% of patients treated with VYVGART HYTRULO compared to 6% of patients who received placebo. The most common of these injection site reactions were injection site bruising and injection site erythema. All injection site reactions were mild to moderate in severity. Most injection site reactions occurred during the first 3 months of treatment.

Efgartigimod-alfa-hyaluronidase having just been approved for use in CIDP by the FDA in 2024, has not yet had its place in treatment defined.

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:
All other uses of efgartigimod are considered experimental/investigational and therefore, will follow Molina's Off- Label policy. Contraindications to Vyvgart (efgartigimod alfa-fcab) include: patients with serious hypersensitivity to efgartigimod alfa products or to any of the excipients of Vyvgart. Contraindications to Vyvgart Hytrulo (efgartigimod alfa and hyaluronidase-qvfc) include: patients with serious hypersensitivity to efgartigimod alfa products, to hyaluronidase, or to any of the excipients of Vyvgart Hytrulo.

OTHER SPECIAL CONSIDERATIONS:
Because VYVGART and VYVGART HYTRULO cause transient reduction in IgG levels, immunization with live-attenuated or live vaccines is not recommended during treatment with VYVGART and VYVGART HYTRULO. Evaluate the need to administer age appropriate immunizations according to immunization guidelines before initiation of a new treatment cycle with VYVGART and VYVGART HYTRULO.
VYVGART should be administered via intravenous infusion by a healthcare professional. Infuse the total 125 mL of diluted solution intravenously over one hour via a 0.2 micron in-line filter.
VYVGART HYTRULO is for subcutaneous use only and administered by a healthcare professional only.
If a scheduled infusion or dose is missed, VYVGART and VYVGART HYTRULO may be administered up to 3 days after the scheduled time point. Thereafter, resume the original dosing schedule until the treatment cycle is completed.

CODING/BILLING 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

HCPCS CODE	DESCRIPTION
J9332	Injection, efgartigimod alfa-fcab, 2mg
J9334	Injection, efgartigimod alfa, 2 mg and hyaluronidase-qvfc

AVAILABLE DOSAGE FORMS:
Vyvgart Hytrulo SOLN 180-2000MG-UNIT/ML single-dose vial
Vyvgart SOLN 400MG/20ML single-dose vial

REFERENCES

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SUMMARY OF REVIEW/REVISIONS	DATE
REVISION- Notable revisions: Diagnosis Required Medical Information Continuation of Therapy Quantity Route of Administration FDA-Approved Uses Background Contraindications/Exclusions/Discontinuation Coding/Billing Information References	Q3 2024
REVISION- Notable revisions: Products Affected Required Medical Information Continuation of Therapy Quantity Place of Administration Background Other Special Considerations Coding/Billing Information Available Dosage Forms References	Q4 2023
New Development	Q2 2022