Oscar Clinical Guideline: Vyvgart (efgartigimod alfa-fcab) and Vyvgart Hytrulo (efgartigimod alfa and hyaluronidase-qvfc) (PG191, Ver. 4)

Vyvgart (efgartigimod alfa-fcab) and Vyvgart Hytrulo (efgartigimod alfa and hyaluronidase-qvfc)

Disclaimer

Clinical guidelines are developed and adopted to establish evidence-based clinical criteria for utilization management decisions. Clinical guidelines are applicable according to policy and plan type. The Plan may delegate utilization management decisions of certain services to third parties who may develop and adopt their own clinical criteria.

Coverage of services is subject to the terms, conditions, and limitations of a member's policy, as well as applicable state and federal law. Clinical guidelines are also subject to in-force criteria such as the Centers for Medicare & Medicaid Services (CMS) national coverage determination (NCD) or local coverage determination (LCD) for Medicare Advantage plans. Please refer to the member's policy documents (e.g., Certificate/Evidence of Coverage, Schedule of Benefits, Plan Formulary) or contact the Plan to confirm coverage.

Summary

Generalized myasthenia gravis (gMG) is a chronic autoimmune neuromuscular disorder characterized by muscle weakness and fatigue. It is caused by the production of autoantibodies that target components of the neuromuscular junction, such as the acetylcholine receptor (AChR) or muscle-specific tyrosine kinase (MuSK). The condition leads to a breakdown in communication between nerves and muscles, resulting in weakness and fatigue of voluntary muscles.

Symptoms of gMG can vary but commonly include weakness of the eye muscles (ocular myasthenia), drooping eyelids (ptosis), blurred or double vision (diplopia), changes in facial expressions, difficulty swallowing, and shortness of breath. The severity of gMG is often classified using the Myasthenia Gravis Foundation of America (MGFA) Clinical Classification, which categorizes the disease into five main classes (I-V) based on signs, symptoms, and degree of impairment. This classification helps guide treatment decisions and assess disease progression.

Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) is a neurological disorder characterized by progressive weakness and impaired sensory function in the legs and arms. It is caused by damage to the myelin sheath of peripheral nerves.

Vyvgart (efgartigimod alfa-fcab) and Vyvgart Hytrulo (efgartigimod alfa and hyaluronidase-qvfc) target the underlying cause of gMG by blocking the neonatal Fc receptor, leading to a reduction in autoantibodies and improvement in muscle weakness and fatigue.

- Vyvgart (efgartigimod alfa-fcab) is a medication that acts as a neonatal Fc receptor blocker. It is indicated for the treatment of generalized myasthenia gravis (gMG) in adult patients who are anti-acetylcholine receptor (AChR) antibody positive.
- Vyvgart Hytrulo (efgartigimod alfa and hyaluronidase-qvfc) a combination of efgartigimod alfa, a neonatal Fc receptor blocker, and hyaluronidase, an endoglycosidase. Vyvgart Hytrulo (efgartigimod alfa-fcab and hyaluronidase-qvfc) is indicated for the treatment of:
    - Generalized myasthenia gravis (gMG) in adult patients who are anti-acetylcholine receptor (AChR) antibody positive.
    - Chronic inflammatory demyelinating polyneuropathy (CIDP) in adult patients.

Definitions

"Anti-acetylcholine receptor (anti-AChR) antibodies" are autoantibodies directed against the nicotinic acetylcholine receptor found at the neuromuscular junction.

"Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)" is a neurological disorder characterized by progressive weakness and impaired sensory function in the legs and arms due to damage to peripheral nerves.

"Documentation" refers to written information, including but not limited to:

- Up-to-date chart notes, relevant test results, and/or relevant imaging reports to support diagnoses; or
- Prescription claims records, and/or prescription receipts to support prior trials of formulary alternatives.

"Generalized myasthenia gravis (gMG)" is a chronic autoimmune neuromuscular disorder characterized by fluctuating weakness of voluntary muscles.

"INCAT (Inflammatory Neuropathy Cause and Treatment) Disability Score" is a scale used to measure disability in immune-mediated peripheral neuropathies, particularly useful in assessing CIDP.

"Medical Research Council (MRC) Sum Score" for muscle strength assessed muscle strength at 6 different sites: shoulder abductors, elbow flexors, wrist extensors, hip flexors, knee extensors, foot dorsiflexor. The score ranges from 0 to 60, with lower scores indicating greater muscle weakness.

"Modified Rankin Scale" refers to a scale used to assess CIDP. Scoring ranges from 0 to 6, with lower scores associated with no symptoms, and 6 associated with death.

"Myasthenia Gravis Foundation of America (MGFA) Clinical Classification" is a system that categorizes disease severity into five main classes (I-V) with subclasses based on signs, symptoms, and degree of impairment.

"Myasthenia Gravis Activities of Daily Living (MG-ADL)" is an 8-item patient-reported questionnaire that assesses daily functions often impacted by myasthenia gravis. Total score ranges from 0 to 24, with a higher score indicating more disability. A positive change in the score indicates worsening and a negative change indicates improvement.

"No evidence of" indicates that the reviewer has not identified any records of the specified item or condition within the submitted materials or claims history. In the absence of such evidence, the member is considered eligible. If any evidence of the item or condition is present upon review of the request, the member does not qualify.

"Quantitative Myasthenia Gravis (QMG)" is a comprehensive 13-item scale specifically designed to accurately assess the severity of myasthenia gravis. It evaluates various aspects such as endurance, fatigability, and fluctuations in symptoms. The scale assigns scores ranging from 0 to 39, with higher scores indicating a more severe manifestation of the disease. A positive change in the score indicates worsening and a negative change indicates improvement.

"[s]" indicates state mandates may apply.

"Six minute walk test (6-MWT)" is an objective evaluation of functional capacity. The individual is asked to walk a flat, 30-meter marked corridor in 6 minutes.

Clinical Indications

Medical Necessity Criteria for Clinical Review

General Medical Necessity Criteria

The Plan considers Vyvgart (efgartigimod alfa) or Vyvgart Hytrulo (efgartigimod alfa and hyaluronidase-qvfc) medically necessary when ALL of the following criteria are met:

1. Prescribed by or in consultation with a neurologist or neuromuscular disease specialist; ***AND***
2. The member is 18 years of age or older; ***AND***
3. Will not be used concomitantly with other immunomodulatory biologic therapies for generalized myasthenia gravis (e.g., efgartigimod alfa, inebiluzumab, nipocalimab, rituximab, rozanolixizumab, ravulizumab, zilucoplan, etc.); ***AND***
4. IF the request is for Vyvgart (efgartigimod alfa) or Vyvgart Hytrulo (efgartigimod alfa and hyaluronidase-qvfc) vial, the member meets ONE (1) of the following:
    a. The member has tried the self-administered Vyvgart Hytrulo (efgartigimod alfa and hyaluronidase-qvfc) prefilled syringe***; or***
    b. There is support for use of a provider-administered product (vial) over the self-administered product (Vyvgart Hytrulo [efgartigimod alfa and hyaluronidase-qvfc] prefilled syringe)***; AND***
5. Vyvgart (efgartigimod alfa) or Vyvgart Hytrulo (efgartigimod alfa and hyaluronidase-qvfc) is being prescribed at a dose and frequency that is within FDA approved labeling OR is supported by compendia or evidence-based published dosing guidelines for the requested indication; ***AND***
6. The member meets the applicable Medical Necessity Criteria for Initial Clinical Review or Subsequent Clinical Review listed below.

Medical Necessity Criteria for Initial Clinical Review

Initial Indication-Specific Criteria

Generalized Myasthenia Gravis (gMG)

The Plan considers Vyvgart (efgartigimod alfa) or Vyvgart Hytrulo (efgartigimod alfa and hyaluronidase-qvfc) medically necessary when ALL of the following criteria are met:

7. The member meets the above General Medical Necessity Criteria; ***AND***
8. The member has a confirmed diagnosis of generalized myasthenia gravis (gMG) AND documentation of ALL of the following:
    a. Positive serologic test for anti-acetylcholine receptor (anti-AChR) antibodies; *and*

b. Myasthenia Gravis Foundation of America (MGFA) Clinical Classification Class II to IV (*see* Appendix A, Table 1); *and*
c. Baseline Myasthenia Gravis-Activities of Daily Living (MG-ADL) total score of at least (≥) 5; *AND*

9. The member is unable to use, limited by toxicity, or has adequately tried and failed or experienced insufficient response to at least TWO (2) standard therapies for gMG, such as[s]:
    a. Cholinesterase inhibitors (e.g., pyridostigmine); *and/or*
    b. Corticosteroids (e.g., prednisone) or inability to taper steroids below a reasonably acceptable level without return of symptoms; *and/or*
    c. Non-steroidal immunosuppressive therapies (e.g., azathioprine, cyclosporine, mycophenolate mofetil, cyclophosphamide, tacrolimus).

If the above prior authorization criteria are met, the requested product will be authorized for 6-months.[s]

Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)

The Plan considers Vyvgart Hytrulo (efgartigimod alfa and hyaluronidase-qvfc) medically necessary when ALL of the following criteria are met:

7. The member meets the above General Medical Necessity Criteria; *AND*
8. The member has a confirmed diagnosis of Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) with ALL of the following:
    a. Disease course is progressive or relapsing and remitting for 2 months or longer; *and*
    b. Electrodiagnostic testing indicating demyelination; *and*
    c. Baseline strength/weakness documented using an objective clinical measuring tool (e.g., INCAT, MRC muscle strength, 6-MWT, Rankin, Modified Rankin); *AND*
9. The member meets ONE (1) of the following:
    a. Has had an inadequate response or intolerable adverse event to at least ONE (1) of the following therapies:
        i. Immunoglobulins (i.e., intravenous Immunoglobulin (IVIG), subcutaneous Immunoglobulin); *or*
        ii. Corticosteroids (e.g., prednisone, dexamethasone); *or*
        iii. Plasma exchange (i.e. plasmapheresis); *or*
    b. Has a documented clinical reason that precludes the use of immunoglobulins, corticosteroids, and plasma exchange.

If the above prior authorization criteria are met, the requested product will be authorized for 6-months.[s]

Continued Care

Medical Necessity Criteria for Subsequent Clinical Review

The Plan considers Vyvgart (efgartigimod alfa) or Vyvgart Hytrulo (efgartigimod alfa and hyaluronidase-qvfc) medically necessary when ALL of the following criteria are met:

1. Prescribed by or in consultation with a neurologist or neuromuscular disease specialist; *AND*
2. Will not be used concomitantly with other immunomodulatory biologic therapies for generalized myasthenia gravis (e.g., efgartigimod alfa, inebiluzumab, nipocalimab, rituximab, rozanolixizumab, ravulizumab, zilucoplan, etc.); *AND*
3. Vyvgart (efgartigimod alfa) or Vyvgart Hytrulo (efgartigimod alfa and hyaluronidase-qvfc) is being prescribed at a dose and frequency that is within FDA approved labeling OR is supported by compendia or evidence-based published dosing guidelines for the requested indication; *AND*
4. There is no unacceptable toxicity or adverse reaction to therapy, such as:
    a. Serious infections (e.g. serious respiratory or urinary tract infections); *and/or*
    b. Severe hypersensitivity reactions; *and/or*
    c. Severe immunosuppression; *and/or*
    d. Other intolerable side effects or reactions; *AND*
5. There is documentation of positive clinical response to therapy, as evidenced by ONE (1) of the following:
    a. For Generalized Myasthenia Gravis (gMG) (Vyvgart or Vyvgart Hytrulo):
        i. Improvement in Myasthenia Gravis-Activities of Daily Living (MG-ADL), MG Manual Muscle Test (MMT), MG-Composite, OR Quantitative Myasthenia Gravis (QMG) score from baseline; *or*
        ii. Achievement of minimal symptom expression or pharmacological remission; *or*
        iii. Lack of relapses or reduced frequency/severity of relapses compared to baseline; *or*
    b. For Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) (Vyvgart Hytrulo ONLY):
        i. Improvement based on an objective clinical measuring tool (e.g., INCAT, MRC muscle strength, 6-MWT, Rankin, Modified Rankin); *AND*
6. Ongoing therapy is required to maintain disease stability and control.

If the above reauthorization criteria are met, the requested product will be authorized for up to 6-months.[s]

Experimental or Investigational / Not Medically Necessary[s]

Vyvgart (efgartigimod alfa-fcab) and Vyvgart Hytrulo (efgartigimod alfa-fcab and hyaluronidase-qvfc) for any other indication or use is considered not medically necessary by the Plan, as it is deemed to be experimental, investigational, unproven, or not medically necessary. Non-covered indications include, but are not limited to, the following:

- Guillain-Barré Syndrome (GBS). There are no high quality studies to support the safety and efficacy of Vyvgart (efgartigimod alfa-fcab) or Vyvgart Hytrulo (efgartigimod alfa-fcab and hyaluronidase-qvfc) for the management of GBS.
- Pemphigus Foliaceus orPemphigus Vulgaris (PV) . Only one small (n=34) open-label study has found promising results with Vyvgart (efgartigimod alfa-fcab) for the management of pemphigus foliaceus or vulgaris, however larger, high-quality studies are needed to support this indication.
- Primary Immune Thrombocytopenia (ITP). Two clinical trials have shown promising results for Vyvgart (efgartigimod alfa-fcab) and the management of ITP, however further studies are needed to support the safety and efficacy of Vyvgart (efgartigimod alfa-fcab) in ITP. Several studies are currently in recruitment (NCT07194850, NCT06831058, NCT06544499) or active phases (NCT04812925, NCT04225156)) which may further support this indication in the future.
- Thrombocytopenia. There are no high quality studies to support the safety and efficacy of Vyvgart (efgartigimod alfa-fcab) or Vyvgart Hytrulo (efgartigimod alfa-fcab and hyaluronidase-qvfc) for the management of thrombocytopenia.

Applicable Billing Codes

Table 1	
Service(s) name	
CPT/HCPCS Codes for myasthenia gravis and chronic inflammatory demyelinating polyneuropathy considered medically necessary if criteria are met:	
Code	*Description*
96365	Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); initial, up to 1 hour
96372	Therapeutic, prophylactic, or diagnostic injection (specify substance or drug); subcutaneous or intramuscular
J9332	Injection, efgartigimod alfa-fcab, 2mg
J9334	Injection, efgartigimod alfa, 2 mg and hyaluronidase-qvfc

Table 2	
ICD-10 codes considered medically necessary for myasthenia gravis and chronic inflammatory demyelinating polyneuropathy with Table 1 (CPT/HCPCS) codes if criteria are met:	
Code	*Description*
G61.81	Chronic inflammatory demyelinating polyneuritis

G70.0	Myasthenia gravis
G70.00	Myasthenia gravis without (acute) exacerbation
G70.01	Myasthenia gravis with (acute) exacerbation

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Appendix A

Table 3: Summary of Myasthenia Gravis Foundation of America (MGFA) Disease Clinical Classification

Class	*Description*
I	Ocular muscle weakness; All other muscles - normal strength
II	Mild generalized weakness
IIa	Predominantly limb/axial weakness; Lesser oropharyngeal involvement possible
IIb	Predominantly oropharyngeal/respiratory weakness; Lesser limb/axial involvement possible

III	Moderate generalized weakness
IIIa	Predominantly limb/axial weakness; Lesser oropharyngeal involvement possible
IIIb	Predominantly oropharyngeal/respiratory weakness; Lesser limb/axial involvement possible
IV	Severe generalized weakness
IVa	Predominantly limb/axial weakness; Lesser oropharyngeal involvement possible
IVb	Predominantly oropharyngeal/respiratory weakness; Lesser limb/axial involvement possible
V	Intubation, with or without ventilation; Not for routine postoperative care

NOTE: The preceding table summarizes key aspects of the Myasthenia Gravis Foundation of America (MGFA) Disease Classifications. This is provided only for quick reference. For the exact definitions and details on the MGFA Disease Classifications, please refer to the original MGFA Classification document available at https://myasthenia.org/Portals/0/MGFA%20Classification.pdf.

Clinical Guideline Revision / History Information

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