Policy Title:	Vyvgart (efgartigimod alfa-fcab) and Vyvgart Hytrulo (efgartigimod alfa and hyaluronidase-qvtc) (Intravenous and Subcutaneous)		
		Department:	PHA
Effective Date:	03/01/2022		
Review Date:	02/17/2022, 8/4/2022, 4/27/2023, 12/14/2023, 01/10/2024, 05/08/2024, 07/17/2024		

Purpose: To support safe, effective, and appropriate use of Vyvgart (efgartigimod alfa-fcab) and Vyvgart Hytrulo (efgartigimod alfa and hyaluronidase-qvtc).

Scope: Medicaid, Commercial, Medicare-Medicaid Plan (MMP)

Policy Statement:

Vyvgart (efgartigimod alfa-fcab) and Vyvgart Hytrulo (efgartigimod alfa and hyaluronidase-qvtc) are covered under the Medical Benefit when used within the following guidelines. Use outside of these guidelines may result in non-payment unless approved under an exception process.

Procedure:

Coverage of Vyvgart (efgartigimod alfa-fcab) and Vyvgart Hytrulo (efgartigimod alfa and hyaluronidase-qvtc) will be reviewed prospectively via the prior authorization process based on criteria below.

Summary of Evidence:
Vyvgart (efgartigimod) and Vyvgart Hytrulo (efgartigimod alfa and hyaluronidase-qvtc) are indicated for the treatment of generalized myasthenia gravis (gMG) in adults who test positive for the anti-acetylcholine receptor (AChR) antibody. The medication causes a reduction in overall levels of IgG, including the abnormal AChR antibodies that are present in myasthenia gravis. The safety and efficacy of Vyvgart were evaluated in a 26-week clinical study of 167 patients with myasthenia gravis who were randomized to receive either Vyvgart or placebo. The study showed that more patients with myasthenia gravis with antibodies responded to treatment during the first cycle of Vyvgart (67.7%) compared to those who received placebo (29.7%) on a measure that assesses the impact of myasthenia gravis on daily function. More patients receiving Vyvgart also demonstrated response on a measure of muscle weakness compared to placebo. 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). Vyvgart Hytrulo was evaluated in patients with chronic inflammatory demyelinating polyneuropathy (CIDP) using the adjusted Inflammatory Neuropathy Cause and Treatment (aINCAT) disability scale, ranging from 0 to 10 points with a higher number representing more disability. 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 most common side effects associated with the use of Vyvgart include respiratory tract infections, headache, and urinary tract infections. Injection site reactions were also common (≥15%) with Vyvgart Hytrulo treatment. 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.

Initial Criteria:

MMP members who have previously received this medication within the past 365 days are not Subject to Step Therapy Requirements.

- Patient is at least 18 years of age; AND
- Only one formulation of efgartigimod will be used (intravenous or subcutaneous); AND
- Will not be administered with live-attenuated or live vaccines during treatment; AND
- Patient does not have an active infection, including clinically important localized infections; AND
- Patient does not have a deficiency of immunoglobulin G (IgG) necessitating supplementation with IgG level; AND

Generalized Myasthenia Gravis (gMG) † Φ [1,2,4-6, ,8]

- Submission of medical records (e.g., chart notes, laboratory values, etc.) to support the diagnosis of generalized myasthenia gravis (gMG); AND
- Prescribed by, or in consultation with, a neurologist; AND
- Patient has a positive serologic test for anti-acetylcholine receptor (AChR) antibodies; AND
- Patient has Myasthenia Gravis Foundation of America (MGFA) Clinical Classification of Class II to IV disease§; AND
- Physician has assessed objective signs of neurological weakness and fatigability on a baseline neurological examination (e.g., including, but not limited to, the Quantitative Myasthenia Gravis (QMG) score or the MG-Activities of Daily Living (MG-ADL) score, etc.); AND

- Patient has a baseline MG-Activities of Daily Living (MG-ADL) total score of at least 5; AND
- Patient had an inadequate response after a minimum six-month trial of concurrent use with two (2) or more immunosuppressive therapies (e.g., corticosteroids plus an immunosuppressant such as azathioprine, methotrexate, cyclosporine, mycophenylate, etc.) OR
- Patient has required at least one acute or chronic treatment with plasmapheresis or plasma exchange (PE) or intravenous immunoglobulin (IVIG) in addition to immunosuppressant therapy; AND
- Will not be used in combination with other immunomodulatory biologic therapies (e.g., Rituxan (rituximab), Soliris (eculizumab), Ultomiris (ravulizumab), Empaveli or Syfovre (pegcetacoplan), Enspryng (satralizumab), Uplizna(inebilizumab), Rystiggo (rozanolixizumab), Zilbrysq (zilucoplan), etc.); AND
- Patient will avoid or use with caution medications known to worsen or exacerbate symptoms of MG (e.g., certain antibiotics, beta-blockers, botulinum toxins, hydroxychloroquine, etc.); AND
- For Medicaid members requesting Vyvgart IV at a weekly dose requiring 3 vials (>800mg to 1200mg), documentation that patient is unable to tolerate Vyvgart Hytrulo and medical rationale has been provided

Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) [2,10,11]

- Request is for Vyvgart Hytrulo; AND
- Patient's disease course is progressive or relapsing and remitting for >2 months; AND
- Patient has decreased or absent deep tendon reflexes in upper or lower limbs; AND
- Electrodiagnostic testing indicating demyelination:
  - Partial motor conduction block in at least 2 motor nerves or in 1 nerve plus one other demyelination criterion listed here in at least 1 other nerve; OR
  - Distal CMAP duration increase in at least 1 nerve plus one other demyelination criterion listed here in at least 1 other nerve; OR
  - Abnormal temporal dispersion conduction must be present in at least 2 motor nerves; OR
  - Reduced motor conduction velocity in at least 2 motor nerves; OR
  - Prolonged distal motor latency in at least 2 motor nerves; OR
  - Absent F wave in at least 2 motor nerves plus one other demyelination criterion listed here in at least 1 other nerve; OR
  - Prolonged F wave latency in at least 2 motor nerves; AND
- Baseline CIDP Disease Activity Status (CDAS) score ≥2; AND

- Baseline in strength/weakness has been documented using an objective clinical measuring tool (e.g., INCAT, Medical Research Council (MRC) muscle strength, 6-MWT, Rankin, Modified Rankin, etc.; AND
- Patient has tried and failed on at least 3-month trial of immunoglobulin (IG) or plasma exchange therapy; AND
- Will not be used as maintenance therapy in combination with immunoglobulin or Vyvgart IV (intravenous efgartigimod)

† FDA approved indication(s); ‡ Compendia recommended indication(s); Φ Orphan Drug

§ Myasthenia Gravis Foundation of America (MGFA) Disease Classifications:

- Class I: Any ocular muscle weakness; may have weakness of eye closure. All other muscle strength is normal.
- Class II: Mild weakness affecting muscles other than ocular muscles; may also have ocular muscle weakness of any severity.
  - IIa. Predominantly affecting limb, axial muscles, or both. May also have lesser involvement of oropharyngeal muscles.
  - IIb. Predominantly affecting oropharyngeal, respiratory muscles, or both. May also have lesser or equal involvement of limb, axial muscles, or both.
- Class III: Moderate weakness affecting muscles other than ocular muscles; may also have ocular muscle weakness of any severity.
  - IIIa. Predominantly affecting limb, axial muscles, or both. May also have lesser involvement of oropharyngeal muscles.
  - IIIb. Predominantly affecting oropharyngeal, respiratory muscles, or both. May also have lesser or equal involvement of limb, axial muscles, or both.
- Class IV: Severe weakness affecting muscles other than ocular muscles; may also have ocular muscle weakness of any severity.
  - IVa. Predominantly affecting limb, axial muscles, or both. May also have lesser involvement of oropharyngeal muscles.
  - IVb. Predominantly affecting oropharyngeal, respiratory muscles, or both. May also have lesser or equal involvement of limb, axial muscles, or both.
- Class V: Defined as intubation, with or without mechanical ventilation, except when employed during routine postoperative management. The use of a feeding tube without intubation places the patient in class IVb.

Continuation of Therapy Criteria:

- Patient continues to meet universal and other indication-specific relevant criteria identified in initial criteria section; AND

- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include infection, severe hypersensitivity reactions (e.g., rash, angioedema, and dyspnea, etc.), severe infusion related reactions, etc.; AND

Generalized Myasthenia Gravis (gMG)

- Patient has had an improvement (i.e., reduction) of at least 2-points from baseline in the Myasthenia Gravis-Specific Activities of Daily Living scale (MG-ADL) total score sustained for at least 4-weeks *; AND
- Improvement in muscle strength testing with fatigue maneuvers as evidenced on neurologic examination when compared to baseline; AND
- Patient requires continuous treatment, after an initial beneficial response, due to new or worsening disease activity (Note: a minimum of 50 days must have elapsed from the start of the previous treatment cycle)

*(*May substitute an improvement of at least 3-points from baseline in the Quantitative Myasthenia Gravis (QMG) total score sustained for at least 4-weeks, if available)*

Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)

- Patient has demonstrated a clinical response to therapy based on an objective clinical measuring tool (e.g., INCAT, Medical Research Council (MRC) muscle strength, 6-MWT, Rankin, Modified Rankin, etc.)

Coverage Durations:

- Initial coverage: 6 months
- Continuation of therapy coverage: 6 months

Dosage/Administration:

Generalized Myasthenia Gravis (gMG)

Drug	Dose for gMG	Maximum dose (1 billable unit = 2 mg)
Vyvgart IV	• 10mg/kg IV over 1 hour once weekly for four doses per 50 days (for patients weighing ≥120 kg, the recommended dose is 1200mg) • 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.	600 billable units weekly for four doses per 50 days
Vyvgart Hytrulo	• Vyvgart Hytrulo is supplied as a single-dose 5.6 ml vial containing 1,008 mg efgartigimod alfa and	504 billable units weekly for four doses per 50 days

	11,200 units hyaluronidase administered subcutaneously over approximately 30 to 90 seconds in cycles of once weekly injections for 4 weeks by a healthcare professional only. • 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.	

Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)

Drug	Dose for CIDP	Maximum dose (1 billable unit = 2 mg)
Vyvgart Hytrulo	• Vyvgart Hytrulo is supplied as a single-dose 5.6 ml vial containing 1,008 mg efgartigimod alfa and 11,200 units hyaluronidase administered subcutaneously over approximately 30 to 90 seconds as once weekly injections by a healthcare professional only.	504 billable units weekly

Investigational use: All therapies are considered investigational when used at a dose or for a condition other than those that are recognized as medically accepted indications as defined in any one of the following standard reference compendia: American Hospital Formulary Service Drug information (AHFS-DI), Thomson Micromedex DrugDex, Clinical Pharmacology, Wolters Kluwer Lexi-Drugs, or Peer-reviewed published medical literature indicating that sufficient evidence exists to support use. Neighborhood does not provide coverage for drugs when used for investigational purposes.

Applicable Codes:
Below is a list of billing codes applicable for covered treatment options. The below tables are provided for reference purposes and may not be all inclusive. Requests received with codes from tables below do not guarantee coverage. Requests must meet all criteria provided in the procedure section.

The following HCPCS/CPT codes are:

HCPCS/CPT Code	Description
J9332	Injection, efgartigimod alfa-fcab, 2mg

J9334	Injection, efgartigimod alfa, 2 mg and hyaluronidase-qvfc

NDC:

- Vyvgart 400 mg/20 mL single-dose vial: 73475-3041-xx
- Vyvgart Hytrulo 1,008 mg efgartigimod alfa and 11,200 units hyaluronidase per 5.6 mL (180 mg/2,000 units per mL) single-dose vial: 73475-3102-xx

References:

1. Vyvgart [package insert]. Boston, MA; Argenx, Inc., December 2021. Accessed July 2024.
2. Vyvgart Hytrulo [package insert]. Boston, MA; Argenx US, Inc., June 2023. Accessed July 2024.
3. Sussman J, Farrugia ME, Maddison P, et al. Myasthenia gravis: Association of British Neurologists' management guidelines. Pract Neurol 2015; 15: 199-206.
4. Narayanaswami P, Sanders D, Wolfe G, Benatar M, et al. International consensus guidance for management of myasthenia gravis, 2020 update. Neurology® 2021;96:114-122. doi:10.1212/WNL.0000000000011124.
5. Howard JF Jr, Bril V, Vu T, Karam C, ADAPT Investigator Study Group, et al. Safety (ADAPT): a multicentre, randomised, placebo-controlled, phase 3 trial. Lancet Neurol. 2021 Jul;20(7):526-536. doi: 10.1016/S1474-4422(21)00159-9. Erratum in: Lancet Neurol. 2021 Aug;20(8):e5.
6. Jayam-Trouth A, Dabi A, Solieman N, Kurukumbi M, Kalyanam J. Myasthenia gravis: a review. Autoimmune Dis. 2012;2012:874680. doi:10.1155/2012/874680.
7. Institute for Clinical and Economic Review. Eculizumab and Efgartigimod for the Treatment of Myasthenia Gravis: Effectiveness and Value. Draft evidence report. July 22, 2021. https://icer.org/wp-content/uploads/2021/03/ICER_Myasthenia-Gravis_Draft-Evidence-Report_072221.pdf. Accessed December 5, 2023.
8. Guidon AC, Muppidi S, Nowak RJ, et al. Telemedicine visits in myasthenia gravis: expert guidance and the Myasthenia Gravis Core Exam (MG-CE). Muscle Nerve 2021; 64:270-276
9. Gronseth GS, Barohn R, Narayanaswami P. Practice advisory: Thymectomy for myasthenia gravis (practice parameter update): Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. Neurology. 2020;94(16):705. Epub 2020 Mar 25.
10. Van den Bergh PY, Hadden RD, Bouche P, et al. European Federation of Neurological Societies/Peripheral Nerve Society guideline on management of chronic inflammatory demyelinating polyradiculoneuropathy: report of a joint task force of the European Federation of Neurological Societies [trunc]. Eur J Neurol 2010 Mar;17(3):356-63.
11. Van den Bergh PYK, van Doorn PA, Hadden RDM, et al. European Academy of Neurology/Peripheral Nerve Society guideline on diagnosis and treatment of chronic inflammatory demyelinating polyradiculoneuropathy: Report of a joint Task Force-Second

revision. J Peripher Nerv Syst. 2021 Sep;26(3):242-268. doi: 10.1111/jns.12455. Erratum in: J Peripher Nerv Syst. 2022 Mar;27(1):94. Erratum in: Eur J Neurol. 2022 Apr;29(4):1288.

12. Allen J, Basta I, Eggers C, et al. Efficacy, Safety, and Tolerability of Efgartigimod in Patients with Chronic Inflammatory Demyelinating Polyneuropathy: Results from the ADHERE Trial (PL5.002). Neurology. April 9, 2024 issue; 102 (17_supplement_1). https://doi.org/10.1212/WNL-.0000000000206324.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
G70.0	Myasthenia gravis
G70.00	Myasthenia gravis without (acute) exacerbation
G70.01	Myasthenia gravis with (acute) exacerbation
G61.81	Chronic inflammatory demyelinating polyneuritis
G61.89	Other inflammatory polyneuropathies
G62.89	Other specified polyneuropathies

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

The preceding information is intended for non-Medicare coverage determinations. Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determinations (NCDs) and/or Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. Local Coverage Articles (LCAs) may also exist for claims payment purposes or to clarify benefit eligibility under Part B for drugs which may be self-administered. The following link may be used to search for NCD, LCD, or LCA documents: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications, including any preceding information, may be applied at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC

Policy Rationale:
Vyvgart and Vyvgart Hytrulo were reviewed by the Neighborhood Health Plan of Rhode Island Pharmacy & Therapeutics (P&T) Committee. Neighborhood adopted the following clinical coverage criteria to ensure that its members use Vyvgart and Vyvgart Hytrulo according to Food and Drug Administration (FDA) approved labeling and/or relevant clinical literature. Neighborhood worked with network prescribers and pharmacists to draft these criteria. These criteria will help ensure its members are using this drug for a medically accepted indication, while minimizing the risk for adverse effects and ensuring more cost-effective options are used first, if applicable and appropriate. For INTEGRITY (Medicare-Medicaid Plan) members, these coverage criteria will only apply in the absence of National Coverage Determination (NCD) or Local Coverage Determination (LCD) criteria. Neighborhood will give individual consideration to each request it reviews based on the information submitted by the prescriber and other information available to the plan.