Medical Drug Clinical Criteria

Subject:	Vyvgart (efgartigimod alfa-fcab) and Vyvgart Hytrulo (efgartigimod alfa and hyaluronidase-qvfc)		
Document #:	CC-0207	**Publish Date:**	09/01/2023
Status:	Revised	**Last Review Date:**	08/18/2023

Table of Contents

Overview

This document addresses the use of Vyvgart (efgartigimod alfa-fcab) and Vyvgart Hytrulo (efgartigimod alfa and hyaluronidase-qvfc). Both agents are human immunoglobulin G1 (IgG1) antibody Fc fragments that target the neonatal Fc receptor (FcRn) and are approved for the treatment of generalized myasthenia gravis in adult patients who are anti-acetylcholine receptor (AchR) antibody positive. Vyvgart is administered intravenously (IV) by a healthcare professional. Vyvgart Hytrulo contains the same active ingredient as Vyvgart but is formulated with hyaluronidase to allow for subcutaneous administration by a healthcare professional.

Generalized myasthenia gravis (gMG) is an autoimmune neuromuscular disorder characterized by fluctuating motor weakness causing dyspnea, dysphagia, diplopia, dysarthria, and ptosis. Generalized myasthenia gravis is commonly mediated by IgG autoantibodies directed against the neuromuscular junction. Treatment strategies include symptomatic therapy (with anticholinesterase agents such as pyridostigmine), chronic immunotherapy with steroids or other immunosuppressive drugs (such as azathioprine, cyclosporine, or methotrexate), rapid immunotherapy (with plasmapheresis or IV immune globulin), and/or surgical treatment. Soliris and Ultomiris are immunotherapies which block complement activation triggered by acetylcholine receptor antibodies at the neuromuscular junction. Vyvgart (efgartigimod alfa-fcab), Vyvgart Hytrulo (efgartigimod alfa and hyaluronidase-qvfc), and Rystiggo (rozanolixizumab-noli) reduce autoantibodies by binding to the neonatal Fc receptor (FcRn), but differ in product administration, frequency, and population. Only Rystiggo is additionally approved for anti-muscle-specific tyrosine kinase (MuSK)-positive individuals. Myasthenia Gravis Foundation of America (MGFA) international consensus guidelines, published prior to approval FcRn inhibitors, recommend immunosuppressive drugs and/or corticosteroids for individuals who have not met treatment goals after an adequate trial of pyridostigmine.

Current published evidence includes one phase 3, multicenter, randomized, placebo-controlled trial that included individuals with non-ocular symptoms and were on a stable dose of at least one gMG treatment (cholinesterase inhibitors, corticosteroids, or non-steroidal immunosuppressants) prior to screening and throughout the study. Trial inclusion criteria required Myasthenia Gravis Foundation of America (MGFA) Clinical Classification Class II to IV disease and a Myasthenia Gravis Activities of Daily Living (MG-ADL) score of at least 5 or higher. Individuals with hepatitis B, hepatitis C, HIV, or severe infections were excluded. While individuals with acetylcholine receptor (AChR) antibody negative disease were included, the trial was not statistically powered to assess efficacy in this population. Participants in the trial were treated with Vyvgart (efgartigimod alfa-fcab) 10 mg/kg administered intravenously as four infusions per cycle (one infusion every week for 4 weeks). The primary endpoint was proportion of acetylcholine receptor antibody-positive patients who were MG-ADL responders (≥2-point MG-ADL improvement sustained for ≥4 weeks) in the first treatment cycle. Subsequent cycles were administered according to clinical response when the MG-ADL score was at least 5 and, for responders, when they no longer had a clinically meaningful decrease in MG-ADL score compared to baseline. Not all patients were responders after 1 cycle of therapy: and some achieved response after the second cycle. Vyvgart Hytrulo was approved by the FDA based on the clinical efficacy of IV Vyvgart and a study demonstrating comparable pharmacodynamic effect on AChR Antibody reduction with the subcutaneous formulation.

Clinical Criteria

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

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

Initial requests for Vyvgart (efgartigimod alfa-fcab) or Vyvgart Hytrulo (efgartigimod alfa and hyaluronidase-qvfc) may be approved if the following criteria are met:

I. Individual is 18 years of age or older; **AND**
II. Individual has a diagnosis of acetylcholine receptor antibody-positive (AChR-Ab+) generalized myasthenia gravis (gGM); **AND**
III. Documentation is provided that individual has a positive serologic test for the presence of acetylcholine receptor antibodies (AchR-Ab+); **AND**
IV. Individual has Myasthenia Gravis Foundation of America (MGFA) Clinical Classification Class II to IV disease; **AND**
V. Documentation is provided that individual has a Myasthenia Gravis Activities of Daily Living (MG-ADL) score of at least 5 or higher; **AND**
VI. Documentation is provided that individual meets both of the following (A and B):
    A. Individual has had a trial and inadequate response or intolerance to an acetylcholinesterase inhibitor; **OR**
        1. Individual is on a stable dose of an acetylcholinesterase inhibitor; **OR**
        2. Individual has a contraindication to acetylcholinesterase inhibitors;

    AND
    B. Individual has had a trial and inadequate response or intolerance to one or more immunosuppressive agents (including but not limited to systemic corticosteroids or non-steroidal immunosuppressants); **OR**
        1. Individual is on a stable dose of one or more immunosuppressive agents (including but not limited to systemic corticosteroids or non-steroidal immunosuppressants); **OR**
        2. Individual has a contraindication to systemic corticosteroids and non-steroidal immunosuppressants.

Initial Approval Duration: 26 weeks

Requests for continued use of Vyvgart (efgartigimod alfa-fcab) or Vyvgart Hytrulo (efgartigimod alfa and hyaluronidase-qvfc) may be approved if the following criteria are met:

I. Individual has experienced a prior clinical response to efgartigimod treatment as defined by the following:
    A. Reduction in signs or symptoms that impact daily function; **AND**
    B. Documentation is provided to show at least a 2-point reduction in MG-ADL total score from pre-treatment baseline;

    AND
II. Individual requires continued treatment to maintain response or to regain clinically meaningful response.

Requests for Vyvgart (efgartigimod alfa-fcab) or Vyvgart Hytrulo (efgartigimod alfa and hyaluronidase-qvfc) may not be approved for the following:

I. Individual is using in combination with maintenance immunoglobulin treatment, eculizumab, ravulizumab, rituximab, or rozanolixizumab-noli; **OR**
II. If the above criteria are not met and for all other indications.

Continuation Approval Duration: 1 year

Quantity Limits

Vyvgart (efgartigimod alfa-fcab) Quantity Limit

Drug	Limit	
Vyvgart (efgartigimod alfa-fcab) 400 mg/20 mL intravenous solution	Less than 120 kg	10 mg/kg once weekly for 4 weeks (4 weeks = 1 cycle)*
	120 kg and above	1200 mg (total of 3 vials) once weekly for 4 weeks (4 weeks = 1 cycle)*
Override Criteria		

*May approve for additional treatment cycles (4 weeks = 1 cycle) based on clinical relapse/response, but no sooner than 50 days from the start of the previous treatment cycle.

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

Drug	Limit
Vyvgart Hytrulo 1,008 mg efgartigimod alfa and 11,200 units hyaluronidase (180mg/2,000 units per mL) in a single dose vial	One vial once weekly for 4 weeks (4 weeks= 1 cycle)*
Override Criteria	
*May approve for additional treatment cycles (4 weeks = 1 cycle) based on clinical relapse/response, but no sooner than 50 days from the start of the previous treatment cycle.	

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

HCPCS	
J9332	Injection, efgartigimod alfa-fcab, 2mg [Vyvgart] (efgartigimod alfa-fcab)
J3490	Unclassified drugs when specified as [Vyvgart Hytrulo] (efgartigimod alfa-fcab and hyaluronidase-qvfc)
C9399	Unclassified drugs or biologicals when specified as [Vyvgart Hytrulo] (efgartigimod alfa-fcab and hyaluronidase-qvfc)
ICD-10 Diagnosis	
G70.00-G70.01	Myasthenia gravis

Document History

Revised: 08/18/2023
Document History:

- 08/18/2023 – Annual Review: Include new dosage form, Vyvgart Hytrulo within clinical criteria; add new quantity limit for Vyvgart Hytrulo; update combination exclusion list to include rozanolixizumab; wording and formatting updates. Coding Reviewed: Added HCPCS J3490, C9399.
- 08/19/2022 – Annual Review: Add ravulizumab to combination exclusion list; wording and formatting updates. Coding Reviewed: No changes.
- 1/4/2022 – Select Review: Add new clinical criteria document for Vyvgart (efgartigimod). Administrative update to add documentation language. Coding Reviewed: Added HCPCS codes J3490, J3590, C9399. All diagnoses pend. Effective 7/1/2022 Added HCPCS J9332. Removed J3490, J3590, C9399. Added G70.00-G70.01. Removed All diagnoses pend.

References

1. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm. Accessed: July 6, 2023.
2. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
3. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2023; Updated periodically.
4. Howard JF Jr, Bril V, Vu T, et al. Safety, efficacy, and tolerability of efgartigimod in patients with generalised myasthenia gravis (ADAPT): a multicentre, randomised, placebo-controlled, phase 3 trial. *Lancet Neurol*. 2021;20(7):526-536.
5. Gable KL, Guptill JT. Antagonism of the Neonatal Fc Receptor as an Emerging Treatment for Myasthenia Gravis. Front Immunol. 2020 Jan 10;10:3052. doi: 10.3389/fimmu.2019.03052. PMID: 31998320; PMCID: PMC6965493.
6. Lascano AM, Lalive PH. Update in immunosuppressive therapy of myasthenia gravis. Autoimmun Rev. 2021 Jan;20(1):102712. doi: 10.1016/j.autrev.2020.102712. Epub 2020 Nov 13. PMID: 33197578.
7. Narayanaswami P, Sanders DB, Wolfe G, et al for the Task Force of the Myasthenia Gravis Foundation of America (MGFA). International consensus guidance for management of myasthenia gravis 2020 update. Neurology 2021; 96:114-122

Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.