09-J4000-18

Original Effective Date: 03/15/22

Reviewed: 06/08/22

Revised: 07/15/22

Subject: Efgartigimod alfa-fcab (Vyvgart) injection

THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.

DESCRIPTION:

Generalized myasthenia gravis is an autoimmune neuromuscular disorder characterized by muscle weakness and fatigue. IgG antibodies occur in up to 85% of patients which are most frequently directed at the acetylcholine receptor. Treatment includes the use of cholinesterase inhibitors to prevent the breakdown of acetylcholine at the neuromuscular junction, immunosuppressive therapies, and thymectomy. Myasthenic crisis may occur which is a medical emergency due to respiratory failure and treatment includes plasmapheresis, IVIG, and corticosteroids.

Efgartigimod alfa-fcab (Vyvgart) is FDA-approved for the treatment of generalized myasthenia gravis (gMG) in adult patients who are anti-acetylcholine receptor (AChR) antibody positive. It is a human immunoglobulin G1 (IgG1) derived Fc fragment that binds to the neonatal Fc receptor (FcRn) and reduces IgG. The amount of AChR autoantibodies is also reduced.

Efgartigimod was compared to placebo in 167 patients with AChR antibody positive generalized myasthenia gravis a 26-week study. The patients were included if they had a Myasthenia Gravis Foundation of America (MGFA) clinical classification of class II – IV and a Myasthenia Gravis Activities of Daily Living (MG-ADL) total score of greater than or equal to 5. The patients also had to be on a stable dose of medication that included acetylcholinesterase (AChE) inhibitors, steroids, or non-steroidal immunosuppressive therapies alone or in combination. There were over 80% of patients who received AChE inhibitors, over 70% receiving steroids, and approximately 60% received non-steroidal immunosuppressive therapies. Patients had IgG levels of at least 6 g/L, a median time since diagnosis of MG of 9 years, a median MG-ADL total score of 9, and the median Quantitative Myasthenia Gravis (QMG) total score of 16. The MG-ADL was used to evaluate the efficacy of treatment. The MG-ADL quantifies the impact of gMG on 8 signs or symptoms with a score ranging from 0 to 24, with a higher score indicating less ability to perform a function. A 2-point or greater reduction in the total MG-ADL score from baseline over 4 weeks was considered a responder. The primary endpoint was the

percentage of MG-ADL responders during the first treatment cycle. A statistically significant improvement in the percentage of MG-ADL responders was demonstrated with the use of efgartigimod as compared to placebo (67.7% vs 29.7%, p<0.0001). The QMG was used to assess the impact on muscle weakness (range 0-39 with higher score indicating severe weakness). A responder was defined as a 3 point or greater reduction in the total QMG score as compared from baseline for at least 4 consecutive weeks. The percentage of QMG responders was significantly higher in the patients treated with efgartigimod vs the placebo group (63.1% vs 14.1%, p<0.0001). The most common adverse reactions in patients with treated with efgartigimod included respiratory tract infections, headache, and urinary tract infection.

POSITION STATEMENT:

Site of Care: If efgartigimod (Vyvgart) is administered in a hospital-affiliated outpatient setting, additional requirements may apply depending on the member's benefit. Refer to 09-J3000-46: Site of Care Policy for Select Specialty Medications.

Initiation of efgartigimod (Vyvgart) **meets the definition of medical necessity** when **ALL** of the indication- specific criteria are met:

1. Generalized Myasthenia Gravis (MG)
    a. Member meets **ALL** of the following - documentation must be provided:
        i. Anti-acetylcholine receptor (AchR) antibody positive disease
        ii. Myasthenia Gravis Foundation of America (MGFA) Clinical Classification Class II – IV
        iii. Myasthenia Gravis Activities of Daily Living (MG-ADL) total score greater than or equal to 5
        iv. **BOTH** of the following[a]:
            1. Member had an inadequate response to at least **ONE** of the following immunosuppressants:
                a. azathioprine
                b. cyclosporine
                c. mycophenolate mofetil
                d. tacrolimus
                e. methotrexate
                f. cyclophosphamide
                g. rituximab
            2. Member had an inadequate response to a corticosteroid
    b. The member will receive treatment in combination with **ONE** of the following:
        i. Acetylcholinesterase inhibitor (e.g. pyridostigmine)
        ii. Corticosteroid

iii. Oral immunosuppressant (e.g., azathioprine, cyclosporine, mycophenolate mofetil)

c. Efgartigimod is not used concurrently with rituximab, eculizumab, ravulizumab, or IVIG

d. Treatment is prescribed by or in consultation with a neurologist

e. There is no evidence of an active infection

f. The dose does not exceed the following:

i. 10 mg/kg[b] weekly for 4 weeks (4 doses per 4 week cycle)

ii. A minimum of 50 days is required between the first dose of each 4 week cycle

Approval duration: 6 months

Continuation of efgartigimod (Vyvgart) **meets the definition of medical necessity** when **ALL** of the following criteria are met:

1. An authorization or reauthorization for efgartigimod has been previously approved by Florida Blue or another health plan in the past 2 years for the treatment of myasthenia gravis, **OR** the member has previously met **ALL** indication-specific criteria.
2. For continuation of therapy for Generalized Myasthenia Gravis, member's diagnosis has been confirmed by the following – documentation must be provided:
   a. Anti-acetylcholine receptor (AchR) antibody positive disease
3. Member has a history of beneficial response to therapy– examples of beneficial response include improved MG-ADL total score, Quantitative myasthenia gravis total score – documentation must be provided
4. There is no evidence of an active infection
5. Efgartigimod is not used concurrently with rituximab, eculizumab, ravulizumab, or IVIG
6. The dose does not exceed the following:
   a. 10 mg/kg[b] weekly for 4 weeks (4 doses per 4 week cycle)
   b. A minimum of 50 days is required between the first dose of each 4 week cycle

Approval duration: 1 year

[a] Not required if the member is switching to efgartigimod and member and was previously approved by Florida Blue for the use of eculizumab or ravulizumab for the treatment of myasthenia gravis.

[b] For members 120 kg or greater, the dose does not exceed 1200 mg

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approved

- For the treatment of generalized myasthenia gravis in adults who are anti-acetylcholine receptor (AChR) antibody positive: 10 mg/kg administered as an IV infusion over one hour once weekly for 4 weeks. In patients weighing 120 kg or more, the dose is 1200 mg per infusion.
- Subsequent treatment cycles are based on clinical evaluation. The safety of administering subsequent cycles sooner than 50 days from the start of the previous treatment has not been established.

Dose Adjustments

- None

Drug Availability

- 400 mg in 20 mL (20 mg/mL) single-dose vial

PRECAUTIONS:

Boxed Warning

- None

Contraindications

- None

Precautions/Warnings

- Infection: Delay administration to patients with an active infection. Monitor for signs and symptoms of infection in patients receiving therapy. If serious infection occurs administer appropriate treatment and consider withholding until the infection has resolved.
- Hypersensitivity reaction: Angioedema, dyspnea, and rash have occurred. If a hypersensitivity reaction occurs, discontinue the infusion and institute appropriate therapy.
- Avoid combined use of efgartigimod with immunoglobulin products, monoclonal antibodies, or antibody derivatives containing the human Fc domain of the IgG subclass due to lower systemic exposure and reduced effectiveness of medications.

BILLING/CODING INFORMATION:

HCPCS Coding

J9332	Injection, efgartigimod alfa-fcab, 2 mg

ICD-10 Diagnosis Codes That Support Medical Necessity

G70.00 – G70.01	Myasthenia gravis

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Part D: BCBSF has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

Medicare Advantage: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline review date.

DEFINITIONS:

Table 1: Myasthenia Gravis Foundation of America (MGFA) Clinical Classification System

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.

Table 2: Myasthenia Gravis Activities of Daily Living (MG-ADL)

Grade	0	1	2	3	Score
Talking	Normal	Intermittent slurring or nasal speech	Constant slurring or nasal, but can be understood	Difficult to understand speech	

Chewing	Normal	Fatigue with solid food	Fatigue with soft food	Gastric tube	
Swallowing	Normal	Rare episode of choking	Frequent choking necessitating changes in diet	Gastric tube	
Breathing	Normal	Shortness of breath with exertion	Shortness of breath at rest	Ventilator dependence	
Impairment of ability to brush teeth or comb hair	None	Extra effort, but no rest periods needed	Rest periods needed	Cannot do one of these functions	
Impairment of ability to arise from a chair	None	Mild, sometimes uses arms	Moderate, always uses arms	Severe, requires assistance	
Double vision	None	Occurs, but not daily	Daily, but not constant	Constant	
Eyelid droop	None	Occurs, but not daily	Daily, but not constant	Constant	
Total Score					

Table 3: Quantitative Myasthenia Gravis Score for Disease Severity

Test item	None	Mild	Moderate	Severe	Score
Grade	**0**	**1**	**2**	**3**	
(1) Double vision on lateral gaze, seconds	61	11-60	1-10	Spontaneous	
(2) Ptosis on upward gaze, seconds	61	11-60	1-10	Spontaneous	
(3) Weakness of facial muscles	Normal lid closure	Complete, weak, some resistance	Complete, without resistance	Incomplete	
(4)Swallowing water	Normal	Minimal coughing or throat clearing	Severe coughing/choking or nasal regurgitation	Cannot swallow (test not attempted)	
(5) Speech after counting aloud from 1-50	None at 50	Dysarthria at 30-49	Dysarthria at 10-29	Dysarthria at 9	

(6) Ability to keep right arm outstretched, seconds	240	90-239	10-89	0-9	
(7) Ability to keep left arm outstretched, seconds	240	90-239	10-89	0-9	
(8) Vital capacity as percent of predicted	Greater or equal to 80	65-79	50-64	Less than 50	
(9) Right hand grip strength, kgW	Men – 45 or greater Women – 30 or greater	Men – 15-44 Women – 10-29	Men – 5-14 Women – 5-9	Men –0-4 Women – 0-4	
(10) Left hand grip strength, kgW	Men – 45 or greater Women – 30 or greater	Men – 15-44 Women – 10-29	Men – 5-14 Women – 5-9	Men –0-4 Women – 0-4	
(11) Ability to keep head lifted when lying supine, seconds	120	30-119	1-29	0	
(12) Ability to keep the right leg outstretched, seconds	100	31-99	1-30	0	
(13) Ability to keep the left leg outstretched, seconds	100	31-99	1-30	0	
				Total QMG Score:	

RELATED GUIDELINES:

Immune Globulin Therapy, 09-J0000-06
Rituximab Products, 09-J0000-59
Eculizumab (Soliris) Injection, 09-J1000-17

Ravulizumab (Ultomiris), 09-J3000-26

OTHER:

None.

REFERENCES:

1. Clinical Pharmacology [Internet]. Tampa (FL): Gold Standard, Inc. Accessed Jan 27, 2022.
2. DRUGDEX® System [Internet]. Greenwood Village (CO): Thomson Micromedex; Accessed Jan 27, 2022.
3. Howard JF, Bril V, Vu T et al. Safety, efficacy, and tolerability of efgartigimod in patients with generalized myasthenia gravis (ADAPT): a multicentre, randomized, placebo-controlled, phase 3 trial. Lancet Neurol 2021; 20: 526-36.
4. National Organization of Rare Diseases. https://rarediseases.org/rare-diseases.
5. Orphan Drug Designations and Approval [Internet]. Silver Spring (MD): US Food and Drug Administration; 2022 [cited Jan 27, 2022]. Available from: http://www.accessdata.fda.gov/scripts/opdlisting/oopd/index.cfm/.
6. Vyvgart (efgartigimod alfa-fcab) injection. Argenx US, Inc. Boston, MA. December 2021.

COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 06/08/22.

GUIDELINE UPDATE INFORMATION:

03/15/22	New Medical Coverage Guideline.
06/15/22	Updated position statement to include site of care policy.
07/01/22	Revision: Added HCPCS code J9332 and deleted code J3590.
07/15/22	Revision to guideline consisting of updating the position statement.