Medical Drug Clinical Criteria

Subject:	Vyvgart (efgartigimod alfa-fcab) and Vyvgart Hytrulo (efgartigimod alfa and hyaluronidase-qvfc)		
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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. Vyvgart Hytrulo is additionally approved for the treatment of adults with Chronic Inflammatory Demyelinating Polyneuropathy (CIDP).

Myasthenia Gravis (MG): 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.

Chronic Inflammatory Demyelinating Polyneuropathy (or polyradiculoneuropathy) (CIDP): CIDP is an acquired, immune-mediated neuropathy which currently lacks consensus on one gold standard for confirming diagnosis via electrophysiologic findings and for determining therapeutic improvement. The clinical trial for Vyvgart Hytrulo required individuals to have a diagnosis of definite or probable CIDP as defined in the European Federation of Neurological Societies/Peripheral Nerve Society (EFNS/PNS) Guidelines on management of paraproteinemic demyelinating neuropathies from 2010. The guidelines were updated in 2021 and include many of the same diagnostic features. Overall, a diagnosis of CIDP includes clinical features and electrodiagnostic testing with or without other supportive criteria. The clinical diagnosis of CIDP may be made based on features of either typical or atypical CIDP with an exclusion of other causes of neuropathy. Electrodiagnostic testing reveals characteristic findings, including prolongation of motor distal latency, reduction of motor conduction velocity, prolongation of F-wave latency, absence of F-waves, motor conduction block, abnormal temporal dispersion, and distal compound muscle action potential (CMAP) duration increase in one or more nerves. Though not widely used in clinical practice, various clinical assessment tools have been developed, including Inflammatory Neuropathy Cause and Treatment (INCAT) scale, Inflammatory Rasch-built Overall Disability Scale (I-RODS), Medical Research Council (MRC) scale for muscle strength, and tools assessing grip strength. In clinical practice, objective measures of function are often used to assess response to therapy.

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 Hytrulo (efgartigimod alfa and hyaluronidase-qvfc)

Initial requests for Vyvgart Hytrulo (efgartigimod alfa and hyaluronidase-qvfc) in myasthenia gravis 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 anti-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 Hytrulo (efgartigimod alfa and hyaluronidase-qvfc) in myasthenia gravis 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.

Initial requests for Vyvgart Hytrulo (efgartigimod alfa and hyaluronidase-qvfc) in chronic inflammatory demyelinating polyneuropathy 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 chronic inflammatory demyelinating polyneuropathy (CIDP); **AND**
III. Diagnosis has been verified by all of the following:
    A. Clinical presentation aligned with one of the following (EFNS/PNS 2010):
        1. Typical CIDP; defined as chronically progressive, stepwise, or recurrent symmetric proximal and distal weakness and sensory dysfunction of all extremities, developing over at least 2 months and absent or reduced tendon reflexes in all extremities; **OR**
        2. Atypical CIDP; defined as in typical CIDP but with one of the following: predominately distal, asymmetric, focal, pure motor, or pure sensory);

    AND
    B. Characteristic electrodiagnostic findings (prolongation of motor distal latency, reduction of motor conduction velocity, prolongation of F-wave latency, absence of F-waves, motor conduction block, abnormal temporal dispersion, and distal compound muscle action potential (CMAP) duration increase) in at least one nerve (EFNS/PNS 2010);

AND

C. Other causes of neuropathy (including but not limited drug or toxin induced neuropathy, Lyme disease, IgM neuropathy, hereditary neuropathy, prominent sphincter disturbance, multifocal motor neuropathy, and diabetic neuropathy) have been ruled out (EFNS/PNS 2010).

AND

IV. Documentation is provided that individual demonstrates objective functional impairment from CIDP (including but not limited to requiring support to walk or upper limb symptoms affecting or preventing ability to perform certain functions [such as zips and buttons, washing or brushing hair, using a knife and fork together, or handling small coins]); **AND**

V. Vyvgart Hytrulo (efgartigimod alfa and hyaluronidase-qvfc) is prescribed by or in consultation with a neurologist.

Initial Approval Duration: 6 months

Requests for continued use of Vyvgart Hytrulo (efgartigimod alfa and hyaluronidase-qvfc) in chronic inflammatory demyelinating polyneuropathy may be approved if the following criteria are met:

I. Documentation is provided that there is clinically significant improvement in neurological symptoms on physical examination (for example, an objective change in function that is clinically meaningful, such as the individual can now work or perform tasks that they previously could not).

Requests for 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, zilucoplan, or rozanolixizumab-noli; **OR**

II. If the above criteria are not met and for all other indications.

Continuation Approval Duration: 1 year

Vyvgart (efgartigimod alfa-fcab)

Initial requests for Vyvgart (efgartigimod alfa-fcab) 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 (gMG); **AND**

III. Documentation is provided that individual has a positive serologic test for the presence of anti-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) 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) may not be approved for the following:

I. Individual is using in combination with maintenance immunoglobulin treatment, eculizumab, ravulizumab, rituximab, zilucoplan, or rozanolixizumab; **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	4 vials per 28 days

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)
J9334	Injection, efgartigimod alfa, 2 mg and hyaluronidase-qvfc [Vyvgart Hytrulo]
ICD-10 Diagnosis	
G61.81	Chronic inflammatory demyelinating polyneuritis
G70.00-G70.01	Myasthenia gravis

Document History

Revised: 08/16/2024
Document History:

- 08/16/2024 – Annual Review: Separate Vyvgart and Vyvgart Hytrulo criteria; add new indication for CIDP for Vyvgart Hytrulo; add zilucoplan to combination exclusion list; update Vygart Hytrulo quantity limit. Administrative update to add documentation language. Coding Reviewed: Added ICD-10-CM G61.81.
- 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. Effective 1/1/2024 Added HCPCS J9334. Removed J3490, C9399. Added ICD-10-CM G70.00-G70.01.

- 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.

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