Vyvgart and Vyvgart Hytrulo
(efgartigimod alfa-fcab; efgartigimod alfa and hyaluronidase-qvfc)
PAM – 052

Iowa Medicaid Program	Prior Authorization	**Effective Date**	07/01/2022
Revision Number	3	**Last Reviewed**	04/18/2025
Reviewed By	Medicaid Medical Director	**Next Review**	01/16/2026
Approved By	Medicaid Clinical Advisory Committee	**Approved Date**	01/20/2023

Overview

Medication:	efgartigimod alfa-fcab[1]	efgartigimod alfa and hyaluronidase-qvfc[2]
Brand Name:	Vyvgart®	Vyvgart Hytrulo®
Pharmacologic Category:	Neonatal Fc receptor blocker	Neonatal Fc receptor blocker + endoglycosidase
FDA-Approved Indication(s):	<u>Vyvgart® and Vyvgart Hytrulo®</u> 1. Treatment of generalized myasthenia gravis (gMG) in adult patients who are anti-acetylcholine receptor (AChR) antibody positive <u>Vyvgart Hytrulo® ONLY</u> 2. Chronic inflammatory demyelinating polyneuropathy (CIDP) in adult patients ▶ **NEW** indication (FDA-approved June 21, 2024)	
How Supplied:	• Single-dose vial • 400 mg/20 mL	• Single-dose vial • 1,008 mg efgartigimod alfa and 11,200 units hyaluronidase per 5.6 mL
Benefit Category:	Medical	

DOSAGE AND ADMINISTRATION	
Vyvgart® (efgartigimod alfa-fcab)	
gMG	• Intravenous (IV) infusion • 10 mg/kg once weekly for 4 weeks • For patients weighing ≥ 120 kg, dose is 1,200 mg • Administer subsequent treatment cycles based on clinical evaluation • The safety of initiating subsequent treatment cycles sooner than 50 days from the start of the previous treatment cycle has not been established.
Vyvgart Hytrulo® (efgartigimod alfa and hyaluronidase-qvfc)	
gMG	• Subcutaneous (SC) injection by a healthcare professional only • 1,008 mg/11,200 units SC injection once weekly for 4 weeks • Administer subsequent treatment cycles based on clinical evaluation • The safety of initiating subsequent treatment cycles sooner than 50 days from the start of the previous treatment cycle has not been established.
CIDP	• Subcutaneous (SC) injection by a healthcare professional only • 1,008 mg/11,200 units SC injection once weekly

Descriptive Narrative

Neuromuscular junction (NMJ) disorders comprise several dysfunctions that ultimately lead to muscle weakness. Some of these diseases, such as congenital myasthenic syndromes, are genetic. Others are acquired autoimmune forms, such as myasthenia gravis, the most prevalent neuromuscular junction disorder.

Myasthenia gravis (MG) is characterized by muscle weakness and fatigue. The weakness is due to an antibody-mediated immunologic attack directed at proteins in the postsynaptic membrane of the neuromuscular junction. Myasthenia gravis can affect all ages, but it is considered "a disease of young women and old men." The most common onset age is between 20 and 39 years in women and between 50 and 70 years in men. [3] Autoimmune myasthenia gravis has a reported worldwide prevalence of 40 to180 per million people, and an annual incidence of 4-12 per million people. In the United States, there are an estimated 60,000 patients diagnosed with myasthenia gravis.

Autoimmune myasthenia gravis is characterized by the presence of antibodies against several components of the neuromuscular junctions. The most common antibody found in autoimmune myasthenia gravis is directed against post-synaptic acetylcholine receptors (AChRs). Anti-AChR antibodies are present in approximately 80 percent of all autoimmune MG patients. Less frequent autoantibodies found in autoimmune MG include the anti-muscle-specific kinase (MuSK) antibody (4 percent of the cases) and the anti-lipoprotein receptor-related protein-4 (LRP4) antibody (2 percent of the cases) directed against LPR4. All these autoantibodies belong to the immunoglobulin G (IgG) class.[4]

Chronic inflammatory demyelinating polyneuropathy (CIDP) is an acquired, immune-mediated neuropathy affecting peripheral nerves and nerve roots, typically characterized by a relapsing-remitting or progressive course of symmetric weakness of proximal and distal muscles. CIDP is identified by electrodiagnostic and/or pathologic features of demyelination and responsiveness to immunomodulatory treatments. Although the cause of CIDP and its variants is unknown, there is evidence to support the hypothesis that the disorder(s) are immunologically mediated and can have multiple triggers. Both the cellular and humoral components of the adaptive immune system appear to be involved in the pathogenesis of CIDP and its variants.

The reported prevalence of CIDP ranges from 0.7 to 10.3 cases per 100,000 people. here is a predominance in males, with a sex rate ratio ranging from 1.5 to 4. CIDP primarily affects adults and the incidence rises with advancing age. The typical age of onset is not well established, but some studies have reported mean ages of presentation in the sixth decade. CIDP may also occur in children. No specific predisposing risk factors for CIDP have been clearly identified. There have been conflicting studies on human leukocyte antigen (HLA) type associations, but no clear genetic predisposition has been found.[5]

Guidelines

The International Consensus Guidance for Management of Myasthenia Gravis was last updated in 2020.[6] Vyvgart® and Vyvgart Hytrulo® are not yet included in the consensus guidance.

The goals of therapy in myasthenia gravis (MG) are to render patients minimally symptomatic or better while minimizing side effects from medications.

There are four primary therapies currently used to treat MG.

- Symptomatic treatment (acetylcholinesterase inhibition) to increase the amount of acetylcholine (ACh) available at the neuromuscular junction
- Chronic immunotherapies (glucocorticoids and nonsteroidal immuno-suppressive and immunomodulatory agents) to target the underlying immune dysregulation
- Rapid but short-acting immunomodulating treatments (therapeutic plasma exchange and intravenous immune globulin [IVIG])
- Surgical treatment (thymectomy)

In addition to the pace and severity of the disease, the time to onset of clinical effect for each of these therapies varies considerably, which plays a large role in choosing the appropriate therapy for a given patient.[7]

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Commonly used therapies for myasthenia gravis [8] (estimated times are rough guidelines based upon clinical experience in myasthenia gravis)		Time to onset of effect	Time to maximal effect
Symptomatic therapy – *increases the amount of acetylcholine available at the neuromuscular junction*	pyridostigmine	10-15 minutes	2 hours
Chronic immunotherapies – *target underlying immune dysregulation*	prednisone	2 to 3 weeks	5 to 6 months
	azathioprine	~12 months	1 to 2 years
	mycophenolate mofetil	6 to 12 months	1 to 2 years
	cyclosporine	~6 months	~7 months
	tacrolimus	~6 months	~12 months
	efgartigimod alfa	1 to 2 weeks	~4 weeks
	ravulizumab	1 to 2 weeks	~4 to 10 weeks
Rapid immunotherapies – *manage myasthenia crisis*	plasmapheresis	1 to 7 days	1 to 3 weeks
	intravenous immune globulin (IVIG)	1 to 2 weeks	1 to 3 weeks
Surgery – *therapeutic option in select patients*	thymectomy	1 to 10 years	1 to 10 years

Outcomes Measurements[9]

The Myasthenia Gravis Foundation of America Classification (MGFA)	
MGFA classification separates patients in groups based on disease severity and the localization of the symptoms.	
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, ± 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, ± 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, ± 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.

The Myasthenia Gravis Activities of Daily Living (MG-ADL)				
The MG-ADL assesses the impact of generalized myasthenia gravis (gMG) on daily functions by assigning a score to 8 signs or symptoms that are commonly affected in gMG, then totaling the individual scores for a composite MG-ADL score. Each item is measured on a 4-point scale, where a score of 0 represents normal function and a score of 3 represents the loss of ability to perform that function.				
Grade	0	1	2	3
1. Talking	Normal	Intermittent slurring or nasal speech	Constant slurring or nasal, but can be understood	Difficult to understand speech
2. Chewing	Normal	Fatigue with solid food	Fatigue with soft food	Gastric tube
3. Swallowing	Normal	Rare episode of choking	Frequent choking necessitating changes in diet	Gastric tube
4. Breathing	Normal	Shortness of breath with exertion	Shortness of breath at rest	Ventilator dependence
5. 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
6. Impairment of ability to arise from a chair	None	Mild, sometimes uses arms	Moderate, always uses arms	Severe, requires assistance
7. Double vision	None	Occurs, but not daily	Daily, but not constant	Constant
8. Eyelid droop	None	Occurs, but not daily	Daily, but not constant	Constant

Goals of Therapy – Chronic inflammatory demyelinating polyneuropathy

Early administration of effective treatment is important in chronic inflammatory demyelinating polyneuropathy (CIDP). The goal is to stop the immune attack against the myelin sheath of peripheral nerves so that secondary axonal degeneration is minimized. This can improve symptoms and function and can prevent or minimize long-term disability. Once symptoms stabilize, the treatment objective is for sustained improvement and to promote remission.

For most treatment-naïve patients with CIDP who are more than mildly affected or for mildly affected patients who are rapidly worsening, initial immunomodulatory treatment is recommended, using either intravenous immune globulin, plasma exchange, or glucocorticoids. Vyvgart Hytrulo was approved for use as an induction and maintenance therapy in CIDP, but its place in the spectrum of CIDP treatment has not yet been defined.[10]

Criteria

Prior authorization is required.

Generalized Myasthenia Gravis (gMG)

Vyvgart® or Vyvgart Hytrulo® are considered medically necessary when **ALL** of the following are met:

1. Documented diagnosis of acetylcholine receptor antibody-positive (AChR-Ab+) generalized myasthenia gravis (gMG); **AND**
2. Member is 18 years of age or older; **AND**
3. Member has Myasthenia Gravis Foundation of America (MGFA) Clinical Classification of Class II to IV; **AND**
4. Member has a Myasthenia Gravis – Activities of Daily Living (MG-ADL) score of at least 5 or higher, with at least 50 percent of the baseline MG-ADL score due to non-ocular symptoms; **AND**
5. Member is on a stable dose (for the duration specified, if indicated) of at least ONE (or documentation of inadequate response, intolerance, or labeled contraindication to ALL) of the following standard-of-care treatments for gMG:
    a. Acetylcholine inhibitors (e.g., pyridostigmine); and/or
    b. Steroids (at least 3 months of treatment); and/or
    c. Non-steroidal immunosuppressive therapy, e.g., azathioprine, cyclophosphamide, cyclosporine, mycophenolate mofetil, or tacrolimus (at least 6 months of treatment); **AND**
6. Vyvgart® or Vyvgart Hytrulo® are not prescribed concurrently with eculizumab (Soliris®), rituximab, ravulizumab (Ultomiris®), or maintenance immunoglobulin treatment; **AND**
7. Prescribed by, or in consultation with, an immunologist, neurologist, or rheumatologist; **AND**
8. Request meets one of the following (a or b):
    a. The regimen prescribed does not exceed the FDA-approved labeling:
        i. Vyvgart®: 10 mg/kg intravenously once weekly (1,200 mg per infusion for members weighing 120 kg or more) for 4 weeks; or
        ii. Vyvgart Hytrulo®: 1,008 mg/11,200 units subcutaneously once weekly for 4 weeks; **OR**
    b. Regimen is supported by clinical practice guidelines. Supporting clinical documentation must be provided with any request for which regimen prescribed does not align with FDA-approved labeling.

Vyvgart® or Vyvgart Hytrulo® are considered medically necessary for continuation of therapy when **ALL** of the following are met:

1. Member is currently receiving medication through the Iowa Medicaid benefit or has previously met initial approval criteria; **AND**
2. Documentation of positive clinical response to therapy, as demonstrated by at least a 2-point reduction in the total Myasthenia Gravis Activities of Daily Living (MG-ADL) score from pre-treatment baseline; **AND**
3. Vyvgart® or Vyvgart Hytrulo® are not prescribed concurrently with eculizumab (Soliris®), rituximab, ravulizumab (Ultomiris®), or maintenance immunoglobulin treatment; **AND**
4. Prescribed by, or in consultation with, an immunologist, neurologist, or rheumatologist; **AND**
5. Request meets one of the following (a or b):
    a. The regimen prescribed does not exceed the FDA-approved labeling:
        i. Vyvgart®: 10 mg/kg intravenously (1,200 mg per infusion for members weighing 120 kg or more) once weekly for 4 weeks **AND** at least 50 days have passed since the start of the previous cycle; or
        ii. Vyvgart Hytrulo®: 1,008 mg/11,200 units subcutaneously once weekly for 4 weeks **AND** at least 50 days have passed since the start of the previous cycle; **OR**
    b. Regimen is supported by clinical practice guidelines. Supporting clinical documentation must be provided with any request for which regimen prescribed does not align with FDA-approved labeling.

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Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)
Vyvgart Hytrulo® ONLY

Vyvgart Hytrulo® is considered medically necessary when **ALL** of the following are met:

1. Diagnosis of chronic inflammatory demyelinating polyneuropathy (CIDP) confirmed by **BOTH** of the following (a and b):
    a. Electrodiagnostic testing (consistent with EFNS/PNS≠ guidelines); **AND**
    b. Clinical presentation aligned with one of the following (i or ii):
        i. Typical CIDP: 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
        ii. Atypical CIDP: defined as in typical CIDP but with one of the following: predominately distal, asymmetric, focal, pure motor, or pure sensory; **AND**
2. Documentation provided that member 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**
3. 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; **AND**
4. Member is 18 years of age or older; **AND**
5. Documentation of trial and failure of at least one of the following standard of care treatments (a, b, and/or c):
    a. Corticosteroids (minimum 3-month trial duration); and/or
    b. Immune globulin; and/or
    c. Plasma exchange; **AND**
6. Vyvgart Hytrulo® is not prescribed concurrently with immune globulin therapy; **AND**
7. Prescribed by, or in consultation with, a neurologist or neuromuscular specialist; **AND**
8. Request meets one of the following (a or b):
    a. Regimen prescribed does not exceed 1,008 mg/11,200 units subcutaneously once weekly; or
    b. Regimen is supported by clinical practice guidelines. Supporting clinical documentation must be provided with any request for which regimen prescribed does not align with FDA-approved labeling.

Vyvgart Hytrulo® is considered medically necessary for continuation of therapy when **ALL** of the following are met:

1. Member is currently receiving medication through the Iowa Medicaid benefit or has previously met initial approval criteria; **AND**
2. Documentation of positive clinical response to therapy (e.g., improvement or stabilization in a CIDP disability or impairment scale, disability improvement, symptom improvement in affected limbs); **AND**
3. Prescribed by, or in consultation with, a neurologist or neuromuscular specialist; **AND**
4. Request meets one of the following (a or b):
    a. Regimen prescribed does not exceed 1,008 mg/11,200 units subcutaneously once weekly; or
    b. Regimen is supported by clinical practice guidelines. Supporting clinical documentation must be provided with any request for which regimen prescribed does not align with FDA-approved labeling.

≠ EFNS/PNS: European Federation of Neurological Societies/Peripheral Nerve Society

Approval Duration and Quantity Limits

Approval Duration	
Initial Authorization	6 months
Subsequent Authorization(s)	12 months
Quantity Limits – Myasthenia Gravis (gMG)	
Vyvgart	Dose not to exceed 10 mg/kg (1,200 mg per infusion for members ≥ 120 kg): ▪ administered as an IV infusion once weekly for 4 weeks; **AND** ▪ (for subsequent cycles) at least 50 days have passed since the start of the previous cycle
Vyvgart Hytrulo	Dose not to exceed 1,008 mg/11,200 units: ▪ administered subcutaneously once weekly for 4 weeks; **AND** ▪ (for subsequent cycles) at least 50 days have passed since the start of the previous cycle
Quantity Limits – Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)	
Vyvgart Hytrulo	Dose not to exceed 1,008 mg/11,200 units: ▪ administered subcutaneously once weekly

oding and Product Information

The following list(s) of codes and product information are provided for reference purposes only and may not be all inclusive. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment, nor does the exclusion of a code imply that its association to the HCPCS code is inappropriate.

HCPCS	Description
J9332	Injection, efgartigimod alfa-fcab, 2 mg [Vyvgart®]
J9334	Injection, efgartigimod alfa, 2 mg and hyaluronidase-qvfc [Vyvgart Hytrulo®]

ICD-10	Description
G61.81	Chronic inflammatory demyelinating polyneuritis
G70.00	Myasthenia gravis without (acute) exacerbation
G70.01	Myasthenia gravis with (acute) exacerbation

NDC	Labeler	Dosage	Pkg Size	Pkg Qty	Units/ Pkg
73475-3041-05 [Vyvgart®]	argenx US, Inc.	2 mg	1	EA	200
73475-3102-03 [Vyvgart Hytrulo®]	argenx US, Inc.	2 mg	1	EA	504

Compliance

1. Should conflict exist between the policy and applicable statute, the applicable statute shall supersede.
2. Federal and State law, as well as contract language, including definitions and specific contract provisions or exclusions, take precedence over medical policy and must be considered first in determining eligibility for coverage.
3. Medical technology is constantly evolving, and Iowa Medicaid reserves the right to review and update medical policy on an annual or as-needed basis.

Medical necessity guidelines have been developed for determining coverage for member benefits and are published to provide a better understanding of the basis upon which coverage decisions are made. Medical necessity guidelines are developed for selected physician-administered medications found to be safe and proven to be effective in a limited, defined population or clinical circumstances. They include concise clinical coverage criteria based on current literature review, consultation with practicing physicians in the service area who are medical experts in the particular field, FDA and other government agency policies, and standards adopted by national accreditation organizations. Criteria are revised and updated annually, or more frequently if new evidence becomes available that suggests needed revisions.

References

[1] Vyvgart prescribing information (10/2024). argenx US, Inc.: Boston, MA. Available online at www.vyvgarthcp.com. Accessed November 4, 2024.

[2] Vyvgart Hytrulo prescribing information (08/2024). argenx US, Inc.: Boston, MA. Available online at www.vyvgarthcp.com. Accessed November 4, 2024.

[3] Bubuioc AM, Kudebayeva A, Turuspekova S, Lisnic V, Leone MA. The epidemiology of myasthenia gravis. J Med Life. 2021 Jan-Mar;14(1):7-16. PMID: 33767779.

[4] Gilhus NE, Verschuuren JJ. Myasthenia gravis: subgroup classification and therapeutic strategies. Lancet Neurol. 2015 Oct;14(10):1023-36. PMID: 26376969.

[5] Lewis RA, Muley SA. Chronic inflammatory demyelinating polyneuropathy: Etiology, clinical features, and diagnosis. Goddeau RP, ed. UpToDate. Waltham, MA: UpToDate Inc. www.uptodate.com. Accessed March 27, 2025.

[6] Narayanaswami P, Sanders DB, et al. International Consensus Guidance for Management of Myasthenia Gravis: 2020 Update. Neurology. 2021 Jan 19;96(3):114-122. Epub 2020 Nov 3. PMID: 33144515.

[7] Bird SJ. Overview of the treatment of myasthenia gravis. Goddeau RP, ed. UpToDate. Waltham, MA: UpToDate Inc. www.uptodate.com. Accessed March 25, 2025.

[8] Bird SJ. Chronic immunotherapy for myasthenia gravis. Goddeau RP, ed. UpToDate. Waltham, MA: UpToDate Inc. www.uptodate.com. Accessed March 25, 2025.

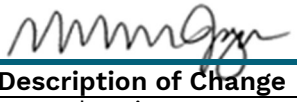
[9] Barnett C, Herbelin L, Dimachkie MM, Barohn RJ. Measuring Clinical Treatment Response in Myasthenia Gravis. Neurol Clin. 2018 May;36(2):339-353. PMID 29655453.

[10] Lewis RA, Muley SA. Chronic inflammatory demyelinating polyneuropathy: Treatment and prognosis. Goddeau RP, ed. UpToDate. Waltham, MA: UpToDate Inc. www.uptodate.com. Accessed March 27, 2025.

Development of utilization management criteria may also involve research into other state Medicaid programs, other payer policies, consultation with experts and review by the Medicaid Clinical Advisory Committee (CAC). These sources may not be referenced individually unless they are specifically published and are otherwise applicable to the criteria at issue.

Criteria Change History

Change Date	Changed By	Description of Change	Version
[mm/dd/yyyy]	CAC		
Signature			

Change Date	Changed By	Description of Change	Version
04/18/2025	CAC	Annual review. Vyvgart Hytrulo approved for treatment of CIDP on 6/21/2024. Added information to Overview section (moved Dosage and Administration into a separate table). Added information on CIDP to Descriptive Narrative and added criteria for new indication. Return policy to January review cadence for 2026.	3
Signature William (Bill) Jagiello, DO			

Change Date	Changed By	Description of Change	Version
01/19/2024	CAC	Annual review. New SC formulation Vyvgart Hytrulo®, updated policy to include this formulation. Updated criteria with dosing information. Updated criteria, quantity limits, approval duration, and coding information to include Vyvgart Hytrulo®.	2
Signature William (Bill) Jagiello, DO			

Change Date	Changed By	Description of Change	Version
01/20/2023	CAC	Criteria implementation.	1
Signature William (Bill) Jagiello, DO			

CAC = Medicaid Clinical Advisory Committee