efgartigimod alfa and Hyaluronidase (Vyvgart Hytrulo®) EOCCO POLICY

Policy Type:PA/SP Pharmacy Coverage Policy: EOCCO327

Description

Efgartigimod alfa and hyaluronidase (Vyvgart Hytrulo) is a subcutaneously administered human immunoglobin G1 (IgG1)-derived antibody that works by reducing circulating IgG in a patient's blood stream decreasing the autoimmune attack of the postsynaptic membrane in the neuromuscular junction in those with myasthenia gravis and chronic inflammatory demyelinating polyneuropathy.

Length of Authorization

- Initial: Six months
- Renewal: 12 months

Quantity Limits

Product Name	Indication	Dosage Form	Quantity Limit
efgartigimod alfa and hyaluronidase (Vyvgart Hytrulo)	Generalized Myasthenia Gravis; Chronic inflammatory demyelinating polyneuropathy	1,000mg/5mL / 10,000u/5mL prefilled syringe	20mL/28 days
Provider Administered Agents*			
efgartigimod alfa and hyaluronidase (Vyvgart Hytrulo)	Generalized Myasthenia Gravis; Chronic inflammatory demyelinating polyneuropathy	1,008mg/5.6mL / 11,200u/5.6mL vial*	22.4mL/28 days

**Medical drug that requires administration by a healthcare professional and is not available for self-administration by the member, considered one of the excluded classes under the prescription benefit. Subcutaneous vial is only FDA approved for provider administration.*

Initial Evaluation

I. **Efgartigimod alfa and hyaluronidase (Vyvgart Hytrulo)** may be considered medically necessary when the following criteria are met:
   A. Member is 18 years of age or older; **AND**
   B. The request is for efgartigimod alpha and hyaluronidase (Vyvgart Hytrulo) prefilled syringe; **AND**
   C. Medication is prescribed by, or in consultation with, a specialist (e.g., neurologist or rheumatologist); **AND**
   D. Member has a diagnosis of one of the following:
      1. **Generalized myasthenia gravis (gMG)**; **AND**
         i. Provider attestation that the member has myasthenia gravis class II to IV (i.e., not defined as ocular myasthenia gravis and not intubated); **AND**

ii. Member has previously had an inadequate response to pyridostigmine and at least one immunosuppressant therapy (i.e., azathioprine, cyclosporine, mycophenolate), unless all agents were not tolerated or are contraindicated; **AND**

iii. Member will continue on standard of care therapies (i.e., azathioprine, cyclosporine, mycophenolate); **AND**

iv. Member has a baseline Myasthenia Gravis-activities of daily living (MG-ADL) total score of at least 5; **AND**

v. Medication will **NOT** be used in combination with maintenance immunoglobulin therapy (IVIG), eculizumab (Soliris), ravulizumab (Ultomiris), rozanolixizumab (Rystiggo), zilucoplan (Zilbrysq) or rituximab; **OR**

2. Chronic inflammatory demyelinating polyneuropathy (CIDP); AND

i. Provider attestation that the member has typical chronic inflammatory demyelinating polyneuropathy (CIDP) (characterized by symmetric muscle weakness and sensory loss); **AND**

ii. Documentation of progressing or relapsing disease course based on ONE of the following:

a. Chronic inflammatory demyelinating polyneuropathy (CIDP) disease activity status (CDAS) score of 2 or more; **OR**

b. Inflammatory Neuropathy Cause and Treatment (INCAT) disability scale of 2 more; **AND**

iii. Treatment with immunoglobulin (Ig) has been ineffective, not tolerated, or contraindicated; **AND**

iv. Medication will **NOT** be used in combination with maintenance immunoglobulin therapy or IV efgartigimod.

II. Efgartigimod alfa and hyaluronidase (Vyvgart Hytrulo) is considered investigational when used for all other conditions, including but not limited to:

A. Ocular Myasthenia Gravis
B. Myasthenia Gravis at dosing frequencies more often than 50 days before the next initial dose
C. Pediatric Myasthenia Gravis
D. Postural Orthostatic Tachycardia Syndrome
E. Primary Immune Thrombocytopenia
F. Atypical Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)
G. Bullous Pemphigoid (BALLAD) or Pemphigus (Vulgaris or Foliaceus)

Renewal Evaluation

I. Member has received a previous prior authorization approval for this agent through this health plan or has been established on therapy from a previous health plan; **OR**
   A. Member has a previous prior authorization on efgartigimod alfa and hyaluronidase (Vyvgart Hytrulo) intravenously through a medical approval and is transitioning to subcutaneous; **AND**

II. Member is not continuing therapy based off being established on therapy through samples, manufacturer coupons, or otherwise. If they have, initial policy criteria must be met for the member to qualify for renewal evaluation through this health plan; **AND**

III. Member has exhibited improvement or stability of disease symptoms (e.g., an improvement in the MG-ADL score, improvement/stability in CIDP disease activity status (CDAS) score, improvement in INCAT score, improvement in grip strength, a reduction/elimination of oral steroids/immunosuppressants required, etc); **AND**

IV. Medication will **NOT** be used in combination with maintenance therapies (i.e., immunoglobulin therapy (IVIG), eculizumab (Soliris), ravulizumab (Ultomiris), or rituximab).

Supporting Evidence

I. Efgartigimod alfa (Vyvgart) is FDA approved for the use of adult patients with generalized myasthenia gravis (gMG) and chronic inflammatory demyelinating polyneuropathy (CIDP). Efficacy and safety for use in those under the age of 18 has not yet been established.

II. Due to the complexity of diagnosis and treatment, a specialist provider, or consultation with a specialist (e.g., neurologist, rheumatologist) is required.

III. Myasthenia gravis is a chronic, autoimmune, neuromuscular disease characterized by fluctuating motor weakness involving the ocular, spinal column, limb and/or respiratory muscles. The weakness is due to an antibody-mediated, immunologic attack directed at the postsynaptic membrane of the neuromuscular junction (acetylcholine receptors [AChR] or receptor associated proteins, such as MUSK) led by the patient's IgG immune response. This causes common symptoms such as drooping eyelids (ptosis), double vision (diplopia), muscle weakness and fatigue, trouble swallowing or pronouncing words, and facial muscle involvement causing a mask-like appearance or sneer.

IV. Acetylcholine receptors are the most common receptor affected; about 85% of patients will test positive for AChR antibodies, which is considered a positive indicator of a MG diagnosis. Those who do not test positive for AChR, may then test positive for a different receptor protein, such as Muscle-specific tyrosine kinase (MuSK) or LR4 antibody. AChR antibody (AChR-AB) negative patients do not tend to respond as well to regular standards of care as the AB positive patients do and tend to respond better to rituximab (Inflectra) instead.

V. Additionally, there are two clinical forms of MG: ocular and generalized. Although the majority of patients present with a vision symptom as the first indicator of MG, roughly only 15% of patients remain as ocular MG, while the rest become generalized MG. Those with ocular MG are less likely to be AChR-AB positive and have mixed response to traditional therapies usually favoring eye patches or eye "crutches" to assist with drooping eyelids, and in severe cases, surgery.

VI. MG patients are staged by ocular versus generalized and the severity of their symptoms. Stage I is ocular only and Stage V is those patients who require intubation; Stages II-IV encompass those patients in between as mild to moderate and the systems involved. MG patients are further assessed by two common scoring systems: the Quantitative Myasthenia Gravis (QMG) and the MG activity of daily living (MG-ADL). Both are quality of life scales assessing muscle strength and weakness, higher scores on each scale indicate more severe disease. Quantitative Myasthenia Gravis is a 13-item scale with a possible worst score of 39 and MG-ADL is an 8-item scale with a possible worst score of 24. Based on clinical data and physician input, a three-point change is clinically meaningful in QMG for moderate-severe patients and a two-point change for a milder patient; a two-point change is clinically meaningful in MG-ADL for mild-moderate, there is not an agreement on severe patients in the MG-ADL scale.

VII. Currently there is not a cure for MG, patients tend to reach their peak in symptoms and severity within the first three years of diagnosis and then stabilize or move into remission. Available treatments control symptoms and prevent relapses allowing patients to live a relatively high quality of life with a normal life expectancy. Treatment options include symptomatic treatment (e.g., acetylcholinesterase inhibitors [e.g., pyridostigmine]), corticosteroids, long-term immunosuppressive therapy (e.g., azathioprine, cyclosporine, methotrexate), plasma exchange, and rapid immunomodulating treatments (e.g., immune globulin IV). Thymectomy is also an option and according to the Internal Consensus Guidelines on MG 2020 it should be considered early in the disease over those under 50 with generalized MG or those who fail to respond to an adequate trial of immunotherapy. The only biologic currently included in these same guidelines is eculizumab (Soliris) which is recommended in the treatment of severe, refractory, AChR-AB+ generalized MG. Refractory disease is defined by Internal consensus guidelines, as MG-ADL/QMG unchanged or worse after corticosteroids and a least two other immunosuppressant agents, used in adequate doses for an adequate duration (usually 12 weeks), with persistent symptoms or side effects that limit functioning.

VIII. Pyridostigmine should be the initial therapy in the treatment of patients with gMG and patients should remain on this, unless there is an intolerance to it, throughout the lifetime of the patient's disease. The ability to discontinue pyridostigmine can be an indicator that the patient has met therapy goals and may lead to tapering of other therapies. Next line agents, which are considered for patients still having bothersome symptoms, are nonsteroidal immunosuppressants (NISTs), those that can be used in MG include azathioprine, cyclosporine, mycophenolate mofetil, methotrexate, and tacrolimus. NIST can be used in combination with a corticosteroid (prednisone) for flares or more rapid deceleration of exacerbation/crisis.

Myasthenia crisis can occur from concurrent infection, surgery, pregnancy, certain medication classes; mild flares may simply respond to changes in standard of care doses or frequency, such as increasing pyridostigmine, or beginning a course of prednisone. More severe cases where patients are experiencing increased dysphagia or dyspnea, initiation of intravenous immune globulin (IVIG) or plasmapheresis, to return to clinical baseline.

IX. The safety and efficacy of efgartigimod alfa (Vyvgart) intravenously (IV) was studied in a 26-week, Phase 3, randomized, double-blind, placebo-controlled, global trial (ADAPT). One hundred and sixty-seven adult patients with generalized myasthenia gravis staged between II and IV, and had a MG-ADL score of at least 5 with 50% of that score not being from ocular assessment. Patients were randomized 1:1 to receive efgartigimod alfa (n=84, Vyvgart) 10mg/kg or placebo (n=83) as four weekly infusions per one cycle. Patients could remain on standard of care therapies at stable doses; plasmapheresis and IVIG were not allowed during the study. The majority of patients were AChR-AB+, 65 in the treatment arm and 64 in the placebo arm. The primary endpoint was the number of responders in AChR-AB+ patients on the MG-ADL score at week four in efgartigimod alfa (Vyvgart) versus placebo. A responder was defined as a patient who had a two-point or greater reduction in the MG-ADL maintained for four consecutive weeks after the last infusion of the cycle.

X. A statistically significant difference favoring efgartigimod alfa (Vyvgart) over placebo in AChR-AB+ patients was seen at the end of the first treatment cycle. Forty-four of 68 patients in the treatment arm and 19 of 64 patients in the placebo arm experienced a response, OR 4.95 (95CI: 2.21, 11.53; *p<0.0001*). Secondary endpoints looked at response in QMG in AChR-AB+ patients at end of cycle one, MG-ADL response in all patients at the end of cycle one. Endpoints are shown in the following table:

Primary Endpoint	**Efgartigimod alfa (n= 65)***	**Placebo (n=64)***	**Odds Ratio (95% CI); *p* value**
MG-ADL responder in cycle 1 (n, %)	44 (68)	19 (30)	4.95 (2.21-11.53); *p <0.0001*
Secondary Endpoints	**Efgartigimod alfa**	**Placebo**	**Odds Ratio (95% CI); *p* value**
Quantitative Myasthenia Gravis (QMG) responder in cycle one (n,%)	41 (63)*	9 (14)*	10.84 (4.18-31.20); *p<0.0001*
MG-ADL responder in cycle 1 (n,%)	57 (68)±	31 (37)±	3.70 (1.85-7.58); *p<0.0001*

**AChR-AB+ patients; ±All study patients, Efgartigimod alfa (n=84), placebo (n=83)*

XI. Patients could continue to repeat cycles of either efgartigimod alfa (Vyvgart) or placebo during the 26-week trial as long as they had a minimum eight-week period between the first doses of each cycle, had an MG-ADL score of at least 5 with 50% due to non-ocular symptoms, and the patient had a sustained two-point improvement for at least four weeks post last cycle dose. Patients who required rescue therapy (change in standard of care medications, addition of IVIG/plasmapheresis, added glucocorticoid therapy) were discontinued from the trial. Those that did not maintain a four-week sustained two-point improvement were considered non-responders and discontinued from the trial.

XII. Approximately 15%-20% of patients with generalized myasthenia gravis (gMG) are classified as anti-acetylcholine receptor antibody (AChR-Ab) seronegative. ADAPT SERON evaluated efgartigimod alfa (Vyvgart) in this patient population in an 8-week, randomized double-blind, placebo-controlled study. Patients had an MGFA Clinical Classification Class II to IV, MG-ADL total score of at least 5, were on stable doses of MG therapy prior to screening (e.g., AChE inhibitors, steroids or NSISTs, either in combination or alone) and had IgG levels of at least 4 g/L prior to enrollment in the study. Sixty-one percent of patients were triple seronegative (i.e., anti-AChR, anti-MuSK, and anti-low density lipoprotein receptor-related protein 4 [LRP4] antibodies negative). The primary efficacy endpoint was the comparison of the mean change from baseline at Week 4 between treatment groups in the MG-ADL total score. A statistically significant difference favoring efgartigimod alfa (Vyvgart) was observed (LS mean difference [95% CI] = - 1.46 [-2.50 to -0.41]; p-value = 0.0068).

XIII. The data for subcutaneous injections (SC) comes from ADAPTsc, a pharmacodynamic noninferiority, Phase 3, open-label study comparing 10mg/kg IV to 1000mg SC. The primary endpoint evaluated the percentage change from baseline in total IgG levels from week 0 to week 4 in both groups; the body's IgG is partially responsible for the autoimmune activity attacking the ACh receptors in the synapse. Those using SC had a decrease of 66.4 and IV had a decrease of 62.2; a least mean squares difference of 4.2 (0.66-7.73 95%CI, *p<0.0001*) confirming noninferiority. Secondary exploratory endpoints showed consistent similar outcomes of the SC vs. IV for MG-ADL, QMG during one treatment cycle.

XIV. Patients who completed ADAPT without losing response to efgartigimod alfa (Vyvgart) could enroll in a three-year open-label extension (OLE; ADAPT+, N=151) tracking safety, tolerability, and efficacy. To date, the incidence of adverse events (AEs) is similar to ADAPT and efgartigimod alfa (Vyvgart) treatment has shown repeatable and consistent decreases in MG-ADL and QMG scores over multiple cycles. There has been one patient receiving 13 cycles with the majority receiving eight cycles and an average cycle duration of 55 days without additional adverse events with longer-term use.

XV. A reach out to an expert in the field of neurology indicated that efgartigimod alfa (Vyvgart) has been being used as rescue therapy in patients not controlled on conventional therapy (e.g., pyridostigmine, NISTs). If the patient is asymptomatic (MG-ADL less than 5) on SOC medication it is unlikely they would qualify for efgartigimod alfa (Vyvgart). Therefore if a patient improved on efgaritigmod alfa (Vyvgart) over a one-year period, there could potentially be a titration off of standard of care (SOC) medications, first with oral steroids, or a NIST later in the course of the disease, noting disease progression is worse than the AE of SOC medications or efgartigimod alfa (Vyvgart).

XVI. There are currently four other biologics approved in the treatment of MG: eculizumab (Soliris), raculizumab (Ultomiris), zilucoplan (Zilbrysq), and rozanolixizumab (Rystiggo). Soliris is included in the latest guidelines, the Internal Consensus Guidelines on Myasthenia Gravis 2020, in refractory MG with a recommendation after failure of IVIG, plasmapheresis, and

immunosuppressive agents. The exclusion criteria for three of these trials, eculizumab (Soliris), raculizumab (Ultomiris), and efgartigimod alfa (Vyvgart), did not allow concurrent use of each other or IVIG, plasmapheresis, or rituximab within at least four weeks of the trial onset. The combination use of any of these therapies would be experimental.

XVII. The minimum time to the initiation of another treatment cycle in ADAPT was 56 days; however, ADAPT+ defined its protocol to allow the minimum time to another treatment cycle of 50 days. Doses sooner than 50 days between the initial dose of each cycle have not been assessed for safety or efficacy and would be experimental in use.

XVIII. Chronic inflammatory demyelinating polyneuropathy (CIDP) is an acquired immune-mediated neuropathy that primarily affects peripheral nerves, and nerve roots and commonly presents with a relapsing-remitting or progressive course. Over time, symmetric weakness of muscles can exceed the extent of sensory loss, is the most common type affecting 50 to 60% of all cases and considered 'typical' CIDP. Disease not characterized by symmetrical weakness is considered atypical CIDP.

XIX. The European Academy of Neurology/Peripheral Nerve Society (EAN/PNS) recommends induction and maintenance therapy with first-line treatment such as corticosteroids, IVIG and plasma exchange. Subcutaneous immune globulin (SCIG) can also be considered for maintenance treatment. The guidelines do not report one therapy over another and consideration of treatment should be assessed based on patient disease factors and treatment tolerability. In a disease with no cure, the goal of therapy for CIDP is to stop the immune attach against the myelin sheath of peripheral nerves to minimize axonal degeneration and improve symptom control and function.

XX. Efgartigimod alfa and hyaluronidase (Vyvgart Hytrulo) was studied in a Phase 2, randomized-withdrawal, double-blind, multicentered trial (ADHERE) that enrolled a total of 322 participants. The study was done in two stages: stage A participants (n=322) received 1000mg weekly of efgartigimod PH20 subcutaneous injection for 12 weeks and stage B participants (n=221) were randomized (1:1) to receive either continuing efgartigimod PH20 therapy weekly or matched placebo for 48 weeks. Baseline characteristics included a median age of 54 years, predominantly male (65%), and a diagnosis of typical CIDP (85%). Treatment-experienced patients were required to discontinue their current standard-of-care therapies during the study.

XXI. The results of stage A had 66% of participants have a confirmed clinical improvement on therapy based on an improvement of INCAT by at least ≥1 point or ≥4 points on I-RODS or ≥8kPa on grip strength. In stage B, there was a risk reduction rate of 61% between the treatment group and placebo (HR 0.39; 95% CI 0.253, 0.614; p<0.0001). There was a total of 31 participants in the treatment group that experienced a relapse as compared to 59 participants in the placebo group (ARR: 25%) which is comparable to immunoglobulin therapy.

XXII. About 63-64% of patients reported an adverse event (AE) who received efgartigimod alfa and hyaluronidase (Vyvgart Hytrulo) as compared to 56% in the placebo group. The most common AE reported in the treatment group was injection site erythema (10%), CIDP worsening (5%),

and headaches (5%) in stage A. In stage B, common AEs reported include COVID-19 (17% vs. 13%) and inject site reactions (14% vs. 6%). There was a total of 3 reported deaths all deemed not related to the study drug.

Investigational or Not Medically Necessary Uses

I. Efgartigimod alfa (Vyvgart) has not been FDA-approved, or sufficiently studied for safety and efficacy for the conditions or settings listed below:
   A. Ocular Myasthenia Gravis
   B. Myasthenia Gravis at dosing frequencies more often than 50 days before the next initial dose
   C. Pediatric Myasthenia Gravis
   D. Postural Orthostatic Tachycardia Syndrome
   E. Primary Immune Thrombocytopenia
   F. Atypical chronic Inflammatory Demyelinating Polyneuropathy (CIDP)
   G. Bullous Pemphigoid (BALLAD) or Pemphigus (Vulgaris or Foliaceus)

Appendix

I. MGFA Clinical Classification

Class	Distribution and Severity	
1	Any ocular muscle weakness, all other muscle strength is normal	
2	Mild, generalized	• 2a: Mainly limp, axial muscles
		• 2b: mainly oropharyngeal/respiratory muscles
3	Moderate, generalized	• 3a: Mainly limp, axial muscles
		• 3B: Mainly oropharyngeal/respiratory muscles
4	Severe, generalized	• 4a: Mainly limp, axial muscles
		• 4B: Mainly oropharyngeal/respiratory muscles
5	Intubation	

II. MG-ADL Score

	Score=0	Score=1	Score=2	Score=3	Your Score
Talking	Normal	Intermittent slurring or nasal speech	Constant slurring or nasal speech, 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	Gastric tube	

			necessitating changes in diet		
Breathing	Normal	Shortness of breath with exertion	Shortness of breath at rest	Ventilatory dependence	
Brushing teeth or hair	Normal	Extra effort, but no rest periods needed	Rest periods needed	Cannot do one of these functions	
Arising from chair	Normal	Mild, sometimes uses arms	Moderate, always uses arms,	Severe, requires assistance	
Double vision	Normal	Occurs, but not daily	Daily, but not constant	Constant	
Eyelid droop	Normal	Occurs, but not daily	Daily, but not constant	Constant	
				Total Score =	

References

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Related Policies

Policies listed below may be related to the current policy. Related policies are identified based on similar indications, similar mechanisms of action, and/or if a drug in this policy is also referenced in the related policy.

Policy Name	Disease state
zilucoplan (Zilbrysq®)	Myasthenia Gravis

Policy Implementation/Update

Action and Summary of Changes	Date
Updated criteria to remove requirement of AChR-AB positive disease. Updated E/I criteria to remove reference to MUSK antibody positive disease.	07/2026
Policy created	08/2025