Clinical Policy: Efgartigimod Alfa-fcab, Efgartigimod/-Hyaluronidase-qvfc (Vyvgart, Vyvgart Hytrulo)

Reference Number: PA.CP.PHAR.555
Effective Date: 09/2022
Last Review Date: 10/2024

Description

- Efgartigimod alfa-fcab (Vyvgart®) is a neonatal Fc receptor (FcRn) antagonist.
- Efgartigimod alfa/hyaluronidase-qvfc (Vyvgart® Hytrulo) is a combination of efgartigimod alfa, a neonatal Fc receptor blocker, and hyaluronidase, an endoglycosidase.

FDA Approved Indication(s)

Vyvgart and Vyvgart Hytrulo are indicated for the treatment of generalized myasthenia gravis (gMG) in adult patients who are anti-acetylcholine receptor (AChR) antibody positive.

Vyvgart Hytrulo is also indicated for the treatment of adult patients with chronic inflammatory demyelinating polyneuropathy (CIDP).

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of PA Health & Wellness® that Vyvgart and Vyvgart Hytrulo are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Generalized Myasthenia Gravis (must meet all)**:**

1. Diagnosis of gMG;
2. Prescribed by or in consultation with a neurologist;
3. Age ≥ 18 years;
4. Myasthenia Gravis-Activities of Daily Living (MG-ADL) score ≥ 5 at baseline;
5. Greater than 50% of the baseline MG-ADL score is due to non-ocular symptoms;
6. Myasthenia Gravis Foundation of America (MGFA) clinical classification of Class II to IV;
7. Member has positive serologic test for anti-AChR antibodies;
8. Failure of a cholinesterase inhibitor (see Appendix B), unless contraindicated or clinically significant adverse effects are experienced;
9. Failure of a corticosteroid (see Appendix B), unless contraindicated or clinically significant adverse effects are experienced;
10. Failure of at least one immunosuppressive therapy (see Appendix B), unless clinically significant adverse effects are experienced or all are contraindicated;
11. The requested agent is not prescribed concurrently with Soliris®, Ultomiris® or Zilbrysq® ;
12. For Vyvgart requests: Documentation of member's current weight (in kg);
13. Request meets one of the following (a or b):

a. Vyvgart: Dose does not exceed 10 mg/kg (1,200 mg per infusion for members weighing 120 kg or more) IV once weekly for the first 4 weeks of every 8-week cycle;
b. Vyvgart Hytrulo: Dose does not exceed 1,008 mg/11,200 units SC once weekly for the first 4 weeks of every 8-week cycle weekly.

Approval duration: 6 months

B. Chronic Inflammatory Demyelinating Polyneuropathy (must meet all)**:**

1. Request is for Vyvgart Hytrulo;
2. Diagnosis of CIDP;
3. Prescribed by or in consultation with a neurologist or neuromuscular specialist;
4. Age ≥ 18 years;
5. Disease is progressive or relapsing for ≥ 2 months;
6. Member has either of the following (a or b):
   a. Both of the following, characterizing typical CIDP (i and ii):
      i. Progressive or relapsing symmetric, proximal, and distal muscle weakness of upper and lower limbs, and sensory involvement of ≥ 2 limbs;
      ii. Absent or reduced tendon reflexes in all limbs;
   b. One of the following CIDP variants (i-v):
      i. Distal CIDP;
      ii. Multifocal CIDP;
      iii. Focal CIDP;
      iv. Motor CIDP;
      v. Sensory CIDP;
7. Diagnosis has been confirmed via electrodiagnostic testing;
8. Member does not have any of the following (a-f):
   a. Borrelia burgdorferi infection (Lyme disease), diphtheria, or drug or toxin exposure probable to have caused the neuropathy;
   b. Hereditary demyelinating neuropathy;
   c. Prominent sphincter disturbance;
   d. Multifocal motor neuropathy;
   e. IgM monoclonal gammopathy with high titer antibodies to myelin-associated glycoprotein;
   f. Other causes for a demyelinating neuropathy, including POEMS syndrome, osteosclerotic myeloma, and diabetic and nondiabetic lumbosacral radiculoplexus neuropathy;
9. Failure of at least one immune globulin therapy* (*see Appendix B*), unless clinically significant adverse effects are experienced or all are contraindicated;
   **Prior authorization may be required for immune globulins*
10. For members who do not have pure motor symptoms, failure of a corticosteroid (e.g., dexamethasone) at up to maximally indicated doses unless contraindicated or clinically significant adverse effects are experienced;
11. Vyvgart Hytrulo is not prescribed concurrently with immune globulin therapy;
12. Dose does not exceed 1,008 mg/11,200 units SC once weekly.

Approval duration: 6 months

C. Other diagnoses/indications
1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

II. Continued Therapy

A. Generalized Myasthenia Gravis (must meet all)**:**
1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies;
2. Member is responding positively to therapy as evidenced by a 2-point reduction in MG-ADL total score;
3. The requested agent is not prescribed concurrently with Soliris, Ultomiris or Zilbrysq;
4. For Vyvgart requests: Documentation of member's current weight (in kg);
5. If request is for a dose increase, request meets one of the following (a or b):
   a. Vyvgart: New dose does not exceed 10 mg/kg (1,200 mg per infusion for members weighing 120 kg or more) IVonce weekly for the first 4 weeks of every 8-week cycle;
   b. Vyvgart Hytrulo: Dose does not exceed 1,008 mg/11,200 units SC once weekly for the first 4 weeks of every 8-week cycle weekly.

Approval duration: 6 months

B. Chronic Inflammatory Demyelinating Polyneuropathy (must meet all)**:**
1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies;
2. Request is for Vyvgart Hytrulo;
3. Member is responding positively to therapy as evidenced by one of the following (a, b, or c):
   a. Improvement or stabilization in a CIDP disability or impairment scale (*see Appendix E for scales*);
   b. Disability improvement;
   c. Symptom improvement in affected limbs;
4. Vyvgart Hytrulo is not prescribed concurrently with immune globulin therapy;
5. If request is for a dose increase, new dose does not exceed 1,008 mg/11,200 units SC once weekly

Approval duration: 6 months

C. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies .
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – PA.CP.PMN.53;

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

AChR: acetylcholine receptor
CIDP: chronic inflammatory demyelinating polyneuropathy
EAN/PNS: European Academy of Neurology/Peripheral Nerve Society
FcRn: neonatal Fc receptor
FDA: Food and Drug Administration
gMG: generalized myasthenia gravis
IgG: immunoglobulin G
INCAT: inflammatory neuropathy cause and treatment
MG-ADL: Myasthenia Gravis-Activities of Daily Living
MGFA: Myasthenia Gravis Foundation of America

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Corticosteroids		
betamethasone	**gMG** Oral: 0.6 to 7.2 mg PO per day	7.2 mg/day
dexamethasone	**gMG** Oral: 0.75 to 9 mg/day PO **CIDP** Oral: 40 mg QD x 4 days repeated q 4 weeks	Varies
methylprednisolone	**gMG** Oral: 12 to 20 mg PO per day; increase as needed by 4 mg every 2-3 days until there is marked clinical improvement **CIDP** Oral/IV: 500 mg QD x 4 days repeated q 4 weeks (pulsed regimen)	Varies
prednisone	**gMG** Oral: 15 mg/day to 20 mg/day; increase by 5 mg every 2-3 days as needed	60 mg/day
prednisolone	**CIDP** Oral: 30 mg QD x 4 weeks followed by slow tapering over months	Varies
Cholinesterase Inhibitors for gMG		
pyridostigmine (Mestinon®)	Oral immediate-release: 600 mg daily in divided doses (range, 60-1,500 mg daily in divided doses)	Immediate-release: 1,500 mg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	Oral sustained release: 180-540 mg QD or BID	Sustained-release:1,080 mg/day
neostigmine (Bloxiverz®)	Oral: 15 mg TID. The daily dosage should be gradually increased at intervals of 1 or more days. The usual maintenance dosage is 15-375 mg/day (average 150 mg) IM or SC: 0.5 mg based on response to therapy	Oral: 375 mg/day
Immunosuppressants for gMG		
azathioprine (Imuran®)	Oral: 50 mg QD for 1 week, then increase gradually to 2 to 3 mg/kg/day	3 mg/kg/day
mycophenolate mofetil (Cellcept®)*	Oral: Dosage not established. 1 gram BID has been used with adjunctive corticosteroids or other non-steroidal immunosuppressive medications	2 g/day
cyclosporine (Sandimmune®)*	Oral: initial dose of cyclosporine (non-modified), 5 mg/kg/day in 2 divided doses	5 mg/kg/day
Rituxan® (rituximab), Riabni™ (rituximab-arrx), Ruxience™ (rituximab-pvvr), Truxima® (rituximab-abbs)*†	IV: 375 mg/m^2 once a week for 4 weeks; an additional 375 mg/m^2 dose may be given every 1 to 3 months afterwards	375 mg/m^2
Immune Globulins for CIDP		
intravenous immune globulin (e.g., Gammagard Liquid®, Gamunex®-C, Gammaked™)	Induction: 2 g/kg divided over 2-5 days Maintenance: 1 g/kg q 3 weeks	Not applicable
subcutaneous immune globulin (e.g., Hizentra®, HyQvia®)	Varies	Not applicable

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.
**Off-label; †Prior authorization is required for rituximab products*

Appendix C: Contraindications/Boxed Warnings
None reported

Appendix D: General Information
- gMG
  - The MG-ADL scale is an 8-item patient-reported scale that measures functional status in 8 domains related to MG – talking, chewing, swallowing, breathing, impairment of ability to brush teeth or comb hair, impairment of ability to arise from a chair, double

vision, and eyelid droop. Each domain is given a score of 0-3, with 0 being normal and 3 being most severe impairment. A 2-point decrease in the MG-ADL score is considered a clinically meaningful response.
    - In the Phase 3 ADAPT trial, all study patients received an initial 4-week treatment cycle of Vyvgart, with subsequent cycles administered according to individual clinical response when MG-ADL score was ≥ 5 (i.e., symptoms are at least the minimum threshold required for necessitating treatment) and, if the patient was an MG-ADL responder to the 4-week treatment cycle, when they no longer had a clinically meaningful decrease (MG-ADL clinically meaningful improvement defined as having ≥ 2-point improvement in total MG-ADL score) compared with baseline. Subsequent cycles could commence no sooner than 8 weeks from initiation of the previous cycle.
- CIDP
    - CIDP is divided into typical CIDP and CIDP variants. CIDP variants are now well characterized entities, each presenting with a specific clinical and electrodiagnostic phenotype.
    - Diagnostic criteria for CIDP: If the electrodiagnostic study does not fulfill the minimal electrodiagnostic criteria (i.e., conclusion is "possible CIDP"), then ≥ 2 additional supportive criteria can be met for some CIDP variants. Supportive criteria include response to CIDP standard treatment, cerebrospinal fluid analysis, nerve imaging, and nerve biopsy. Not all CIDP diagnostic categories allow for 2 supportive criteria to meet for CIDP diagnosis and hence were not included in the Vyvgart Hytrulo CIDP criteria. For diagnostic criteria specific to each of the CIDP variants, refer to the 2021 EAN/PNS CIDP guideline.
    - Immune globulins, corticosteroids, and plasma exchange are recommended treatments for patients with disabling symptoms. Plasma exchange is similarly effective to immune globulins and corticosteroids but is typically reserved for treatment-refractory patients; it may be less well tolerated and more difficult to administer. Patient-specific factors may determine the appropriate choice of therapy.

Appendix E: Examples of CIDP Disability and Impairment Scales
- Inflammatory neuropathy cause and treatment (INCAT) disability score
- Inflammatory Rasch-built overall disability scale (I-RODS)
- Modified INCAT sensory sum scale (mISS)
- Medical Research Council (MRC) sum score
- Grip strength (with Martin Vigorimeter or Jamar hand grip dynamometer)

V. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
Efgartigimod alfa-fcab (Vyvgart)	gMG	10 mg/kg IV once weekly for the first 4 weeks of every 8-week cycle	10 mg/kg/week (1,200 mg per infusion for members weighing ≥ 120 kg)
Efgartigimod alfa/ hyaluronidase-	gMG	1,008 mg efgartigimod alfa and 11,200 units hyaluronidase SC once weekly injections for the	1,008 mg/11,200 units/ week

Drug Name	Indication	Dosing Regimen	Maximum Dose
qvfc (Vyvgart Hytrulo)		first 4 weeks of every 8-week cycle	
	CIDP	1,008 mg efgartigimod alfa and 11,200 units hyaluronidase SC once weekly	

VI. Product Availability

Drug Name	Availability
Efgartigimod alfa-fcab (Vyvgart)	Single-dose vial: 400 mg/20 mL injection solution
Efgartigimod alfa-hyaluronidase-qvfc (Vyvgart Hytrulo)	Single-dose vial: 1,008 mg (efgartigimod alfa)/11,200 units (hyaluronidase)/5.6 mL

VII. References

1. Vyvgart Prescribing Information. Boston, MA: argenx US, Inc.; April 2022. Available at: https://argenx.com/product/vyvgart-prescribing-information.pdf. Accessed November 29, 2023.
2. Vyvgart Hytrulo Prescribing Information. Boston, MA: agrenx US, Inc.; June 2024. Available at: https://www.argenx.com/product/vyvgart-hytrulo-prescribing-information.pdf. Accessed July 8, 2024.
3. Howard JF, Bril V, Vu T, et al. Safety, efficacy, and tolerability of efgartigimod in patients with generalized myasthenia gravis (ADAPT): a multicenter, randomised, placebo-controlled, phase 3 trial. Lancet Neurology July 2021;20(7):526-36.
4. Sanders DB, Wolfe GI, Benatar M, et al. International consensus guidance for management of myasthenia gravis. Neurology 2016;87:419-425.
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7. ClinicalTrials.gov. A study to assess the safety and efficacy of a subcutaneous formulation of efgartigimod in adults with CIDP (ADHERE). Available at: https://clinicaltrials.gov/study/NCT04281472. Accessed July 8, 2024.
8. Joint Task Force of the EFNS and the PNS. European Federation of Neurological Societies/Peripheral Nerve Society Guideline on management of chronic inflammatory demyelinating polyradiculoneuropathy: report of a joint task force of the European Federation of Neurological Societies and the Peripheral Nerve Society–First Revision. European Journal of Neurology. 2010;17: 356-363. Available at: https://onlinelibrary.wiley.com/doi/10.1111/j.1468-1331.2009.02930.x. Accessed February 16, 2024.
9. Van den Bergh PYK, van Doorn PA, Hadden RDM, et al. European Academy of Neurology/Peripheral Nerve Society (EAN/PNS) guideline on diagnosis and treatment of chronic inflammatory demyelinating polyradiculoneuropathy: Report of a joint Task Force-Second revision [published correction appears in Eur J Neurol. 2022 Apr;29(4):1288.

10. Bus SR, de Haan RJ, Vermeulen M, van Schaik IN, Eftimov F. Intravenous immunoglobulin for chronic inflammatory demyelinating polyradiculoneuropathy. Cochrane Database Syst Rev. 2024;2(2):CD001797.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J9332	Injection, efgartigimod alfa-fcab, 2 mg
J9334	Injection, efgartigimod alfa, 2 mg and hyaluronidase-qvfc

Reviews, Revisions, and Approvals	Date
Policy created	08/2022
1Q 2023 annual review: added to continuation of therapy requirement for no concurrent use with Soliris or Ultomiris; references reviewed and updated.	01/2023
RT4: Vyvgart Hytrulo added to policy.	07/2023
1Q 2024 annual review: added HCPCS code [J9334]; added not prescribed concurrently with Zilbrysq; references reviewed and updated.	01/2024
RT4: added new indication of CIDP for Vyvgart Hytrulo	10/2024