Clinical Policy: Efgartigimod Alfa-fcab (Vyvgart)

Reference Number: ERX.SPA.449
Effective Date: 12.17.21
Last Review Date: 02.22
Line of Business: Commercial, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Efgartigimod alfa-fcab (Vyvgart®) is a neonatal Fc receptor (FcRn) antagonist.

FDA Approved Indication(s)
Vyvgart is indicated for the treatment of generalized myasthenia gravis (gMG) in adult patients who are anti-acetylcholine receptor (AChR) antibody positive.

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.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Vyvgart is **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. Vyvgart is not prescribed concurrently with Soliris® or Ultomiris®;
12. Documentation of member's current weight (in kg);
13. Dose does not exceed 10 mg/kg (1,200 mg per infusion for members weighing 120 kg or more) once weekly for the first 4 weeks of every 8-week cycle.

Approval duration: 6 months

B. Other diagnoses/indications

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

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

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;

2. Member is responding positively to therapy as evidenced by a 2-point reduction in MG-ADL score;
3. Documentation of member's current weight (in kg);
4. If request is for a dose increase, new dose does not exceed 10 mg/kg (1,200 mg per infusion for members weighing 120 kg or more) once weekly for the first 4 weeks of every 8-week cycle.

Approval duration: 6 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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 policy – ERX.PA.01 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

AChR: acetylcholine receptor
FcRn: neonatal Fc receptor
FDA: Food and Drug Administration
gMG: generalized myasthenia gravis
IgG: immunoglobulin G
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	Oral: 0.6 to 7.2 mg per day	7.2 mg/day
dexamethasone	Oral: 0.75 to 9 mg per day	9 mg/day
methylprednisolone	Oral: 12 to 20 mg per day; increase as needed by 4 mg every 2 to 3 days until there is marked clinical improvement or to a maximum of 40 mg/day	40 mg/day
prednisone	Oral: 15 mg/day to 20 mg/day; increase by 5 mg every 2 to 3 days as needed	60 mg/day
Cholinesterase Inhibitors		
pyridostigmine (Mestinon®)	Oral immediate-release: 600 mg daily in divided doses (range, 60-1,500 mg daily in divided doses) Oral sustained release: 180-540 mg QD or BID	Immediate-release: 1,500 mg/day 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		
azathioprine (Imuran®)	Oral: 50 mg QD for 1 week, then increase gradually to 2 to 3 mg/kg/day	3 mg/kg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
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

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.

Appendix C: Contraindications/Boxed Warnings
None reported

Appendix D: General Information
- 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.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
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)

VI. Product Availability
Single-dose vial: 400 mg/20 mL injection solution

VII. References
1. Vyvgart Prescribing Information. Boston, MA: argenx US, Inc.; April 2022. Available at: https://argenx.com/product/vyvgart-prescribing-information.pdf. Accessed August 9, 2022.
2. 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.
3. Sanders DB, Wolfe GI, Benatar M, et al. International consensus guidance for management of myasthenia gravis. Neurology 2016;87:419-425.
4. Narayanaswami P, Sanders DB, Wolfe G, et al. International consensus guidance for management of myasthenia gravis 2020 update. Neurology 2021;96:114-22.

5. Muppidi S, Silvestri N, Tan R, et al. The evolution of Myasthenia Gravis-Activities of Daily Living (MG-ADL) scale utilization to measure myasthenia gravis symptoms and treatment response (1817). Neurology Apr 2021;96(15 Suppl):1817.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created pre-emptively	08.17.21	11.21
Drug is now FDA approved - criteria updated per FDA labeling: revised requirement for a prior trial of two non-steroidal immunosuppressant therapies to a trial of at least one; added requirement for documentation of member's current weight for dose calculation purposes; references reviewed and updated.	01.04.22	02.22
Updated requirement for no concurrent use to include Ultomiris.	08.09.22	

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.