Vyvgart™ (Efgartigimod Alfa-Fcab)

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Instructions for Use

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Coverage Rationale

See Benefit Considerations

Vyvgart™ (efgartigimod alfa-fcab) has been added to the Review at Launch program. Some members may not be eligible for coverage of this medication at this time.

Vyvgart is proven for the treatment of generalized myasthenia gravis. Vyvgart is medically necessary when all of the following criteria are met:

- Initial Therapy
  - Submission of medical records (e.g., chart notes, laboratory values, etc.) to support the diagnosis of generalized myasthenia gravis (gMG) by a neurologist or in consultation with a neurologist confirming all of the following:
    - Patient has not failed a previous course of Vyvgart therapy; and
    - Positive serologic test for anti-AChR antibodies; and
    - One of the following:
      - History of abnormal neuromuscular transmission test demonstrated by single-fiber electromyography (SFEMG) or repetitive nerve stimulation
      - History of positive anticholinesterase test, e.g., edrophonium chloride test
      - Patient has demonstrated improvement in MG signs on oral cholinesterase inhibitors, as assessed by the treating neurologist

    and
    - Patient has a Myasthenia Gravis Foundation of America (MGFA) Clinical Classification of class II, III, or IV at initiation of therapy; and
    - Patient has a Myasthenia Gravis-specific Activities of Daily Living scale (MG-ADL) total score ≥ 5 at initiation of therapy

  and
  - Both of the following: *(for Medicare reviews, refer to the CMS section *)*

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        - History of failure of at least two immunosuppressive agents over the course of at least 12 months [e.g., azathioprine, methotrexate, cyclosporine, mycophenylate, etc.]; and
        - Patient has required 2 or more courses of plasmapheresis/plasma exchanges and/or intravenous immune globulin for at least 12 months without symptom control

      and
    - Patient is currently on a stable dose (at least 2 months) of immunosuppressive therapy; and
    - Patient is not receiving Vyvgart in combination with Soliris (eculizumab); and
    - Vyvgart is initiated and titrated according to the US FDA labeled dosing for gMG, up to a maximum of 1200 mg per dose; and
    - Prescribed by, or in consultation with, a neurologist; and
    - Initial authorization will be for no more than 6 months.
- Continuation of Therapy
    - Patient has previously been treated with Vyvgart; and
    - Submission of medical records (e.g., chart notes, laboratory tests) to demonstrate a positive clinical response from baseline as demonstrated by all of the following:
        - Improvement and/or maintenance of at least a 2 point improvement (reduction in score) in the MG-ADL score from pre-treatment baseline.
        - Reduction in signs and symptoms of myasthenia gravis
        - Maintenance, reduction, or discontinuation of dose(s) of baseline immunosuppressive therapy (IST) prior to starting Vyvgart. Note: Add on, dose escalation of IST, or additional rescue therapy from baseline to treat myasthenia gravis or exacerbation of symptoms while on Vyvgart therapy will be considered as treatment failure.

      and
    - Patient is not receiving Vyvgart in combination with Soliris (eculizumab); and
    - Vyvgart is dosed according to the US FDA labeled dosing for gMG: up to a maximum of 1200 mg per dose; and
    - Prescribed by, or in consultation with, a neurologist; and
    - Reauthorization will be for no more than 12 months.

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

HCPCS Code	Description
C9399	Unclassified drugs or biologicals
J3490	Unclassified drugs
J3590	Unclassified biologics

Diagnosis Code	Description
G70.00	Myasthenia gravis without (acute) exacerbation

Background

Efgartigimod alfa-fcab is a human IgG1 antibody fragment that binds to the neonatal Fc receptor (FcRn), resulting in the reduction of circulating IgG. The pharmacological effect of efgartigimod alfa-fcab was assessed by measuring the decrease in serum IgG levels and AChR autoantibody levels. In patients testing positive for AChR antibodies and who were treated with efgartigimod alfa-fcab, there was a reduction in total IgG levels relative to baseline. Decrease in AChR autoantibody levels followed a similar pattern.

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Benefit Considerations

Some Certificates of Coverage allow for coverage of experimental/investigational/unproven treatments for life-threatening illnesses when certain conditions are met. The member specific benefit plan document must be consulted to make coverage decisions for this service. Some states mandate benefit coverage for off-label use of medications for some diagnoses or under some circumstances when certain conditions are met. Where such mandates apply, they supersede language in the benefit document or in the medical or drug policy. Benefit coverage for an otherwise unproven service for the treatment of serious rare diseases may occur when certain conditions are met. Refer to the Policy and Procedure addressing the treatment of serious rare diseases.

Additional Information: Clinical coverage in this policy addresses the drug only. It does not address coverage for drug administration in a hospital outpatient department. Refer to the member specific benefit plan document and the policy titled Provider Administered Drugs – Site of Care for more information. The member specific benefit plan document determines coverage.

Clinical Evidence

Generalized Myasthenia Gravis

Efgartigimod alfa-fcab is indicated for the treatment of generalized myasthenia gravis (gMG) in adult patients who are anti-acetylcholine receptor (AChR) antibody positive.

The efficacy of efgartigimod alfa-fcab for the treatment of generalized myasthenia gravis (gMG) in adults who are AChR antibody positive was established in a 26-week, multicenter, randomized, double-blind, placebo-controlled trial (Study 1; NCT03669588).

Study 1 enrolled patients who met the following criteria at screening:

- Myasthenia Gravis Foundation of America (MGFA) clinical classification class II to IV
- MG-Activities of Daily Living (MG-ADL) total score of ≥ 5
- On stable dose of MG therapy prior to screening, that included acetylcholinesterase (AChE) inhibitors, steroids, or non-steroidal immunosuppressive therapies (NSISTs), either in combination or alone
- IgG levels of at least 6 g/L

A total of 167 patients were enrolled in Study 1 and were randomized to receive either efgartigimod alfa-fcab 10mg/kg (1200 mg for those weighing 120 kg or more) (n = 84) or placebo (n = 83). Baseline characteristics were similar between treatment groups. Patients had a median age of 46 years at screening (range: 19 to 81 years) and a median time since diagnosis of 9 years. Seventy-one percent were female, and 84% were White. Median MG-ADL total score was 9, and median Quantitative Myasthenia Gravis (QMG) total score was 16. The majority of patients (n = 65 for efgartigimod alfa-fcab; n = 64 for placebo) were positive for AChR antibodies.

At baseline, over 80% of patients in each group received AChE inhibitors, over 70% in each treatment group received steroids, and approximately 60% in each treatment group received NSISTs, at stable doses.

Patients were treated with efgartigimod alfa-fcab at the recommended dosage regimen.

The efficacy of efgartigimod alfa-fcab was measured using the Myasthenia Gravis-Specific Activities of Daily Living scale (MG-ADL) which assesses the impact of gMG on daily functions of 8 signs or symptoms that are typically affected in gMG. Each item is assessed on a 4-point scale where a score of 0 represents normal function and a score of 3 represents loss of ability to perform that function. A total score ranges from 0 to 24, with the higher scores indicating more impairment. In this study, an MGADL responder was defined as a patient with a 2-point or greater reduction in the total MG-ADL score compared to the treatment cycle baseline for at least 4 consecutive weeks, with the first reduction occurring no later than 1 week after the last infusion of the cycle.

The primary efficacy endpoint was the comparison of the percentage of MG-ADL responders during the first treatment cycle between treatment groups in the AChR-Ab positive population. A statistically significant difference favoring efgartigimod alfa-

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fcab was observed in the MG-ADL responder rate during the first treatment cycle [67.7% in the efgartigimod alfa-fcab -treated group vs 29.7% in the placebo-treated group ($p < 0.0001$)].

The efficacy of efgartigimod alfa-fcab was also measured using the Quantitative Myasthenia Gravis (QMG) total score which is a 13-item categorical grading system that assesses muscle weakness. Each item is assessed on a 4-point scale where a score of 0 represents no weakness and a score of 3 represents severe weakness. A total possible score ranges from 0 to 39, where higher scores indicate more severe impairment. In this study, a QMG responder was defined as a patient who had a 3-point or greater reduction in the total QMG score compared to the treatment cycle baseline for at least 4 consecutive weeks, with the first reduction occurring no later than 1 week after last infusion of the cycle.

The secondary endpoint was the comparison of the percentage of QMG responders during the first treatment cycle between both treatment groups in the AChR-Ab positive patients. A statistically significant difference favoring VYVGART was observed in the QMG responder rate during the first treatment cycle [63.1% in the efgartigimod alfa-fcab -treated group vs 14.1% in the placebo-treated group ($p < 0.0001$)].

U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

Vyvgart is a neonatal Fc receptor blocker indicated for the treatment of generalized myasthenia gravis (gMG) in adult patients who are anti-acetylcholine receptor (AChR) antibody positive.

Centers for Medicare and Medicaid Services (CMS)

Medicare does not have a National Coverage Determination (NCD) for Vyvgart™ (efgartigimod alfa-fcab). Local Coverage Determinations (LCDs)/Local Coverage Articles (LCAs) do not exist.

In general, Medicare may cover outpatient (Part B) drugs that are furnished "incident to" a physician's service provided that the drugs are not usually self-administered by the patients who take them. Refer to the Medicare Benefit Policy Manual, Chapter 15, §50 - Drugs and Biologicals. (Accessed December 21, 2021)

*Preferred therapy criteria is not applicable for Medicare Advantage members.

References

1. Vyvgart™ [prescribing information]. Boston, MA: argenx US, Inc.; December 2021.
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3. Bird S. Overview of the treatment of myasthenia gravis. In: *UpToDate*, Post TW (Ed), UpToDate, Waltham, MA. (Accessed on January 6, 2022.)
4. Farmakidis C, Pasnoor M, Dimachkie MM, Barohn RJ. Treatment of Myasthenia Gravis. *Neurol Clin*. 2018;36(2):311-337.
5. Narayanaswami P, Sanders DB, Wolfe G, et al. International Consensus Guidance for Management of Myasthenia Gravis: 2020 Update. *Neurology*. 2021;96(3):114-122.

Policy History/Revision Information

Date	Summary of Changes
06/01/2022	Coverage Rationale • Revised coverage criteria for continuation of therapy; replaced criterion requiring “improvement and/or maintenance of at least a *3* point improvement (reduction in score) in the MG-ADL score from pre-treatment baseline” with “improvement and/or maintenance of at least a *2* point improvement (reduction in score) in the MG-ADL score from pre-treatment baseline”

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Date	Summary of Changes
	Supporting Information • Archived previous policy version 2022D00111A

Instructions for Use

This Medical Policy provides assistance in interpreting UnitedHealthcare standard benefit plans. When deciding coverage, the member specific benefit plan document must be referenced as the terms of the member specific benefit plan may differ from the standard plan. In the event of a conflict, the member specific benefit plan document governs. Before using this policy, please check the member specific benefit plan document and any applicable federal or state mandates. UnitedHealthcare reserves the right to modify its Policies and Guidelines as necessary. This Medical Policy is provided for informational purposes. It does not constitute medical advice.

This Medical Policy may also be applied to Medicare Advantage plans in certain instances. In the absence of a Medicare National Coverage Determination (NCD), Local Coverage Determination (LCD), or other Medicare coverage guidance, CMS allows a Medicare Advantage Organization (MAO) to create its own coverage determinations, using objective evidence-based rationale relying on authoritative evidence (Medicare IOM Pub. No. 100-16, Ch. 4, §90.5).

UnitedHealthcare may also use tools developed by third parties, such as the InterQual® criteria, to assist us in administering health benefits. UnitedHealthcare Medical Policies are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.

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Nondiscrimination & Language Access Policy

Aspirus Health Plan, Inc. complies with applicable Federal civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability, sex, sexual orientation, or gender identity. *We* do not exclude people or treat them differently because of race, color, national origin, age, disability, sex, sexual orientation, or gender identity.

We will:
Provide free aids and services to people with disabilities to communicate effectively with us, such as:
- Qualified sign language interpreters
- Written information in other formats (large print, audio, accessible electronic formats, other formats)

Provide free language services to people whose primary language is not English, such as:
- Qualified interpreters
- Information written in other languages

If *you* need these services, contact *us* at the phone number shown on the inside cover of this *contract*, *your* id card, or aspirushealthplan.com.

If *you* believe that *we* have failed to provide these services or discriminated in another way on the basis of race, color, national origin, age, disability, sex, sexual orientation, or gender identity, *you* can file a grievance with:

Nondiscrimination Grievance Coordinator
Aspirus Health Plan, Inc.
PO Box 1062
Minneapolis, MN 55440
Phone: 1.866.631.5404 (TTY: 711)
Fax: 763.847.4010
Email: customerservice@aspirushealthplan.com

You can file a grievance in person or by mail, fax, or email. If *you* need help filing a grievance, the Nondiscrimination Grievance Coordinator is available to help you.

You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights, electronically through the Office for Civil Rights Complaint Portal, available at https://ocrportal.hhs.gov/ocr/portal/lobby.jsf, or by mail or phone at:

U.S. Department of Health and Human Services
200 Independence Avenue, SW
Room 509F, HHH Building
Washington, D.C. 20201
1-800-368-1019, 800-537-7697 (TDD)

Complaint forms are available at http://www.hhs.gov/ocr/office/file/index.html.

Language Assistance Services

Albanian: KUJDES: Nëse flitni shqip, për ju ka në dispozicion shërbime të asistencës gjuhësore, pa pagesë.Telefononi në 1.866.631.5404 (TTY: 711).

Arabic تنبيه: إذا كنت تتحدث اللغة العربية، فإن خدمات المساعدة اللغوية متاحة لك مجاناً . اتصل بن اعلى رقم الهاتف 1.866.631.5404(رقم هاتف الصم والبك : 711)

French: ATTENTION : Si vous parlez français, des services d'aide linguistique vous sont proposés gratuitement. Appelezle 1.866.631.5404 (ATS : 711).

German: ACHTUNG: Wenn Sie Deutsch sprechen, stehen Ihnen kostenlos sprachliche Hilfsdienstleistungen zurVerfügung. Rufnummer: 1.866.631.5404 (TTY: 711).

Hindi: _यान द_: य_द आप ि◌हंदी बोलते ह_ तो आपके ि◌लए मु_त म_ भाषा सहायता सेवाएं उपल_ध ह_। 1.866.631.5404 (TTY: 711) पर कॉल कर_।

Hmong: LUS CEEV: Yog tias koj hais lus Hmoob, cov kev pab txog lus, muaj kev pab dawb rau koj. Hu rau 1.866.631.5404 (TTY: 711).

Korean: 주의: 한국어를 사용하시는 경우, 언어 지원 서비스를 무료로 이용하실 수 있습니다. 1.866.631.5404 (TTY: 711)번으로 전화해 주십시오.

Polish: UWAGA: Jeżeli mówisz po polsku, możesz skorzystać z bezpłatnej pomocy językowej. Zadzwoń pod numer 1.866.631.5404 (TTY: 711).

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Spanish: ATENCIÓN: si habla español, tiene a su disposición servicios gratuitos de asistencia lingüística. Llame al 1.866.631.5404 (TTY: 711).

Tagalog: PAUNAWA: Kung nagsasalita ka ng Tagalog, maaari kang gumamit ng mga serbisyo ng tulong sa wika nangwalang bayad. Tumawag sa 1.866.631.5404 (TTY: 711)

Traditional Chinese: 注意：如果您使用繁體中文，您可以免費獲得語言援助服務。請 致電 1.866.631.5404 (TTY:711).

Vietnamese: CHÚ Ý: Nếu bạn nói Tiếng Việt, có các dịch vụ hỗ trợ ngôn ngữ miễn phí dành cho bạn. Gọi số 1.866.631.5404 (TTY: 711).

Pennsylvania Dutch: Wann du Deitsch (Pennsylvania German / Dutch) schwetzscht, kannscht du mitaus Koschte ebbergricke, ass dihr helft mit die englisch Schprooch. Ruf selli Nummer uff: Call 1.866.631.5404 (TTY: 711).

Lao: ໂປດຊາບ: ຖ້າວ່າ ທ່ານເວົ້າພາສາ ລາວ, ການບໍລິການຊ່ວຍເຫຼືອດ້ານພາສາ,ໂດຍບໍ່ເສັ້ງຄ່າ, ແມ່ນມີພ້ອມໃຫ້ທ່ານ. ໂທຣ 1.866.631.5404 (TTY:711).

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