Vyvgart® (Efgartigimod Alfa-Fcab)

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Instructions for Use

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Coverage Rationale

See Benefit Considerations

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; or
      - History of positive anticholinesterase test, e.g., edrophonium chloride test; or
      - 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
  - One of the following: (for Medicare reviews, refer to the CMS section*)
    - History of failure of at least two immunosuppressive agents over the course of at least 12 months [e.g., azathioprine, methotrexate, cyclosporine, mycophenolate, etc.]; or
    - Patient has a history of failure of at least one immunosuppressive therapy and has required four or more courses of plasmapheresis/plasma exchanges and/or intravenous immune globulin over the course of at least 12 months without symptom control

and
  - Patient is not receiving Vyvgart in combination with Soliris (eculizumab) or Ultomiris (ravulizumab); 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 at least 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[6]; and
    - Reduction in signs and symptoms of myasthenia gravis; and
    - 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) or Ultomiris (ravulizumab); 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
J9332	Injection, efgartigimod alfa-fcab, 2 mg

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.

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. Studies have used different thresholds of change in MG-ADL score to indicate clinically meaningful change.[6,7] In a validation study that aimed to determine the change in MG-ADL value that would best predict improvement in MG clinical status, results from sensitivity and specificity analyses indicated that a 1-point change in MG-ADL was highly sensitive (96%) but did not have good specificity (71%), and a 3-point change had good specificity (90%) but was not very sensitive (62%). A 2-point change provided a balance between sensitivity (77%) and specificity (82%).

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-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 covers 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 19, 2022)

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

References

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Policy History/Revision Information

Date	Summary of Changes
03/01/2023	Supporting Information • Updated *Clinical Evidence*, *CMS*, and *References* sections to reflect the most current information • Archived previous policy version 2022D00111D

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.