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Policy Number: 052.001
Title: Coverage Determination Policy for Vyvgart (efgartigimod alfa-fcab); Vyvgart Hytrulo (efgartigimod alfa and hyaluronidase-qvfc); Rystiggo (rozanolixizumab-noli)

Regions: ☒ **Texas** ☒ **New Mexico**

Impacted Areas:

- ☒ Network Management/Provider Services
- ☐ Member services
- ☐ Quality Management
- ☐ Credentialing
- ☐ IT
- ☐ Administration
- ☐ Compliance/delegation
- ☒ Utilization Management
- ☐ Case management
- ☐ Disease management
- ☒ Claims
- ☐ Human resources
- ☐ Finance
- ☒ Pharmacy
- ☐ ALL

Available LCD/NCD/LCA: None

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Doctors helping patients for more than 25 years

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Coverage Policy Number: 052.001

Line of Business: Medicare Part B

Policy Type: Prior Authorization

Coverage Determination:

Initial/New Requests

Vyvgart and Vyvgart Hytrulo are proven for the treatment of **generalized myasthenia gravis (gMG)**. Vyvgart and Vyvgart Hytrulo are medically necessary when **ALL** of the following criteria are met:

A. 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:

- **I.** Patient has not failed a previous course of Vyvgart therapy
- **II.** Patient has not failed a previous course of Vyvgart Hytrulo therapy
- **III.** Positive serologic test for anti-AChR antibodies
- **IV.** ONE of the following
  - **a.** History of abnormal neuromuscular transmission test demonstrated by single-fiber electromyography (SFEMG) or repetitive nerve stimulation
  - **b.** History of positive anticholinesterase test, e.g., edrophonium chloride test
  - **c.** Patient has demonstrated improvement in MG signs on oral cholinesterase inhibitors, as assessed by the treating neurologist
- **V.** Patient has a Myasthenia Gravis Foundation of America (MGFA) Clinical Classification of class II, III, or IV at initiation of therapy
- **VI.** Patient has a Myasthenia Gravis-specific Activities of Daily Living scale (MG-ADL) total score ≥ 5 at initiation of therapy

B. ONE of the following:

- **I.** History of failure of at least **two** immunosuppressive agents over the course of at least 12 months [e.g., azathioprine, corticosteroids, methotrexate, cyclosporine, mycophenolate, etc.]
- **II.** 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

C. Patient is not receiving Vyvgart or Vyvgart Hytrulo in combination with Soliris (eculizumab) or Ultomiris (ravulizumab)

D. Patient is not receiving Vyvgart or Vyvgart Hytrulo in combination with another neonatal Fc receptor blocker [e.g., Rystiggo (rozanolixizumab-noli)

E. Vyvgart or Vyvgart Hytrulo is initiated and titrated according to the FDA labeled dosing for gMG

F. Prescribed by, or in consultation with, a neurologist

G. Initial authorization will be approved for 6 months

Rystiggo is proven for the treatment of **generalized myasthenia gravis**. Rystiggo is medically necessary when **ALL** of the following criteria are met:

1. 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:

A. Patient has not failed a previous course of Rystiggo therapy

B. **One** of the following:

I. Positive serologic test for anti-AChR antibodies

II. Positive serologic test for anti-MuSK antibodies

C. **One** of the following:

I. History of abnormal neuromuscular transmission test demonstrated by single-fiber electromyography (SFEMG) or repetitive nerve stimulation

II. History of positive anticholinesterase test, e.g., edrophonium chloride test

III. Patient has demonstrated improvement in MG signs on oral cholinesterase inhibitors, as assessed by the treating neurologist

D. Patient has a Myasthenia Gravis Foundation of America (MGFA) Clinical Classification of class II, III, or IV at initiation of therapy

E. Patient has a Myasthenia Gravis-specific Activities of Daily Living scale (MG-ADL) total score ≥ 5 at initiation of therapy

F. **One** of the following:

I. History of failure of at least **two** immunosuppressive agents over the course of at least 12 months [e.g., azathioprine, corticosteroids, cyclosporine, methotrexate, mycophenolate, etc.]

II. 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

G. Patient is not receiving Rystiggo in combination with Soliris (eculizumab) or Ultomiris (ravulizumab)

H. Patient is not receiving Rystiggo in combination with another neonatal Fc receptor blocker [e.g., Vyvgart (efgartigimod alfa-fcab), Vyvgart Hytrulo (efgartigimod alfa and hyaluronidase-qvfc)]

I. Rystiggo is dosed according to the US FDA labeled dosing for gMG

J. Prescribed by, or in consultation with, a neurologist

K. Initial authorization will be approved for 6 months.

Renewal/Continuation of Therapy Requests

For **ALL Vyvgart or Vyvgart Hytrulo** requests for continuation of therapy, **ALL** of the following must be met:

A. Patient has previously been treated with Vyvgart or Vyvgart Hytrulo

B. 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:

I. Improvement and/or maintenance of at least a 2 point improvement (reduction in score) in the MG-ADL score from pre-treatment baseline

II. Reduction in signs and symptoms of myasthenia gravis

III. Maintenance, reduction, or discontinuation of dose(s) of baseline immunosuppressive therapy (IST) prior to starting Vyvgart or Vyvgart Hytrulo. ***Note:*** *Add on, dose escalation of IST, or additional rescue therapy from baseline to treat myasthenia gravis or exacerbation of symptoms while on Vyvgart or Vyvgart Hytrulo therapy will be considered as treatment failure*

C. Patient is not receiving Vyvgart or Vyvgart Hytrulo in combination with Soliris (eculizumab) or Ultomiris (ravulizumab)

D. Patient is not receiving Vyvgart or Vyvgart Hytrulo in combination with another neonatal Fc receptor blocker [e.g., Rystiggo (rozanolixizumab-noli)

E. Vyvgart or Vyvgart Hytrulo is dosed according to the FDA labeled dosing for gMG

F. Prescribed by, or in consultation with, a neurologist

For **ALL Rystiggo** requests for continuation of therapy, **ALL** of the following must be met:

A. Patient has previously been treated with Rystiggo

B. 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:

I. Improvement and/or maintenance of at least a 2 point improvement (reduction in score) in the MG-ADL score from pre-treatment baseline

II. Reduction in signs and symptoms of myasthenia gravis

III. Maintenance, reduction, or discontinuation of dose(s) of baseline immunosuppressive therapy (IST) prior to starting Rystiggo. ***Note:*** *Add on, dose escalation of IST, or additional rescue therapy from baseline to treat myasthenia gravis or exacerbation of symptoms while on Rystiggo therapy will be considered as treatment failure*

C. Patient is not receiving Rystiggo in combination with Soliris (eculizumab) or Ultomiris (ravulizumab)

D. Patient is not receiving Rystiggo in combination with another neonatal Fc receptor blocker [e.g., Vyvgart (efgartigimod alfa-fcab), Vyvgart Hytrulo (efgartigimod alfa and hyaluronidase-qvfc)]

E. Rystiggo is dosed according to the US FDA labeled dosing for gMG

F. Prescribed by, or in consultation with, a neurologist

FDA Approved Dose and Indication

Drug Name	FDA Approved Indication	Dosing
Vyvgart	**Myasthenia gravis, Anti-acetylcholine receptor (AChR) antibody positive**	• Weight less than 120 kg- Initial: 10 mg/kg IV infusion over 1 hour once weekly for 4 weeks • Weight 120 kg or greater- Initial: 1200 mg IV infusion over 1 hour once weekly for 4 weeks ***Note:*** *Subsequent treatment cycles can be administered based on clinical evaluation; the safety of initiating subsequent cycles sooner than 50 days from the start of a previous cycle has not been established.*
Vyvgart Hytrulo	**Myasthenia gravis, Anti-acetylcholine receptor (AChR) antibody positive**	• 1008 mg/11,200 units subQ once weekly for 4 weeks ***Note:*** *Administer subsequent treatment cycles according to clinical evaluation, the safety of initiating subsequent cycles sooner than 50 days from the start of the previous treatment cycle has not been established.*
Rystiggo	**Myasthenia gravis, Generalized, anti-acetylcholine receptor or anti-muscle-specific tyrosine kinase antibody positive**	• (Less than 50 kg) 420 mg as a subQ infusion once weekly for 6 weeks • (50 kg to less than 100 kg) 560 mg once weekly for 6 weeks • (100 kg or greater) 840 mg once weekly for 6 weeks ***Note:*** *Administer subsequent treatment cycles based on clinical evaluation; the safety of initiating subsequent cycles sooner than 63 days from the start of the previous treatment cycle has not been established.*

General Background

Myasthenia gravis is an autoimmune condition that causes weakness and rapid fatigue of muscles. The weakness is due to an antibody-mediated, immunologic attack directed at proteins in the postsynaptic membrane of the neuromuscular junction (acetylcholine receptors or receptor-associated proteins). MG is the most common disorder of neuromuscular transmission. The goals of therapy in MG are to render patients minimally symptomatic or better while minimizing side effects from medications. MG is a chronic but treatable disease, and many patients can achieve sustained remission of symptoms and full functional capacity.

Vyvgart (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.

MGFA Clinical Classification[3]

1. Class I: Any ocular muscle weakness; may have weakness of eye closure. All other muscle strength is normal.
2. Class II: Mild weakness affecting non-ocular muscles May also have any ocular weakness
    - IIa. Predominantly affecting limb, axial muscles, or both. May also have lesser involvement of oropharyngeal muscles.
    - IIb. Predominantly affecting oropharyngeal, respiratory muscles, or both. May also have lesser or equal involvement of limb, axial muscles, or both.
3. Class III: Moderate weakness affecting muscles other than ocular muscles; may also have ocular muscle weakness of any severity
    - IIIa. Predominantly affecting limb, axial muscles, or both. May also have lesser involvement of oropharyngeal muscles
    - IIIb. Predominantly affecting oropharyngeal, respiratory muscles, or both. May also have lesser or equal involvement of limb, axial muscles, or both
4. Class IV: Severe weakness affecting muscles other than ocular muscles; may also have ocular muscle weakness of any severity
    - IVa. Predominantly affecting limb, axial muscles, or both. May also have lesser involvement of oropharyngeal muscles.
    - IVb. Predominantly affecting oropharyngeal, respiratory muscles, or both. May also have lesser or equal involvement of limb, axial muscles, or both
5. Class V: Defined as intubation, with or without mechanical ventilation, except when employed during routine postoperative management.
   The use of a feeding tube without intubation places the patient in class IVb

Myasthenia Gravis Activities of Daily Living (MG-ADL) scale[6]

MG-ADL can be accessed at this link.

Assesses the impact of gMG on daily functions by measuring 8 signs or symptoms that are commonly affected in gMG.

- Each item is measured on a 4-point scale, where a score of 0 represents normal function and a score of 3 represents the loss of ability to perform that function.
- Total scores range from 0 to 24 points, with a higher score showing more severe gMG

	0	1	2	3	Score
1. Talking	Normal	Intermittent slurring or nasal speech	Constant slurring or nasal speech, but can be understood	Difficult-to understand speech	
2. Chewing	Normal	Fatigue with solid food	Fatigue with soft food	Gastric tube	
3. Swallowing	Normal	Rare episode of choking	Frequent choking necessitating changes in diet	Gastric tube	
4. Breathing	Normal	Shortness of breath with exertion	Shortness of breath at rest	Ventilator dependence	
5. Impairment of ability to brush teeth or comb hair	None	Extra effort, but no rest periods needed	Rest periods needed	Cannot do one of these functions	
6. Impairment of ability to arise from a chair	None	Mild, sometimes uses arms	Moderate, always uses arms	Severe, requires assistance	
7. Double vision	None	Occurs, but not daily	Daily, but not constant	Constant	
8. Eyelid droop	None	Occurs, but not daily	Daily, but not constant	Constant	
Add items 1-8 for total MG-ADL score					

Clinical Evidence

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 nonsteroidal 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.

In Study 2, the pharmacological effect of Vyvgart Hytrulo administered subcutaneously (SC) at 1,008 mg / 11,200 Units was compared to efgartigimod alfa-fcab administered intravenously at 10 mg/kg (EFG IV) in gMG patients. The maximum mean reduction in AChR-Ab level was observed at week 4, with a mean reduction of 62.2% and 59.7% in the Vyvgart Hytrulo SC and efgartigimod alfa-fcab IV arm, respectively. The decrease in total IgG levels followed a similar pattern. The 90% confidence intervals for the geometric mean ratios of AChR-Ab reduction at day 29 and AUEC0-4w (area under the effect-time curve from time 0 to 4 weeks post dose) were within the range of 80% to 125%, indicating no clinically significant difference between the two formulations

The efficacy of Rystiggo for the treatment of generalized myasthenia gravis (gMG) in adults who are anti-AChR antibody positive or anti-MuSK antibody positive was established in a multicenter, randomized, double-blind, placebo-controlled study (Study 1; NCT03971422). The study included a 4-week screening period and a 6-week treatment period followed by 8 weeks of observation. During the treatment period, RYSTIGGO or placebo were administered subcutaneously once a week for six weeks.

In Study 1, a total of 200 patients were randomized 1:1:1 to receive weight-tiered dosesof Rystiggo (n=133), equivalent to ≈7 mg/kg (n=66) or ≈10 mg/kg (n=67), or placebo (n=67). Baseline characteristics were similar between treatment groups. Patients had a median age of 52 years at baseline (range: 18 to 89 years) and a median time since diagnosis of 6 years. Sixty-one percent of patients were female, 68% were White, 11% were Asian, 3% were Black or African American, 1% were American Indian or Alaska Native, and 7% were of Hispanic or Latino ethnicity. Median MG-ADL total score was 8, and the median Quantitative Myasthenia Gravis (QMG) total score was 15. The majority of patients, 89.5% (n=179) were positive for AChR antibodies and 10.5% (n=21) were positive for MuSK antibodies. At baseline in each group, over 83% of patients received AChE inhibitors, over 56% of patients received steroids, and approximately 50% received NSISTs, at stable doses. Patients were treated with Rystiggo via subcutaneous infusion once per week for a period of 6 weeks [see Dosage and Administration (2.2)], followed by an observation period of up to 8 weeks.

The efficacy of Rystiggo was measured using the MG-ADL scale, 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. The primary efficacy endpoint was the comparison of the change from baseline between treatment groups in the MG-ADL total score at day 43. A statistically significant difference favoring Rystiggo was observed in the MG-ADL total score change from baseline [-3.4 points in Rystiggo -treated group at either dose vs -0.8 points in the placebo-treated group ($p<0.001$)]. The secondary endpoint was the change between treatment groups from baseline to day 43 in the QMG. The QMG 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. A statistically significant difference favoring Rystiggo was observed in the QMG total score change from baseline [-5.4 points and -6.7 points in Rystiggo -treated group at ≈7 mg/kg and ≈10 mg/kg dose level, respectively, vs -1.9 points in the placebo-treated group ($p<0.001$).

HCPCS Code

HCPCS Code	J9332: Vyvgart	C9399, J3490, J3590 (Vyvgart Hytrulo)	C9399, J3490, J3590 (Rystiggo)
Dosage Form	400 mg/20 mL (20 mg/mL) in one single-dose vial	1008 mg-11,200units/5.6 mL (180 mg/2,000 units per mL): single-dose vial	280 mg/2 mL (140 mg/mL) single-dose vial
Route of Administration	Intravenous infusion	Subcutaneous injection by healthcare professional only	Subcutaneous infusion only using an infusion pump

Acronyms

Gmg = Generalized myasthenia gravis

MG-ADL = Myasthenia Gravis-specific Activities of Daily Living scale

MGFA = Myasthenia Gravis Foundation of America

AchR = Anti-acetylcholine receptor

SFEMG= Single-fiber electromyography

anti-MuSK = Anti-muscle-specific kinase

anti-AchR = Anti-acetylcholine receptor

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