Neonatal Fc Receptor Blockers (Vyvgart®, Vyvgart® Hytrulo, & Rystiggo®)

Policy Number: 2024D00111G
Effective Date: January 1, 2024

➲ Instructions for Use

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Related Commercial Policy
- Provider Administered Drugs – Site of Care

Community Plan Policy
- Neonatal Fc Receptor Blockers (Vyvgart®, Vyvgart® Hytrulo, & Rystiggo®)

Coverage Rationale

➲ See Benefit Considerations

Vyvgart and Vyvgart Hytrulo are proven for the treatment of generalized myasthenia gravis in patients who are anti-acetylcholine receptor (AChR) antibody positive. Vyvgart and Vyvgart Hytrulo are medically necessary for the treatment of generalized myasthenia gravis in patients who are anti-AChR antibody positive 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**
    - Patient has not failed a previous course of Vyvgart Hytrulo 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, corticosteroids, cyclosporine, methotrexate, 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 or Vyvgart Hytrulo in combination with Soliris (eculizumab) or Ultomiris (ravulizumab); **and**
    - Patient is not receiving Vyvgart or Vyvgart Hytrulo in combination with another neonatal Fc receptor blocker [e.g., Rystiggo (rozanolixizumab-noli)]; **and**
    - Vyvgart or Vyvgart Hytrulo is dosed according to the US FDA labeled dosing for gMG; **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 or Vyvgart Hytrulo; **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 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

      and
    - Patient is not receiving Vyvgart or Vyvgart Hytrulo in combination with Soliris (eculizumab) or Ultomiris (ravulizumab); **and**
    - Patient is not receiving Vyvgart or Vyvgart Hytrulo in combination with another neonatal Fc receptor blocker [e.g., Rystiggo (rozanolixizumab-noli)]; **and**
    - Vyvgart or Vyvgart Hytrulo is dosed according to the US FDA labeled dosing for gMG; **and**
    - Prescribed by, or in consultation with, a neurologist; **and**
    - Reauthorization will be for no more than 12 months

Rystiggo is proven for the treatment of generalized myasthenia gravis in patients who are anti-acetylcholine receptor (AChR) antibody positive. Rystiggo is medically necessary for the treatment of generalized myasthenia gravis in patients who are anti-AChR antibody positive 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 Rystiggo 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, corticosteroids, cyclosporine, methotrexate, 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 Rystiggo in combination with Soliris (eculizumab) or Ultomiris (ravulizumab); **and**
    - 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)]; **and**
    - Rystiggo is dosed according to the US FDA labeled dosing for gMG; **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 Rystiggo; **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 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

      and
    - Patient is not receiving Rystiggo in combination with Soliris (eculizumab) or Ultomiris (ravulizumab); **and**
    - 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)]; **and**
    - Rystiggo is dosed according to the US FDA labeled dosing for gMG; **and**
    - Prescribed by, or in consultation with, a neurologist; **and**
    - Reauthorization will be for no more than 12 months

Rystiggo is proven for the treatment of generalized myasthenia gravis in patients who are antimuscle-specific tyrosine kinase (MuSK) antibody positive. Rystiggo is medically necessary for the treatment of generalized myasthenia gravis in patients who are anti-MuSK antibody positive 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 Rystiggo therapy; **and**
        - Positive serologic test for anti-MuSK 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
    - History of failure of at least **one** immunosuppressive agent over the course of at least 12 months [e.g., azathioprine, corticosteroids, cyclosporine, methotrexate, mycophenolate, etc.] (for Medicare reviews, refer to the CMS section*); **and**
    - Patient is not receiving Rystiggo in combination with Soliris (eculizumab) or Ultomiris (ravulizumab); **and**

- 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)]; **and**
- Rystiggo is dosed according to the US FDA labeled dosing for gMG; **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 Rystiggo; **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 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

    and
  - Patient is not receiving Rystiggo in combination with Soliris (eculizumab) or Ultomiris (ravulizumab); **and**
  - 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)]; **and**
  - Rystiggo is dosed according to the US FDA labeled dosing for gMG; **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
J9333	Injection, rozanolixizumab-noli, 1 mg
J9334	Injection, efgartigimod alfa, 2 mg and hyaluronidase-qvfc

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.

Efgartigimod alfa and hyaluronidase-qvfc is a coformulation of efgartigimod alfa and hyaluronidase. Efgartigimod alfa is a human IgG1 antibody fragment that binds to the neonatal Fc receptor (FcRn), resulting in the reduction of circulating IgG. Hyaluronidase increases permeability of the subcutaneous tissue by depolymerizing hyaluronan. This effect is transient and permeability of the subcutaneous tissue is restored within 24 to 48 hours.

Rozanolixizumab-noli is a humanized IgG4 monoclonal antibody that binds to the neonatal Fc receptor (FcRn), resulting in the reduction of circulating IgG.

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 Medical Benefit Drug 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 ($p < 0.0001$)].

Efgartigimod alfa and hyaluronidase-qvfc is indicated for the treatment of gMG in adult patients who are anti-acetylcholine receptor (AChR) antibody positive. Study 1 (described above) which established the effectiveness of efgartigimod alfa-fcab for the treatment of gMG in adults who are AChR antibody positive was conducted with efgartigimod alfa-fcab intravenous formulation. In Study 2, efgartigimod alfa and hyaluronidase-qvfc demonstrated a comparable pharmacodynamic effect on AChR antibody reduction as compared to the efgartigimod alfa-fcab intravenous formulation, which established the efficacy of efgartigimod alfa and hyaluronidase-qvfc. In Study 2, the pharmacological effect of efgartigimod alfa and hyaluronidase-qvfc 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 efgartigimod alfa and hyaluronidase-qvfc 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 $AUEC_{0\text{-}4w}$ (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 rozanolixizumab-noli for the treatment of 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, rozanolixizumab-noli or placebo were administered subcutaneously once a week for six weeks.
Study 1 enrolled patients who met the following criteria:

- Presence of autoantibodies against AChR or MuSK
- Myasthenia Gravis Foundation of America (MGFA) Clinical Classification Class II to IVa
- Myasthenia Gravis-Activities of Daily Living (MG-ADL) total score of at least 3 (with at least 3 points from non-ocular symptoms)
- 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
- Serum IgG levels of at least 5.5 g/L

In Study 1, a total of 200 patients were randomized 1:1:1 to receive weight-tiered doses of rozanolixizumab-noli (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, followed by an observation period of up to 8 weeks. The efficacy of rozanolixizumab-noli was measured using the MG-ADL scale. 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 rozanolixizumab-noli was observed in the MG-ADL total score change from baseline [-3.4 points in rozanolixizumab-noli -treated group at either dose vs -0.8 points in the placebo-treated group ($p < 0.001$)]. Reductions from baseline to day 43 in MG-ADL scores were observed in patients with AChR autoantibodypositive generalized myasthenia gravis (rozanolixizumab 7 mg/kg least-squares mean −3·03 [SE 0·89]; rozanolixizumab 10 mg/kg −3·36 [0·87]; placebo −1·10 [0·87]; least-squares mean difference from placebo −1·94 [97·5% CI −3·06 to −0·81] and −2·26 [−3·39 to −1·13] in the rozanolixizumab 7 mg/kg and 10 mg/kg groups, respectively). For patients with MuSK autoantibodypositive gMG, least-squares mean reductions were −7·28 [SE 1·94] in the rozanolixizumab 7 mg/kg group, −4·16 [1·78] in the rozanolixizumab 10 mg/kg group, and 2·28 [1·95] in the placebo group (least-squares mean difference from placebo for rozanolixizumab 7 mg/kg −9·56 [97·5% CI −15·25 to −3·87]; −6·45 [−11·03 to −1·86] for the rozanolixizumab 10 mg/kg group).

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.

Vyvgart Hytrulo is a combination of efgartigimod alfa, a neonatal Fc receptor blocker, and hyaluronidase, an endoglycosidase, indicated for the treatment of generalized myasthenia gravis (gMG) in adult patients who are anti-acetylcholine receptor (AChR) antibody positive.

Rystiggo is a neonatal Fc receptor blocker indicated for the treatment of generalized myasthenia gravis (gMG) in adult patients who are anti-acetylcholine receptor (AChR) or anti muscle-specific tyrosine kinase (MuSK) antibody positive.

Centers for Medicare and Medicaid Services (CMS)

Medicare does not have a National Coverage Determination (NCD) for neonatal Fc receptor blockers: Vyvgart®, Vyvgart® Hytrulon (efgartigimod alfa and hyaluronidase-qvfc) and Rystiggo® (rozanolixizumab-noli). Local Coverage Determinations/Articles (LCDs)/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 July 19, 2023)

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

References

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Policy History/Revision Information

Date	Summary of Changes

01/01/2024	**Coverage Rationale**
	• Removed reference link to the Medical Benefit Drug Policy titled R*eview at Launch for New to Market Medications*
	• Replaced language indicating:
	  ○ "Vyvgart, Vyvgart Hytrulo, and Rystiggo are proven and medically necessary for the treatment of generalized myasthenia gravis" with "Vyvgart, Vyvgart Hytrulo, and Rystiggo are proven and medically necessary for the treatment of generalized myasthenia gravis *in patients who are anti-acetylcholine receptor (AChR) antibody positive*"
	• Revised coverage criteria for Rystiggo for the treatment of generalized myasthenia gravis; removed criterion requiring positive serologic test for anti-MuSK antibodies
	• Added language to indicate Rystiggo is proven for the treatment of generalized myasthenia gravis in patients who are antimuscle-specific tyrosine kinase (MuSK) antibody positive; Rystiggo is medically necessary for the treatment of generalized myasthenia gravis in patients who are anti-MuSK antibody positive 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 Rystiggo therapy
	  ▪ Positive serologic test for anti-MuSK antibodies
	  – 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
	  – Patient has a Myasthenia Gravis Foundation of America (MGFA) Clinical Classification of class II, III, or IV at initiation of therapy
	  – Patient has a Myasthenia Gravis-specific Activities of Daily Living scale (MG-ADL) total score ≥ 5 at initiation of therapy
	  ○ History of failure of at least one immunosuppressive agent over the course of at least 12 months [e.g., azathioprine, corticosteroids, cyclosporine, methotrexate, mycophenolate, etc.] (for Medicare reviews, refer to the CMS section of the policy)
	  ○ Patient is not receiving Rystiggo in combination with Soliris (eculizumab) or Ultomiris (ravulizumab)
	  ○ 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)]
	  ○ Rystiggo is dosed according to the US FDA labeled dosing for gMG
	  ○ Prescribed by, or in consultation with, a neurologist

Date	Summary of Changes
	○ Initial authorization will be for no more than 6 months ***Continuation of Therapy*** ○ Patient has previously been treated with Rystiggo ○ 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 ▪ Reduction in signs and symptoms of myasthenia gravis ▪ 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) ○ Patient is not receiving Rystiggo in combination with Soliris (eculizumab) or Ultomiris (ravulizumab) ○ 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)] ○ Rystiggo is dosed according to the US FDA labeled dosing for gMG ○ Prescribed by, or in consultation with, a neurologist ○ Reauthorization will be for no more than 12 months **Applicable Codes** • Updated list of applicable HCPCS codes to reflect annual edits; replaced C9399, J3490, and J3590 with J9333 and J9334 **Supporting Information** • Archived previous policy version 2023D00111F

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.