BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

EVIDENCE-BASED CRITERIA	**ORIGINAL EFFECTIVE DATE: 07/15/24**
SECTION: SPECIALTY MEDICAL DRUGS	**LAST REVIEW DATE:**
	CURRENT EFFECTIVE DATE: 07/15/24
	LAST CRITERIA REVISION DATE:
NEXT ANNUAL REVIEW DATE: 2ND QTR 2025	**ARCHIVE DATE:**

RYSTIGGO (rozanolixizumab-noli)
VYVGART (efgartigimod alfa-fcab)
VYVGART HYTRULO (efgartigimod alfa and hyaluronidase-qvfc)

Non-Discrimination Statement is located at the end of this document.

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Evidence-Based Criteria must be read in its entirety to determine coverage eligibility, if any.

This Evidence-Based Criteria provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Evidence-Based Criteria are subject to change as new information becomes available.

For purposes of this Evidence-Based Criteria, the terms "experimental" and "investigational" are considered to be interchangeable.

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RYSTIGGO (rozanolixizumab-noli)
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Criteria:

Refer to FDA website for current indications and dosage.

RYSTIGGO (rozanolixizumab-noli)

- **Criteria for initial therapy:** Rystiggo (rozanolixizumab-noli) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with a Neurologist

2. Individual is 18 years of age or older

3. Individual has a confirmed diagnosis of generalized myasthenia gravis with documentation of **ONE** of the following:

   - Anti-acetylcholine receptor (AChR) antibody positive
   - Anti-muscle-specific tyrosine kinase (MuSK) antibody positive

4. Individual meets **ALL** of the following:

   - Class II to IV disease per the Myasthenia Gravis Foundation of America (MGFA) classification system (see Definitions section)
   - MG-Activities of Daily Living (MG-ADL) score of at least 3 or greater from non-ocular symptoms (see Definitions section)
   - Serum IgG levels 5.5g/L or greater

5. Individual has failure, contraindication per FDA label or intolerance to a trial of at least 3 months of **ALL** the following:

   - Pyridostigmine
   - One immunosuppressive therapy (e.g., azathioprine, cyclosporine, methotrexate, mycophenolate, tacrolimus)
   - For AChR antibody positive individuals: Vyvgart or Vyvgart Hytrulo

6. Individual does **NOT** have **ANY** of the following:

   - Evidence of active infection
   - Will not receive live attenuated or live vaccines during treatment with Rystiggo

7. Rystiggo will not be used in combination with the following medications:

- Neonatal Fc Receptor Antagonists (e.g., Vyvgart, Vyvgart Hytrulo)
- Maintenance Immunoglobulins (e.g., IVIG)
- Complement inhibitors (Soliris, Ultomiris, Zilbrysq)
- Monoclonal antibodies (e.g., Dupixent, Remicade, Rinvoq, Xolair, etc.)

Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Rystiggo (rozanolixizumab-noli) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with a Neurologist

2. Individual has a confirmed diagnosis of generalized myasthenia gravis with documentation of **ONE** of the following:

   - Anti-acetylcholine receptor (AChR) antibody positive
   - Anti-muscle-specific tyrosine kinase (MuSK) antibody positive

3. Individual's condition has responded while on therapy with response defined as **BOTH** of the following:

   - Documentation of clinical benefit (e.g., decrease in frequency or severity of myasthenia gravis exacerbations, improvements in speech, swallowing, mobility, or respiratory function)
   - Improvement MG-ADL total score by 2 points or more from baseline

4. Individual has been adherent with the medication

5. Individual has not developed any contraindications or other significant adverse drug effects that may exclude continued use such as hypersensitivity (e.g., angioedema, rash)

6. Individual does **NOT** have **ANY** of the following:

   - Evidence of active infection
   - Will not receive live attenuated or live vaccines during treatment with Rystiggo

7. Rystiggo will not be used in combination with the following medications:

   - Neonatal Fc Receptor Antagonists (e.g., Rystiggo)
   - Immunoglobulins (e.g., IVIG)
   - Complement inhibitors (Soliris, Ultomiris, Zilbrysq)
   - Monoclonal antibodies (e.g., Dupixent, Remicade, Rinvoq, Xolair, etc.)

RYSTIGGO (rozanolixizumab-noli)
VYVGART (efgartigimod alfa-fcab)
VYVGART HYTRULO (efgartigimod alfa and hyaluronidase-qvfc)

Renewal duration: 12 months

- Rystiggo (rozanolixizumab-noli) for all other indications not previous listed is considered ***experimental or investigational*** and will not be covered when any **ONE** or more of the following criteria are met:

1. Lack of final approval from the appropriate governmental regulatory bodies (e.g., Food and Drug Administration); or
2. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes; or
3. Insufficient evidence to support improvement of the net health outcome; or
4. Insufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives; or
5. Insufficient evidence to support improvement outside the investigational setting.

These indications include, *but not limited to:*

- Treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, or duration.

VYVGART (efgartigimod alfa-fcab)
VYVGART HYTRULO (efgartigimod alfa and hyaluronidase-qvfc)

- **Criteria for initial therapy:** Vyvgart (efgartigimod alfa-fcab) or Vyvgart Hytrulo (efgartigimod alfa and hyaluronidase-qvfc) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with a Neurologist

2. Individual is 18 years of age or older

3. Individual has a confirmed diagnosis of generalized myasthenia gravis in individuals who are anti-acetylcholine receptor (AChR) antibody positive

4. Individual meets **ALL** of the following:

   - Class II to IV disease per the Myasthenia Gravis Foundation of America (MGFA) classification system (see Definitions section)
   - MG-Activities of Daily Living (MG-ADL) score of at least 5 or greater (see Definitions section)
   - Serum IgG levels 6 g/L or greater

5. Individual has failure, contraindication per FDA label or intolerance to a trial of at least 3 months of **ALL** the following:

   - Pyridostigmine
   - One immunosuppressive therapy (e.g., azathioprine, cyclosporine, methotrexate, mycophenolate, tacrolimus)

6. Individual does **NOT** have **ANY** of the following:

   - Evidence of active infection
   - Will not receive live attenuated or live vaccines during treatment with Vyvgart or Vyvgart Hytrulo

7. Vyvgart or Vyvgart Hytrulo will not be used in combination with the following medications:

   - Neonatal Fc Receptor Antagonists (e.g., Rystiggo)
   - Immunoglobulins (e.g., IVIG)
   - Complement inhibitors (Soliris, Ultomiris, Zilbrysq)
   - Monoclonal antibodies (e.g., Dupixent, Remicade, Rinvoq, Xolair, etc.)

Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Vyvgart (efgartigimod alfa-fcab) or Vyvgart Hytrulo (efgartigimod alfa and hyaluronidase-qvfc) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with a Neurologist

2. Individual has a confirmed diagnosis of generalized myasthenia gravis in individuals who are anti-acetylcholine receptor (AChR) antibody positive

3. Individual's condition has responded while on therapy with response defined as **BOTH** of the following:

   - Documentation of clinical benefit (e.g., decrease in frequency or severity of myasthenia gravis exacerbations, improvements in speech, swallowing, mobility, or respiratory function)
   - Improvement MG-ADL total score by 2 points or more from baseline

4. Individual has been adherent with the medication

5. Individual has not developed any contraindications or other significant adverse drug effects that may exclude continued use such as:

   - Hypersensitivity (e.g., anaphylaxis, syncope, angioedema, dyspnea, rash, urticaria)
   - Severe Infusion-related reaction

6. Individual does **NOT** have **ANY** of the following:

   - Evidence of active infection
   - Will not receive live attenuated or live vaccines during treatment with Vyvgart or Vyvgart Hytrulo

7. Vyvgart or Vyvgart Hytrulo will not be used in combination with the following medications:

   - Neonatal Fc Receptor Antagonists (e.g., Rystiggo)
   - Maintenance Immunoglobulins (e.g., IVIG)
   - Complement inhibitors (Soliris, Ultomiris, Zilbrysq)
   - Monoclonal antibodies (e.g., Dupixent, Remicade, Rinvoq, Xolair, etc.)

Renewal duration: 12 months

- Vyvgart (efgartigimod alfa-fcab) or Vyvgart Hytrulo (efgartigimod alfa and hyaluronidase-qvfc) for all other indications not previous listed is considered ***experimental or investigational*** and will not be covered when any **ONE** or more of the following criteria are met:

  1. Lack of final approval from the appropriate governmental regulatory bodies (e.g., Food and Drug Administration); or
  2. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes; or
  3. Insufficient evidence to support improvement of the net health outcome; or
  4. Insufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives; or
  5. Insufficient evidence to support improvement outside the investigational setting.

  These indications include, *including but not limited to:*

  - Treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, or duration.

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RYSTIGGO (rozanolixizumab-noli)
VYVGART (efgartigimod alfa-fcab)
VYVGART HYTRULO (efgartigimod alfa and hyaluronidase-qvfc)

Description:

Myasthenia gravis (MG) is an acquired, autoimmune disorder that affects the neuromuscular junction of the skeletal muscles. Approximately 90 percent of individuals with MG have serum antibodies to AChR, which are believed to play a central role in the disease pathway. Approximately 6 percent of individuals are MuSK antibody positive.

There are four primary therapies to treat MG:

- Symptomatic treatment with acetylcholinesterase inhibitors such as pyridostigmine
- Chronic immunotherapies such as glucocorticoids, Fc receptor blockers, rituximab, maintenance IVIG, and complement inhibitors
- Rapid but short-acting treatments such as plasma exchange and IVIG
- Surgical treatment with thymectomy

Vyvgart, Vyvgart Hytrulo, and Rystiggo are Fc receptor blockers that bind to neonatal Fc receptors which results in the reduction of circulating IgG.

Rystiggo (rozanolixizumab-noli) is 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

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

Definitions:

Myasthenia Gravis Foundation of America clinical classification	
Class I	Any ocular muscle weakness May have weakness of eye closure All other muscle strength is normal
Class II	Mild weakness affecting other than ocular muscles May also have ocular muscle weakness of any severity
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
Class III	Moderate weakness affecting 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
Class IV	Severe weakness affecting other than ocular muscles May also have ocular muscle weakness of any severity
IVa	Predominantly affecting limb and/or axial muscles 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
Class V	Defined by 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.
Weakness class is assessed according to the most severely affected muscle or muscle group at the patient's maximum severity	

MG Activities of Daily Living (MG-ADL):

Grade	0	1	2	3
Talking	Normal	Intermittent slurring or nasal speech	Constant slurring or nasal but can be understood	Difficult to understand speech
Chewing	Normal	Fatigue with solid food	Fatigue with soft food	Gastric tube
Swallowing	Normal	Rare episode of choking	Frequent chocking necessitating changes in diet	Gastric tube
Breathing	Normal	Shortness of breath with exertion	Shortness of breath at rest	Ventilator dependence
Impairment of ability to brush teeth or comb hair	Normal	Extra effort but no rest periods needed	Rest periods needed	Cannot do one of these functions
Impairment of ability to arise from a chair	Normal	Mild, sometimes uses arms	Moderate always uses arms	Severe requires assistance
Double vision	Normal	Occurs but not daily	Daily but not constant	Constant
Eyelid droop	Normal	Occurs but not daily	Daily but not constant	Constant

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The total score was the sum of all individual item scores and range from 0 to 24.
Higher scores indicate more severe disability due to MG.
A decrease from baseline score indicate improvement.
A 2-point change in MG-ADL Score is considered clinically meaningful.

History:	**Date:**	**Activity:**
Pharmacy and Therapeutics Committee	05/16/24	Approved guideline (effective 7/15/24)
Clinical Pharmacist	03/04/24	Development

Coding:

HCPCS: J9332, J9333, J9334

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Resources:

Literature reviewed 05/16/24. We do not include marketing materials, poster boards and non-published literature in our review.

1. Bird SJ. Chronic immunotherapy for myasthenia gravis. In: UpToDate, Shefner JM, Goddeau RP (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through March 2024. Topic last updated February 27, 2024. Accessed April 11, 2024.

2. Bird SJ. Overview of the treatment of myasthenia gravis. In: UpToDate, Shefner JM, Goddeau RP (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through March 2024. Topic last updated August 17, 2023. Accessed April 11, 2024.

3. Narayanaswami P, Sanders DB, Wolfe G, et al. International consensus guidance for management of myasthenia gravis: 2020 update. *Neurology* 2021; 96:114-122.

4. Rystiggo (rozanolixizumab-noli) product information revised by UCB, Inc. 06/2023. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed March 4, 2024.

5. Sanders DB, Wolfe GI, Benatar M, et al. International consensus guidance for management of myasthenia gravis. *Neurology* 2016; 87: 419-25.

6. Vyvgart (efgartigimod alfa-fcab) product information revised by argenx BV, Inc. 01/2024. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed March 4, 2024

7. Vyvgart Hytrulo (efgartigimod alfa and hyaluronidase-qvfc) product information revised by Argenx BV, Inc. 01/2024. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed March 4, 2024

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Blue Cross Blue Shield of Arizona (BCBSAZ) complies with applicable Federal civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability or sex. BCBSAZ provides appropriate free aids and services, such as qualified interpreters and written information in other formats, to people with disabilities to communicate effectively with us. BCBSAZ also provides free language services to people whose primary language is not English, such as qualified interpreters and information written in other languages. If you need these services, call (602) 864-4884 for Spanish and (877) 475-4799 for all other languages and other aids and services.

If you believe that BCBSAZ has failed to provide these services or discriminated in another way on the basis of race, color, national origin, age, disability or sex, you can file a grievance with: BCBSAZ's Civil Rights Coordinator, Attn: Civil Rights Coordinator, Blue Cross Blue Shield of Arizona, P.O. Box 13466, Phoenix, AZ 85002-3466, (602) 864-2288, TTY/TDD (602) 864-4823, crc@azblue.com. You can file a grievance in person or by mail or email. If you need help filing a grievance BCBSAZ's Civil Rights 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, DC 20201, 1–800–368–1019, 800–537–7697 (TDD). Complaint forms are available at http://www.hhs.gov/ocr/office/file/index.html