These Clinical Guidelines have been created by CarepathRx solely for its internal use and the use of its contracted clinical partners. All other use of these Guidelines is prohibited without express written permission. Published as Clinical Guidelines, CarepathRx's clinical partners may adopt these as policies subject to the partner's policy adoption processes.

These Clinical Guidelines have been created using resources that were current as of the "Reviewed" date noted at the beginning of the document. Clinicians should refer to the manufacturer's Prescribing Information (or equivalent) for the most up-to-date information. While CarepathRx has published these Clinical Guidelines after a close review of available literature and a clinical review process, given the evolving nature and complexity of modern pharmaceutical products, CarepathRx does not and cannot warrant or guarantee that these Clinical Guidelines reflect the objectively best or highest standard of care at any given time.

Nothing within these Clinical Guidelines is intended to supersede or interfere with any individual clinician's decision-making or professional judgment with respect to either (1) prescribing or dispensing the drug or product in question or (2) the overall treatment plan for an individual patient.

Rozanolixizumab-noli (Rystiggo) Clinical Guideline for Home Subcutaneous Infusion Therapy

Section: Clinical Guideline
Compliance: ACHC Infusion Pharmacy
ACHC Standards: n/a
URAC Standards: n/a
Policy ID: CG003
Effective: 11/1/2023
Reviewed: n/a
Revised: n/a
Approved by, Title and Date Approved: Kathleen Patrick, President, 11/1/23

I. BACKGROUND

Rozanolixizumab-noli (Rystiggo) is a humanized IgG4 monoclonal antibody that binds to and blocks the neonatal Fc receptor and reduces circulating IgG. It is indicated in adult patients for the treatment of generalized myasthenia gravis (MG) who are anti-acetylcholine receptor (AChR) or anti-muscle-specific tyrosine kinase (MuSK) receptor antibody positive. Generalized MG is an autoimmune disorder that is caused pathogenic IgG antibody-mediated attacks on proteins in the postsynaptic membrane of the neuromuscular junction and results in fluctuating motor weakness involving ocular, bulbar, limb and/or respiratory muscles. Generalized MG is the most common disorder of neuromuscular transmission, and approximately 95% of the generalized MG patient population are AChR or MuSK antibody positive. The following outlines the procedures for servicing patients in need of home rozanolixizumab-noli infusions.

II. PATIENT ACCEPTANCE CRITERIA

A. All candidates for home care service must be evaluated by the clinician(s) and deemed appropriate to receive home care based upon the dispensing pharmacy's admission criteria.

B. The decision to administer a first dose in the home by a field nurse will be determined on a case-by-case basis and reviewed by nursing and pharmacy management. The following criteria will be evaluated:

1. Prescriber preference
2. Allergy profile
3. Age ≥18 years
4. Other relevant social and/or medical history

C. Physician orders for rozanolixizumab-noli must include:

1. Patient weight
2. Drug and dose (weight-based dosing)
3. Route of administration
4. Frequency of administration
5. Emergency medications per protocol
6. Orders for pre-medications, if applicable
7. Routine lab monitoring, if applicable

D. Prior to starting therapy, patients should be evaluated for need to administer age-appropriate vaccines and presence of active infection.

E. Dispensing pharmacy treatment protocol for anaphylaxis will be instituted unless a more comprehensive patient-specific orders are provided by physician. See policy, Management of Allergic/Anaphylactic Reactions (Appendix A)

III. PHARMACOLOGY OVERVIEW

Refer to manufacturer's full Prescribing Information for most up to date information.

A. Indication: generalized MG in adult patients who are anti-acetylcholine receptor or anti-muscle-specific tyrosine kinase receptor antibody positive.

B. Dosage: administer weight-based dose once weekly for six weeks

Actual Body Weight	Dose	Volume to be Infused
< 50 kg	420 mg	3 mL
50 kg to < 100 kg	560 mg	4 mL
≥ 100 kg	840 kg	6 mL

*Dosing is based off actual body weight. Rozanolixizumab-noli has not been studied in extremes of body weight. In clinical trials, all patients were ≥35 kg.

C. Dose Adjustment: none.

D. Duration: one cycle is equivalent to six infusions over a period of six weeks. Additional cycles can be considered based on clinical evaluation. Subsequent cycles should begin no sooner than 63 days after the start of previous cycle.

E. Contraindications: None

F. Warnings and Precautions

1. **Infection**: rozanolixizumab-noli may increase the risk of infection. Serious infections occurred in 4% of patients receiving rozanolixizumab-noli in clinical trials. Initiation of treatment should be delayed in patients with active infection. During treatment, monitor for signs and symptoms of infection, administer appropriate treatment and consider holding rozanolixizumab-noli infusions until infection has resolved.

2. Immunization during treatment has not been studied. Administration of live or live-attenuated vaccines during treatment is not recommended. Any age-appropriate vaccines should be administered prior to initiation of a new treatment cycle.

3. **Aseptic meningitis**: in clinical trials, one patient with generalized MG and two patients with other neurological disease experienced aseptic meningitis, leading to hospitalization and discontinuation of rozanolixizumab-noli. During treatment, monitor for signs and symptoms and initiate diagnostic workup and treatment according to standard of care if symptoms appear.

4. **Hypersensitivity reactions**: hypersensitivity reactions, including angioedema and rash were seen in clinical trials. Hypersensitivity reactions occurred within one day to two weeks, and local reactions within one to three days. Appropriate treatment should be started based on severity of reaction.

5. **Pregnancy and lactation:** limit data exists on use of rozanolixizumab-noli in pregnant women. Increases in embryonic death, reduced body weight and impaired immune function were observed in pregnant monkeys receiving supratherapeutic doses of rozanolixizumab-noli without maternal toxicity. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. The background rate of major birth defects and miscarriage in the indicated population is unknown. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

6. There is no data on the presence of rozanolixizumab-noli in human milk, or the effects on milk production or the breastfed infant.

G. Pharmacokinetics:

1. Absorption: peak levels achieved approximately two hours after subcutaneous infusion.
2. Distribution: 6.6 L.
3. Elimination: degraded by proteolytic enzymes into small peptides and amino acids with a rate of clearance of 0.89 L/day.

H. Adverse Reactions:

1. Headache (44%)
2. Any infection (23%), upper respiratory infection (8%)
3. Diarrhea (20%)
4. Pyrexia (17%)
5. Hypersensitivity reactions (11%)
6. Nausea (10%)
7. Administration site reactions (8%)
8. Abdominal pain (8%)
9. Arthralgia (7%)

I. Drug Interactions: use of rozanolixizumab-noli with other drugs that bind to the human neonatal Fc receptor, including immunoglobulin products, monoclonal antibodies or antibody derivatives containing the human Fc domain of the IgG subclass, may lower systemic exposures and reduce effectiveness of such medications. When concomitant administration is required, monitor for reduced effectiveness of medications that bind to the human neonatal Fc receptor, or consider discontinuing rozanolixizumab-noli.

IV. ADMINISTRATIVE GUIDELINES

A. Administration: SC infusions should be given immediately after puncturing the vial. Use within four hours of preparation per current USP Immediate-Use Guidelines.

V. NURSING PROCEDURE

A. Supplies may include but are not limited to:

1. Alcohol Swabs
2. Gloves
3. Chloraprep swabs

4. Microclave cap
5. IV Start Kit
6. Peripheral IV catheter (ex. 22 G x1" and 24 G x ¾")
7. Tape
8. 26 G, 12 mm single-needle high-flow needle set
9. F180 Precision Flow Rate Tubing
10. Syringe (10 mL) with needle (20 G x 1")
11. Syringe (20 mL)
12. Syringe connector
13. Sharps container
14. Freedom Edge Pump, or other appropriate syringe pump
15. Pump return box

B. Prescription items:

1. Vial(s) of rozanolixizumab-noli

C. How Supplied: rozanolixizumab-noli injections is a sterile, preservative-free, clear to slightly opalescent, colorless to pale brownish yellow solution supplied as 280 mg/2 mL (140 mg/mL) single-dose glass vial in a carton.

D. Storage and Handling: store vials refrigerated at 36° to 46° F (2° to 8° C) in the original carton to protect from light. Do not freeze. Do not shake. Vials may be stored at room temperature, up to 77° F (25° C) for a single period of up to 30 days in the original container. Once stored at room temperature, the vial should not be returned to the refrigerator.

E. Procedures: Preparation of product, Infusion rates, post infusion monitoring time.

1. Explain the reasoning for visit and use of rozanolixizumab-noli.
2. Don gloves.
3. Counsel patient on warnings, precautions, and potential side effects including but not limited to: infusion-related reactions (including hypersensitivity and local site reactions), infection, aseptic meningitis, headache, diarrhea, pyrexia, nausea, abdominal pain and arthralgia.
4. Prepare product:
    a. Allow vials to reach room temperature for approximately 30 minutes.
    b. Visually inspect vial(s) prior to mixing for any particulate matter or discoloration. Do not infuse if solution is cloudy, contains particulate matter or has changed color.
    c. Using 10 mL syringe, withdraw required volume according to prescription label from rozanolixizumab-noli vial(s).

5. Infusion:

    a. Select subcutaneous infusion site in lower right or left part of the abdomen below the navel. Avoid where skin is tender, bruised, red or hard or into tattoos, scars or stretch marks.
    b. Administer using F180 tubing and 26 G high-flow needle over approximately 16-17 mL/hr.
    c. Once complete, do not flush the infusion line

6. Post infusion monitoring: monitor patient during infusion and for 15 minutes after completion for clinical signs and symptoms of hypersensitivity reactions.

VI. CLINICAL MONITORING

A. Prior to therapy:

1. Lack of current, active infection.
2. Up-to-date vaccination history.

B. During therapy:

1. Signs and symptoms of hypersensitivity reactions, including rash and angioedema.

2. Signs and symptoms of infections, including pyrexia, chills, polyuria or dysuria, cough, rhinorrhea, wheezing, dyspnea, fatigue, pharyngitis, rhinorrhea, back pain and/or chest pain.

3. Signs and symptoms of septic meningitis, including severe headache, nuchal rigidity, pyrexia, photophobia, painful eye movements, nausea and vomiting.

4. Efficacy and disease progression, including ability to complete activities of daily life as measured by MG-ADL questionnaire.

Please refer to the package insert for the most up to date guidance on this medication.

REFERENCES:

1. Rystiggo [package insert]. Smyrna, GA: UCB, Inc.; 2023.
2. Bird, Shawn J. "Diagnosis of myasthenia gravis." *UpToDate,* 29 Aug. 2022.
3. Guidance for subcutaneous delivery of Rystiggo® (rozanolixizumab-noli) using the Freedom Infusion System®. Koru Medical Systems; Mahwah, NJ.
4. Rystiggo [brochure]. UCB, Inc., https://www.rystiggo.com/pdf/rystiggo-brochure.pdf.

APPENDIX A: ANAPHYLAXIS KIT INTRUCTIONS

Emergency Medication After Your Infusion

Please call your pharmacy if you have any questions or concerns. In the event of an emergency, always call 911.

Your nurse will tell you when you need to use Emergency Medications.
The epinephrine dose will be noted on the Anaphylaxis Protocol included with your kit.

Start with a clean work surface and clean hands.

Open the supply bag labeled Anaphylaxis Kit Contents.

You will need:

1. **Bag containing Pills** (2 Acetaminophen and 2 Diphenhydramine)
2. **Bag containing Alcohol Prep Pads**
3. **Bag labeled IM Epinephrine**

All other contents will not be needed.

Open the IM Epinephrine Bag

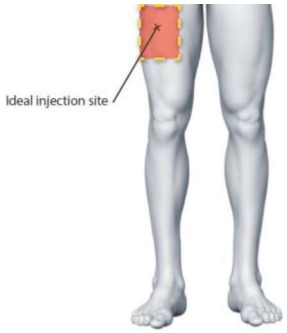
1. **Remove 1 of each item**
    a. 1 -syringe
    b. 1 – brown labeled filter needle (BD Filter Needle)- **for ampul use only**
    c. 1 – black labeled safety needle (Magellan Hypodermic Safety Needle 22G x 1”)
    d. 1 ampul of epinephrine

Prepare IM (intramuscular) injection of Epinephrine:

1. **Attach the brown filtered needle to syringe**
    a. Be careful to not touch the tip of the syringe or the needle.
2. Using an **alcohol swab, wipe the neck of the epinephrine ampul.**
3. Holding the ampul upright, **swirl and flick the ampul until all fluid flows to the bottom chamber** (the top chamber should be empty).
4. Using a new alcohol wipe, grasp the neck of the ampul and with your other hand grasp the bottom chamber of the ampul. **Quickly snap the top of the ampul off, directing the snap way from you.**

5. **Place the tip of the brown filter needle inside the ampul**. Tilting the ampul, **withdraw dose of medication into the syringe** by gently pulling back on the plunger. Be careful to not pull the plunger out of the syringe.
6. Remove the needle from the ampul and h**old the syringe upright** with the needle pointing upward. **Gently tap the side of the syringe to bring any air to the top of the syringe.**
7. **Push the air out of the syringe by gently pushing on the plunger**.
8. Replace the cap on the brown filter needle. Discard remainder in ampul.
9. **Remove the brown filter needle and place the black safety needle onto the syringe.**

Give your IM Epinephrine injection



1. **Grasp your leg muscle at the outer mid-thigh** and **cleanse the area** with a new alcohol wipe.
2. **Push the needle into your leg muscle straight** in at a 90-degree angle.
3. **Inject the medication** by depressing the plunger in a slow and steady motion.
4. **Remove the needle** and wipe the site with the alcohol wipe.
5. May repeat dose every 5 minutes (**maximum 3 doses**) if ordered per protocol.

Take the pills by mouth.

a. 2 – Acetaminophen
b. 2 – Diphenhydramine

Place all trash in the bag the pills came in and take with you when you seek medical care. **Give the bag to the nurse or EMT**, so your doctor will know what medication you already took. They will properly dispose of the syringe and needles.
Call 911 or have someone drive you to the emergency department.