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.

Mirikizumab-mrkz (Omvoh) Clinical Guideline for Home Intravenous Therapy

Section: Clinical Guideline
Compliance: ACHC Infusion Pharmacy
ACHC Standards: N/A
URAC Standards: N/A
Policy ID: CG012
Effective: 7/8/2024
Reviewed: N/A
Revised: N/A
Approved by, Title and Date Approved: Kathleen Patrick, President, 7/8/24

I. BACKGROUND

Mirikizumab-mrkz (Omvoh), a humanized monoclonal antibody, is an interleukin-23 (IL-23) antagonist indicated for the treatment of moderately to severely active ulcerative colitis (UC) in adult patients. UC is a chronic immune-modulated disease characterized by relapsing and remitting episodes of inflammation in the colon in response to the gut microbiota. Activation of the IL-23 cytokine pathway promotes production of proinflammatory cytokines, including tumor necrosis factor-α. Mirikizumab-mrkz binds to the p19 subunit of IL-23 and inhibits its interaction the IL-23 receptor inhibiting downstream mucosal inflammation and symptoms associated with UC.

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
4. Other relevant social and/or medical history

C. Physician orders for mirikizumab-mrkz must include:

1. Drug
2. Dose
3. Route of administration
4. Frequency of administration
5. Specialty Home Infusion Protocol
6. Orders for pre-medications, if applicable
7. Line care protocol
8. Routine lab monitoring, if applicable

D. Prior to starting therapy, patients should be evaluated for tuberculosis (TB) infection, and for need to administer age-appropriate vaccines. Baseline liver enzymes and bilirubin levels should be obtained.

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

III. PHARMACOLOGY OVERVIEW

Refer to manufacturers full Prescribing Information for most up to date information.

A. Indication: treatment of moderately to severely active ulcerative colitis in adult patients.

B. Dosing:

1. Induction: 300 mg IV at weeks 0, 4, and 8.

2. Maintenance: 200 mg SUBQ (as two consecutive 100 mg injections) at week 12 and every 4 weeks thereafter.

C. Dose Adjustments: none.

D. Duration: duration of therapy is dependent on patient response and adverse reactions.

E. Contraindications: history of serious hypersensitivity reaction to mirikizumab-mrkz or any excipient ingredients.

F. Warnings and Precautions

1. **Hypersensitivity reactions**: serious reactions including anaphylaxis, mucocutaneous erythema and pruritis have been reported with mirikizumab-mrkz intravenous induction.

2. **Infections**: mirikizumab-mrkz may increase the risk of infection. Initiation of therapy should be delayed until clinically relevant infections resolve or are adequately treated. Consider risks and benefits of mirikizumba-mrkz in patients with recurrent or chronic infection. If serious infection develops or infection does not respond to standard therapy while on mirikizumba-mrkz, do not administer mirikizumba-mrkz until resolution of infection.

3. **Tuberculosis**: patients with evidence of active tuberculosis, a past history of tuberculosis or were diagnosed with latent tuberculosis were not included in clinical trials. Patients should be evaluated for tuberculosis prior to initiating mirikizumab-mrkz therapy. Do not administer mirikizumab-mrkz to patients with active tuberculosis. Treatment of latent tuberculosis should be initiated before starting mirikizumab-mrkz. Consider anti-tuberculosis therapy in patients with a history of active or latent tuberculosis in whom an adequate course of treatment cannot be confirmed.

4. **Hepatoxicity**: one severe case of reversible liver injury was seen in clinical trials. Consider alternative therapies in patients with evidence of liver cirrhosis. Investigate etiology of liver

enzyme elevations during therapy and interrupt treatment if drug-induced liver injury is suspected.

5. **Immunizations**: avoid administration of live vaccines during mirikizumba-mrkz therapy. There is no data available on the response to live or non-live vaccines in patients treated with mirikizumba-mrkz. Complete all age-appropriate vaccines prior to initiating therapy.

6. **Pregnancy and lactation**: limited data exists on use of mirikizumab-mrkz in pregnant women. Monoclonal antibodies can be actively transported across the placenta and mirikizumab-mrkz may cause immunosuppression in the in utero-exposed infant. Studies of drug at concentrations 69 times the maximum recommended human dose in pregnant monkeys revealed no adverse developmental effects to the developing fetus, or harm to infant monkeys. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. 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. There will be a pregnancy exposure registry to monitor outcomes in women exposed to mirikizumab-mrkz during pregnancy via drug manufacturer. Pregnant women with exposure and their healthcare providers are encouraged to contact manufacturer.

   There is no data on the presence of mirikizumab-mrkz in human milk, or the effects on milk production or the breastfed infant. Endogenous maternal IgG and monoclonal antibodies are transferred in human milk. The benefits of breastfeeding, clinical need for mirikizumab-mrkz and possible adverse effects on the breastfed infant should be considered.

G. Pharmacokinetics:

1. Absorption: peak levels achieved after approximately 5 days and bioavailability is 44% for subcutaneous injection.
2. Distribution: 4.83 L.
3. Metabolism/Elimination: degraded into small peptides and amino acids via catabolic IgG pathways. Rate of clearance is 0.0229 L/hr and elimination half-life is 9.3 days, independent of dose.

H. Adverse Reactions

1. Induction (intravenous): upper respiratory tract infection, arthralgia
2. Maintenance (subcutaneous): upper respiratory tract infection, injection site reaction, arthralgia, rash, headache, herpes viral infection

I. Drug Interactions: drug-drug interactions may exist. Consult interaction database for patient specific assessment.

IV. ADMINISTRATIVE GUIDELINES

A. Administration: IV infusion should be given immediately after reconstitution and dilution. Begin infusion within 4 hours of preparation per current USP Immediate-Use Guidelines.

B. Co-administration with products other than 0.9% sodium chloride or 5% dextrose in the same IV line is not recommended.

V. NURSING PROCEDURE

A. Supplies may include but are not limited to:

1. Alcohol Swabs
2. Gloves
3. Tape
4. IV access supplies as applicable
    a. Peripheral IV access supplies for patients requiring peripheral IV access
        1) IV start Kit
        2) Peripheral IV catheter (ex. 22 Gauge x1" and 24 Gauge x ¾")
        3) Extension set 8" with needless connector
    b. Port access supplies for patients with a port
        1) Port needle (ex. 22 Gauge x ¾ to 1" safe step)
        2) Needless connector
        3) Central line dressing change kit
5. IV Pole
6. IV administration set (flow regulator or gravity tubing)
7. Syringe (20 mL) with needles (20 G x 1")
8. Sharps container

B. Prescription items: (examples below)

1. Drug vial
2. 0.9% sodium chloride (250 mL) diluent bag
3. 0.9% sodium chloride (50 mL) post infusion flush bag
4. Standard flushes per protocol

C. How Supplied: mirikizumab-mrkz injection is sterile, preservative free, clear to opalescent, colorless to slightly yellow to slightly brown solution supplied as:

1. For intravenous infusion: 300 mg/15 mL (20 mg/mL) single dose vial.
2. For subcutaneous injection: 100 mg/mL single dose prefilled pen with 1 mL glass syringe and a fixed 27-gauge ½ inch needle.

D. Storage and Handling: store vials and prefilled pens under refrigeration at 2 to 8 C (36 to 46 F). Do not freeze or shake. Keep in original carton to protect from light. Prefilled pens may be stored at room temperature up to 30 C (86 F) for up to two weeks in original carton if needed. Once stored at room temperature, do not return to refrigerator.

E. Procedures:

1. Explain the reasoning for visit and use of mirikizumab-mrkz
2. Don gloves.
3. Assess for signs and symptoms of infection prior to establishing venous access and preparing medication. Notify ordering physician and pharmacist if signs or symptoms are present.
4. Establish venous access prior to preparation of drug.\
5. Counsel patient on warnings, precautions, and potential side effects including but not limited to: hypersensitivity reactions, risk of infection, elevated liver enzymes, arthralgia.
6. Prepare Product:
7. Inspect vial visually for particulate matter and discoloration.

8. Using 20 mL syringe, withdraw 15 mL mirikizumab-mrkz and add to 0.9% sodium chloride 250 mL bag. Gently invert bag to mix contents. Do not shake.
9. Infusion Rates: administer over 30 minutes (530 mL/hr).
10. Post infusion flush: after administration of mirikizumab-mrkz, flush the administration tubing with 0.9% sodium chloride 50 mL to ensure all of the medication is administered. Administer the flush at the same infusion rate as mirikizumab-mrkz (530 mL/hr).
11. Post infusion monitoring: monitor patient and vital signs periodically during the infusion and 30 minutes after the infusion is complete per "CarePathRx Nursing Best Practice Administration Guidelines."

VI. CLINICAL MONITORING

A. Prior to therapy:
   1. Lack of current, active infection.
   2. Active or latent tuberculosis.
   3. Baseline liver transaminases and bilirubin
   4. Up-to-date vaccination history.

B. During therapy
   1. Signs and symptoms of hypersensitivity reactions.
   2. Signs and symptoms of infection.
   3. Signs and symptoms of tuberculosis.
   4. Efficacy and disease progression, including frequency of diarrhea, hematochezia or melena and abdominal pain.

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

REFERENCES:

Omvoh (mirikizumab-mrkz) [package insert]. Indianapolis, IN: Eli Lilly and Company; 2024.

United States Pharmacopeia (USP). General Chapter, <797> Pharmaceutical Compounding—Sterile Preparations. (2023) USP-NF. Rockville, MD: United States Pharmacopeia. Accessed November 29, 2023.

Noviello D, Mager R, Roda G, Borroni RG, Fiorino G, Vetrano S. The IL23-IL17 Immune Axis in the Treatment of Ulcerative Colitis: Successes, Defeats, and Ongoing Challenges. Front Immunol. 2021;12:611256. Published 2021 May 17. doi:10.3389/fimmu.2021.611256

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

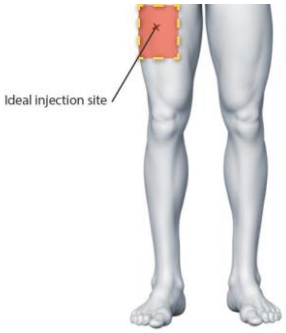
1. **Remove 1 of each item**
    a. 1 -syringe
    b. 1 – brown labeled filter needle (BD Filter Needle)- **for ampule use only**
    c. 1 – black labeled safety needle (Magellan Hypodermic Safety Needle 22G x 1”)
    d. 1 ampule of epinephrine

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 ampule.**
3. Holding the ampule upright, **swirl and flick the ampule 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 ampule and with your other hand grasp the bottom chamber of the ampule. **Quickly snap the top of the ampule off, directing the snap way from you.**

5. **Place the tip of the brown filter needle inside the ampule**. Tilting the ampule, **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 ampule 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 ampule.
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.