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.

Risankizumab (Skyrizi-rzaa) Clinical Guideline for Home Intravenous Therapy

Section: Clinical Guideline
Compliance: ACHC Infusion Pharmacy and/or URAC Specialty Pharmacy
ACHC Standards: N/A
URAC Standards: N/A
TJC Standards: N/A
Policy ID: CG014
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Revised: 9/3/2024
Approved by: Kathleen Patrick, President, 6/29/22, 9/3/24

I. BACKGROUND

Risankizumab-rzaa (Skyrizi) is a humanized immunoglobulin G1 (IgG1) monoclonal antibody that selectively binds to the p19 subunit of human interleukin 23 (IL-23) cytokine and inhibits its interaction with the IL-23 receptor. IL-23 is a naturally occurring cytokine that is involved in inflammatory and immune responses. Risankizumab acts as an interleukin-23 (IL-23) antagonist and inhibits the downstream release of pro-inflammatory cytokines and chemokines. Risankizumab is indicated for the treatment in adult patients with moderate to severe plaque psoriasis, psoriatic arthritis, moderate to severe active Crohn's Disease, and moderate to severe active Ulcerative Colitis. The following outlines the procedures for servicing patients in need of intravenous risankizumab infusions at home.

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 dispensing pharmacy admission criteria.

1. 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:

    a. Prescriber preference
    b. Allergy profile
    c. Age
    d. Other relevant social and/or medical history

B. Physician orders for risankizumab must include:

1. Drug
2. Dose
3. Route of administration
4. Frequency of administration
5. Emergency medications per protocol

6. Orders for pre-medications
7. Line care protocol
8. Routine lab monitoring, if applicable

C. Baseline labs prior to therapy (CBC, CMP, LFTs). Patients receiving this medication for Crohn's Disease or Ulcerative Colitis must have baseline liver enzymes and bilirubin drawn.

D. Patients must have a tuberculosis (TB) screening prior to therapy initiation.

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

F. 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. PHARMACOLOGIC OVERVIEW

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

A. Indications

1. Moderate to severe Plaque psoriasis, (Ps) in adults- approved for subcutaneous (SC) injection
2. Psoriatic arthritis in adults (PsA) - approved for subcutaneous (SC) injection
3. Moderate to severe Crohn's Disease in adults- IV induction and SC maintenance
4. Moderate to severe Ulcerative Colitis in adults – IV induction and SC maintenance

B. Dosing

1. Crohn's Disease

   a. Induction: 600 mg IV at 0,4, and 8 weeks
   b. Maintenance: 180 mg or 360 mg SC at week 12 and then every 8 weeks thereafter

2. Ulcerative Colitis

   a. Induction: 1200 mg IV at 0,4, and 8 weeks
   b. Maintenance: 180mg or 360mg SC at week 12 then every 8 weeks thereafter

   **Subcutaneous administration will not be discussed in the scope of this guideline*

C. Dose Adjustment: No hepatic or renal dose adjustments.

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

E. Contraindications: Patients with a history of hypersensitivity to risankizumab or any component of the formulation.

F. Warnings and Precautions

1. **Hypersensitivity reactions**: Serious hypersensitivity, including anaphylaxis, has been reported with risankizumab
2. **Infections:** Risankizumab may increase the risk of infections. Treatment should not be initiated in patients with active infections until it is resolved or treated. If a serious infection develops, discontinue risankizumab until the infection resolves.
3. **Tuberculosis:** Patients should be evaluated for tuberculosis (TB) infection prior to initiating therapy. Treatment for latent TB should be administered prior to administering risankizumab
4. **Hepatotoxicity:** In psoriatic arthritis trials, the incidence of hepatic events was higher. Drug-induced liver injury was reported in a patient with Crohn's Disease. For the treatment of Crohn's Disease, evaluate liver enzymes and bilirubin at baseline, and during induction at least up to 12 weeks of treatment. Monitor thereafter according to routine patient management. Consider an alternative treatment for patients with evidence of liver cirrhosis. Prompt investigation of the cause of liver enzyme elevation is recommended to identify potential cases of drug-induced liver injury. Interrupt treatment if drug-induced liver injury is suspected, until this diagnosis is excluded. Instruct patients to seek immediate medical attention if they experience symptoms suggestive of hepatic dysfunction.
5. **Immunizations**: Patients should be brought up to date with all age-appropriate immunizations before initiating therapy. Live vaccines should not be given concurrently with risankizumab.
6. **Pregnancy and Lactation**: There is a pregnancy exposure registry that monitors outcomes in women who become pregnant while treated with risankizumab. Patients should be encouraged to enroll by calling 1-877-302-2161 or visiting http://glowpregnancyregistry.com. Available pharmacovigilance and clinical trial data with risankizumab use in pregnant women are insufficient to establish a drug-associated risk of major birth defects, miscarriage or other adverse maternal or fetal outcomes. Although there are no data on risankizumab-rzaa, monoclonal antibodies can be actively transported across the placenta, and risankizumab may cause immunosuppression in the in utero-exposed infant. There are adverse pregnancy outcomes in women with inflammatory bowel disease such as preterm delivery and low birth weight. There is no data on the presence of risankizumab-rzaa in human milk, the effects on the breastfed infant, or the effects on milk production. Endogenous maternal IgG and monoclonal antibodies are transferred in human milk. The effects of local gastrointestinal exposure and limited systemic exposure in the breastfed infant to risankizumab-rzaa are unknown. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for risankizumab and any potential adverse effects on the breastfed infant from risankizumab or from the underlying maternal condition.

G. Pharmacokinetics

1. Volume of distribution: 7.68-11.2 Liters
2. Elimination half-life: 21-28 days
3. Metabolism: degraded into small peptides and amino acids by proteases

H. Adverse Reactions

1. >10%

    a. Antibody development
    b. Infection- Upper respiratory tract infection

2. 1% to 10%:

    a. Elevated liver enzymes
    b. Hypersensitivity reaction (2.3%)
    c. Local Injection site reaction
    d. Fatigue
    e. Headache
    f. Abdominal pain
    g. Anemia
    h. Pyrexia
    i. Arthralgia and back pain

3. <1%:

    a. Folliculitis, urticarial
    b. Anaphylaxis (psoriatic arthritis)
    c. Eczema
    d. Facial Swelling

I. Drug Interactions

1. Live vaccines: concurrent use of risankizumab and live vaccines may result in reduced effectiveness of immunization and increased risk of infection.
2. Biologics and immunosuppressants: may enhance immunosuppressive effect when combined.
3. Consult interaction database for patient specific assessment.

IV. ADMINISTRATIVE GUIDELINES

A. Administrative guidelines: IV infusions should be given immediately after dilution. Complete the infusion within 4 hours of preparation.

B. Do not co-administer other products in the same infusion line.

V. NURSING PROCEDURES

A. Supplies include but are not limited to:

1. Alcohol Swabs
2. Gloves
3. Tape
4. Peripheral IV access supplies for patients requiring peripheral IV access

    a. IV start Kit
    b. Peripheral IV catheter (ex. 22 Gauge x1" and 24 Gauge x ¾")
    c. Extension set 8" with needless connector

5. Port access supplies for patients with a port

a. Port needle (ex. 22 Gauge x ¾ to 1" safe step)
b. Extension set 8" needless connector
c. Central line dressing change kit

6. IV Pole
7. IV injection cap
8. IV administration set (flow regulator [ex: dial-a-flow] or gravity)
9. Syringes (20-35mL) with needles (20 G x 1")
10. Sharps container

B. Prescription Items

1. Risankizumab vials
2. Stock bag of NSS for dilution (100 mL, 250 mL, or 500 mL)
3. Standard flushes per protocol

C. How Supplied

Intravenous Infusion: Risankizumab Vial Injection: 600 mg/10 mL (60 mg/mL), as a colorless to slightly yellow, and clear to slightly opalescent solution in each single-dose vial.

D. Storage and Handling

Store in a refrigerator at 36°F to 46° F (2°C to 8°C). Do not freeze. Do not shake. Keep in the original cartons to protect from light. Not made with natural rubber latex.

E. Compatibility: Intravenous infusion can be diluted in 5% Dextrose Injection Solution or 0.9% Normal Saline Injection Solution.

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

1. Explain the reasoning for visit and use of risankizumab.
2. Don gloves.
3. Assess for signs and symptoms of infection prior to establishing venous access and preparing medication.
4. Establish venous access prior to preparation of drug.
5. Counsel the patient on warnings, precautions, and potential side effects including but not limited to infections, hypersensitivity reactions, fatigue, headache, abdominal pain, and arthralgia.
6. Preparation for Crohn's Disease for induction infusion

   a. Inspect vial. Risankizumab solution should be colorless to slightly yellow.
   b. Withdraw 10 mL of risankizumab solution from the vial and inject into an intravenous infusion bag containing 100 mL, 250 mL, or 500 mL of NSS for a final concentration of approximately 1.2 mg/mL to 6 mg/mL and discard any remaining solution in the vial.
   c. Do not shake the vial or diluted solution in the infusion bag.

7. Preparation for Ulcerative Colitis for induction infusion

a. Inspect vials. Risankizumab solution should be colorless to slightly yellow.
b. Withdraw 10 mL of Risankizumab solution from each of the 2 vials (1,200 mg/20 mL total) and inject into an intravenous infusion bag containing 250mL or 500 mL of NSS for a final concentration of approximately 1.2 to 6 mg/mL and discard any remaining solution in the vial.
c. Do not shake the vial or diluted solution in the infusion bag.

8. Infusion Rates for induction:

    a. Infuse the diluted solution intravenously over a period of at least one hour for **Crohn's Disease (600mg dose)**
    b. Infuse the diluted solution intravenously over a period of at least two hours for **Ulcerative Colitis (1200 mg dose)**

9. Monitor patient and vital signs periodically throughout the infusion and for at least 30 minutes after the infusion has ended per CarepathRx Nursing Best Practice Administration Guidelines.

VI. CLINICAL MONITORING

A. Prior to therapy

1. TB screening
2. Baseline labs including liver enzymes and bilirubin
3. Complete all age-appropriate vaccinations as recommended by current immunization guidelines.

B. During therapy

1. Signs/symptoms of infection
2. Signs of hypersensitivity reactions
3. Liver enzymes and bilirubin during induction and routinely thereafter
4. CBC and BMP routinely

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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 <u>Anaphylaxis Kit Contents</u>.

You will need:

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

All other contents will not be needed.

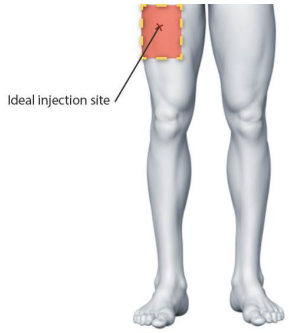
Open the IM Epinephrine Bag

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.