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.

Guidelines for In-Home Intravenous Spesolimab-sbzo (Spevigo) Therapy

Section: Clinical Guidelines
Compliance: ACHC Infusion Pharmacy
ACHC Standards: N/A
URAC Standards: N/A
Policy ID: NUR264
Effective: 8/1/2023
Reviewed:
Revised:
Approved by: Kathleen Patrick, President 8/1/2023

I. BACKGROUND

Spesolimab-sbzo (Spevigo) is a s a humanized monoclonal immunoglobulin G1 antibody that inhibits interleukin-36 (IL-36) signaling by specifically binding to the IL-36 receptor. Binding of spesolimab-sbzo to IL-36 receptor prevents the subsequent activation of IL-36 receptor by cognate ligands (IL-36 α, β and γ) and downstream activation of pro-inflammatory and pro-fibrotic pathways. As an interleukin-36 antagonist, spesolimab is indicated for the treatment of generalized pustular psoriasis (GPP) flares in adult patients. Generalized pustular psoriasis can an appear in any age group, but it is most common in adults between 40–50 years old. The following outlines the procedures for servicing patients in need of outpatient spesolimab 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:
   a. Prescriber preference
   b. Allergy profile
   c. Age ≥18 years
   d. Ability to secure contracted nursing for ongoing infusions
   e. Other relevant social and/or medical history

C. Physician orders for spesolimab must include:
   a. Drug and dose
   b. Route of administration
   c. Frequency of administration
   d. Emergency medications per protocol
   e. Orders for pre-medications, if applicable
   f. Line care protocol
   g. Routine lab monitoring, if applicable

D. Baseline labs or tests prior to starting therapy and evaluate patients for tuberculosis (TB) infection

prior to initiating treatment

E. Dispensing pharmacy treatment protocol for anaphylaxis will be instituted unless a more comprehensive patient-specific orders are provided by physician. See policy NUR012 (Appendix A).

III. PHARMACOLOGY OVERVIEW

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

A. Indications: Generalized pustular psoriasis flares in adult patients

B. Dosage: 900 mg IV administered as a single dose. If symptoms persist, a second 900 mg dose can be administered 1 week after the initial dose.

C. Dose Adjustment: No dose adjustments for renal or hepatic impairment. No formal study of the effect of renal or hepatic impairment on the pharmacokinetics of spesolimab was conducted. As a monoclonal antibody, it is not expected to undergo renal or hepatic elimination

D. Duration:
   a. Spesolimab is a one- time infusion. A second infusion may be given one week after initial infusion if generalized pustular psoriasis (GPP) flare symptoms persist.
   b. In clinical trials, after Week 1 to 12, subjects in either treatment groups whose GPP flare reoccurred after achieving a clinical response were eligible to receive an open-label rescue intravenous dose of 900 mg, with a maximum of 3 total doses of spesolimab throughout the study. Six subjects received a single open-label rescue dose of spesolimab. 36 patients received 1 dose of spesolimab, 13 patients received 2 doses of spesolimab, and 2 subjects received 3 doses of spesolimab throughout the study

E. Contraindications: contraindicated in patients with severe or life-threatening hypersensitivity to spesolimab-sbzo or to any of the excipients in spesolimab. Reactions have included drug reaction with eosinophilia and systemic symptoms (DRESS)

F. Warnings and Precautions

   a. **Infections**: Spesolimab may increase the risk of infections. Infections were reported in 14% of subjects treated with spesolimab compared with 6% of subjects treated with placebo in clinical trials. Treatment with spesolimab is not recommended for use in patients with any active infection until the infection resolves or is adequately treated. Consider potential risks versus benefits for patients who experience chronic infections.
   b. **Risk of tuberculosis**: Evaluate patients for tuberculosis (TB) infection prior to initiating treatment with spesolimab. Do not administer spesolimab to patients with active TB infection. Consider initiating anti-TB therapy prior to initiating spesolimab in patients with latent TB or a history of TB in whom an adequate course of treatment cannot be confirmed. Monitor patients for signs and symptoms of active TB during and after spesolimab treatment.
   c. **Hypersensitivity and Infusion-Related Reactions:** hypersensitivity reactions may include immediate reactions such as anaphylaxis and delayed reactions such as drug reaction with eosinophilia and systemic symptoms (DRESS). DRESS has been reported in clinical trials with two cases.

d. **Vaccinations:** Avoid use of live vaccines. No specific studies have been conducted in spesolimab-treated patients who have recently received live viral or live bacterial vaccines.

e. **Pregnancy and Lactation:** The limited data on the use of spesolimab in pregnant women is insufficient to inform a drug-associated risk of adverse pregnancy-related outcomes. Human IgG is known to cross the placental barrier; therefore, spesolimab may be transmitted from the mother to the developing fetus. In an animal reproduction study, intravenous administration of a surrogate antibody against IL36R in mice during the period of organogenesis did not elicit any reproductive toxicity. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. The estimated background risk of major birth defects and miscarriage for 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.

There is no data on the presence of spesolimab in human milk, the effects on the breastfed infant, or the effects on milk production. Spesolimab is a monoclonal antibody and is expected to be present in human milk. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for spesolimab and any potential adverse effects on the breastfed infant from spesolimab or from the underlying maternal condition.

G. Pharmacokinetics
   a. Volume of distribution: 6.4 liters
   b. Half-life: ~25.5 days

H. Adverse Reactions
   a. Diarrhea (11%)
   b. Asthenia and fatigue (9%)
   c. Nausea and vomiting (9%)
   d. Headache (9%)
   e. Otitis externa (7%)
   f. Pruritis (6%)
   g. Infusion site bruising (6%)
   h. Urinary tract infection (6%)
   i. Vulvovaginal candidiasis (4%)
   j. Latent tuberculosis (4%)
   k. Gastritis (4%)
   l. Bacteremia (3%)
   m. Bacteruria (3%)
   n. Cellulitis (3%)
   o. Herpes dermatitis and oral Herpes (3%)
   p. Upper respiratory tract infection (3%)
   q. Dyspnea (3%)
   r. Eye edema (3%)
   s. Urticaria (3%)

I. Drug Interactions: No formal drug interactions studies have been conducted with spesolimab-sbzo

IV. ADMINISTRATIVE GUIDELINES

A. Administration- IV infusions should be given immediately after reconstitution and dilution. Use within 1 hour of preparation per current USP Immediate-Use Guidelines. **Administer using a line containing a sterile, non-pyrogenic, low protein binding in-line filter (pore size of 0.2 micron**).

B. Do not co-administer in the same IV line with other drug products

V. NURSING PROCEDURE

A. Supplies may include but are not limited to:
   a. Alcohol Swabs
   b. Gloves
   c. Dressing change kit
   d. IV Pole
   e. IV Start Kit
   f. Peripheral IV catheter (ex. 22 Gauge x1" and 24 Gauge x ¾" for patients needing peripheral access)
   g. Port access needle (ex. 22 Gauge x ¾ to 1" safe step for patients with a port)
   h. Tape
   i. Extension set 8"
   j. IV injection cap
   k. IV administration set (dial-a-flow or gravity) with in-line or add-on 0.22-micron filter
   l. Syringes (20 mL) with needles (20 G x 1")
   m. Sharps container

B. Prescription items:
   a. Spesolimab vials
   b. 100mL bag of sodium chloride 0.9% for dilution

C. How Supplied:
Spesolimab is a sterile, preservative-free, colorless to slightly brownish-yellow, clear to slightly opalescent solution. Each carton contains two single-dose 450 mg/7.5 mL (60 mg/mL) glass vials

D. Storage and Handling:
Must be refrigerated, store at 2°C to 8°C (36°F to 46°F) in original carton to protect from light. Do not freeze. Prior to use, may store unopened spesolimab vials at room temperature, 20°C to 25°C (68°F to 77°F), for up to 24 hours in the original carton to protect from light

E. Compatibility:
   a. Compatible with 0.9% normal saline
   b. Compatible with polyvinylchloride (PVC), polyethylene (PE), polypropylene (PP), polybutadiene and polyurethane (PUR), and in-line filter membranes composed of polyethersulfone (PES, neutral and positively charged) and positively charged polyamide (PA)

F. Procedures: Preparation of product, Infusion rates, post infusion monitoring time.
    a. Explain the reasoning for visit and use of spesolimab.
    b. Don gloves.
    c. Establish venous access prior to preparation of drug.
    d. Counsel patient on warnings, precautions, and potential side effects including but not limited to: Diarrhea, fatigue, nausea, vomiting, headache, risk of infections, and infusion related reactions
    e. Prepare Product
        (1) Visually inspect vials prior to mixing for any particulate matter or discoloration. Do not use if cloudy, discolored, or if there are large particulate matter.
        (2) From a 100 mL 0.9% sodium chloride bag, withdraw 15 mL
        (3) Slowly withdraw 15 mL of spesolimab (complete content from two vials of 450 mg/7.5 mL) and add to saline bag
        (4) Mix by gently inverting. Do not shake
    f. Infusion Rates
        (1) Administer over 90 minutes
        (2) If the infusion is slowed or temporarily stopped, the total infusion time (including stop time) should not exceed 180 minutes
    g. 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
    a. TB testing
    b. Assess if patient is up-to-date on vaccinations
    c. No current, active infections
B. During and after infusion
    a. Monitor for signs and symptoms of infusion related reactions including DRESS
    b. Monitor for infections
    c. Monitor efficacy and GPP flare symptoms
        (1) If patient's GPP flare symptoms are still present after a week, a second dose of spesolimab may be administered
        (2) GPP flare symptoms include presence of new, painful pustules, at least 5% of body surface area covered in erythema and pustules. Additionally, some patients may experience systemic symptoms including fever, headache, extreme tiredness, and a burning sensation on the skin.
        (3) Generalized Pustular Psoriasis Physician Global Assessment (GPPPGA) may be used to grade the severity of the disease flare.

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

REFERENCES:

Spesolimab [package insert]. Ridgefield, CT; Boehringer Ingelheim Pharmaceuticals, Inc. 2022

Spesolimab. Micromedex. IBM Watson Health Corporation. Greenwood Village, CO. Available at: https://www.micromedexsolutions.com. Accessed November 18, 2022.

APPENDIX A: ANAPHYLAXIS KIT INSTRUCTIONS
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

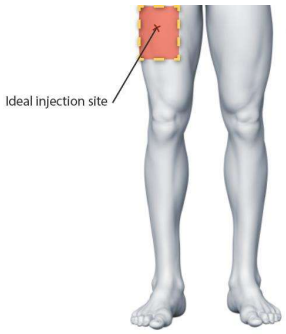
1. **Remove 1 of each item**
    a. 1 -syringe
    b. 1 – brown labeled filter needle (BD Filter Needle)- **for ampule use only**
    c. 1 – black labeled safety needle (Magellan Hypodermic Safety Needle 22G x 1”)
    d. 1 ampule of epinephrine

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.