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.

Ustekinumab (Stelara) Clinical Guideline for Home Intravenous Therapy
Section: Clinical Guideline
Compliance: ACHC Infusion Pharmacy
ACHC Standards: n/a
URAC Standards: n/a
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Approved by, Title and Date Approved: Kathleen Patrick, President, 1/2/2024

I. BACKGROUND

Ustekinumab (Stelara) is a human IgG1k monoclonal antibody indicated adult patients with moderate to severe plaque psoriasis, active psoriatic arthritis, and moderate to severe Crohn's disease. Ustekinumab binds with specificity to the p 40 protein subunit used by both the interleukin-12 and 23 cytokines. The cytokines IL-12 and IL-23 signal inflammation cascades and have been implicated as important contributors to chronic inflammation. Ustekinumab is indicated in adults for the treatment of moderate to severe plaque psoriasis, active psoriatic arthritis, moderate to severe active Crohn's disease, and moderate to severe active ulcerative colitis (UC). In pediatric patients 6 years old and older, ustekinumab can be utilized for the treatment of moderate to severe plaque psoriasis and active psoriatic arthritis. Ustekinumab is utilized in the intravenous form for the induction dosing of Crohn's disease and UC in adult patients. The following outlines the procedures for servicing patients in need of intravenous ustekinumab 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 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 ustekinumab must include:

1. Patient weight
2. Drug and dose (weight-based dosage)
3. Route of administration
4. Frequency of administration
5. Ana-kit per protocol

6. Orders for pre-medications if applicable
7. Line care protocol

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

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. PHARMACOLOGIC OVERVIEW

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

A. Indications for Intravenous Administration:
**Subcutaneous dosing and administration will not be discussed in the scope of this guideline*

1. Crohn's Disease- moderate to severe in adult patients
2. Ulcerative Colitis- moderate to severe in adult patients

B. Dosage:
Crohn's Disease and Ulcerative Colitis: Patients receive a one-time induction infusion and then transition to subcutaneous maintenance injections. The induction infusion is based on the patient's weight according to chart below:

Crohn's Disease and Ulcerative Colitis Initial Adult Intravenous Recommended Dosage (2.3): A single intravenous infusion using weight-based dosing:

Weight Range (kilograms)	Recommended Dosage
up to 55 kg	260 mg (2 vials)
greater than 55 kg to 85 kg	390 mg (3 vials)
greater than 85 kg	520 mg (4 vials)

Crohn's Disease and Ulcerative Colitis Maintenance Adult Subcutaneous Recommended Dosage (2.3): A subcutaneous 90 mg dose 8 weeks after the initial intravenous dose, then every 8 weeks thereafter.

*Dosing is based off actual body weight. Ustekinumab has not been studied in extremes of body weights

C. Dose Adjustments: No renal or hepatic dose adjustments

D. Duration: Induction infusion is a one-time dose. Subcutaneous maintenance duration is based on patient response and adverse reactions.

E. Contraindications: In patients with clinically significant hypersensitivity to ustekinumab or to any of its excipients

F. Warnings and Precautions

1. **Infections**: ustekinumab may increase the risk of infections and reactivation of latent infections. Serious bacterial, mycobacterial, fungal, and viral infections were observed in patients receiving ustekinumab. Treatment with ustekinumab should not be initiated in patients with any clinically active infection until the infection resolves or is adequately treated. Consider the risks and benefits of treatment prior to initiating use of ustekinumab in patients with a chronic infection or a history of recurrent infection.
2. **Tuberculosis:** Do not administer ustekinumab to patients with active tuberculosis infection. Initiate treatment of latent tuberculosis prior to administering ustekinumab. Consider anti-tuberculosis therapy prior to initiation of ustekinumab in patients with a past history of latent or active tuberculosis in whom an adequate course of treatment cannot be confirmed.
3. **Malignancies:** ustekinumab is an immunosuppressant and may increase the risk of malignancy. Malignancies were reported among subjects who received ustekinumab in clinical studies. There have been post-marketing reports of the rapid appearance of multiple cutaneous squamous cell carcinomas in patients receiving ustekinumab who had pre-existing risk factors for developing non-melanoma skin cancer. All patients receiving ustekinumab should be monitored for the appearance of non-melanoma skin cancer. Patients greater than 60 years of age, those with a medical history of prolonged immunosuppressant therapy and those with a history of Psoralen plus Ultraviolet A light (PUVA) treatment should be followed closely.
4. **Hypersensitivity reactions:** Hypersensitivity reactions, including anaphylaxis and angioedema, have been reported with ustekinumab. If an anaphylactic or other clinically significant hypersensitivity reaction occurs, institute appropriate therapy and discontinue ustekinumab.
5. **Posterior Reversible Encephalopathy Syndrome (PRES):** posterior reversible encephalopathy syndrome (PRES), also known as Reversible Posterior Leukoencephalopathy Syndrome (RPLS), were reported in clinical trials. Cases have also been reported in post marketing experience in patients with psoriasis, psoriatic arthritis and Crohn's disease. Clinical presentation included headaches, seizures, confusion, visual disturbances, and imaging changes consistent with PRES a few days to several months after ustekinumab initiation. A few cases reported latency of a year or longer. Patients recovered with supportive care following withdrawal of ustekinumab. Monitor patients for signs and symptoms of PRES. If PRES is suspected, promptly administer appropriate treatment and discontinue ustekinumab
6. **Pregnancy and Lactation**: Limited data on the use of ustekinumab in pregnant women are insufficient to inform a drug associated risk. In animal reproductive and developmental toxicity studies, no adverse developmental effects were observed after administration of ustekinumab to pregnant monkeys at exposures greater than 100 times the human exposure at the maximum recommended human subcutaneous dose. The background risk of major birth defects and miscarriage for the indicated. population(s) are unknown. 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 of clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively. There are no data on the presence of ustekinumab in human milk, the effects on the breastfed infant, or the effects on milk production. Ustekinumab was present in the milk of lactating monkeys administered ustekinumab. Due to species-specific differences in lactation physiology, animal data may not reliably predict drug levels in human milk. Maternal IgG is known to be present in human milk. Published data suggest that the systemic exposure to a breastfed infant is expected to be low because ustekinumab is a large molecule and is degraded in the gastrointestinal tract. However, if ustekinumab is transferred into human milk the effects of local exposure in the gastrointestinal tract are unknown.The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for

therapy and any potential adverse effects on the breastfed child from ustekinumab or from the underlying maternal condition.

G. Pharmacokinetics

1. Volume of distribution: 2.7-3 L
2. Excretion: 0.19L/day
3. Elimination half-life: 14.9-45.6 days

H. Adverse Reactions:

1. Abdominal pain (7%)
2. Diarrhea (2-4%)
3. Nausea (3%)
4. Vomiting (4%)
5. Headache (5-10%)
6. Urinary tract infection (4%)
7. Mycosis (5%)
8. Bronchitis (5%)
9. Nasopharyngitis (7-24%)
10. Sinusitis (3-4%)
11. Upper respiratory tract infection (4-5%)
12. Fatigue (3-4%)
13. Hypersensitivity reactions (0.08%)

I. Drug Interactions:

1. Concurrent use of immunosuppressants or other biologics may cause an increased risk of infection and immunosuppression. Examples include abatacept, tofacitinib, infliximab, baricitinib, and anifrolumab-fnia.
2. Concurrent use of ustekinumab and live vaccines may result in an increased risk of secondary transmission of infection by the live vaccine.
3. The formation of CYP450 enzymes can be altered by increased levels of certain cytokines (IL-1, IL-6, IL-10, TNFα, IFN) during chronic inflammation. Thus, ustekinumab, an antagonist of IL-12 and IL-23, could normalize the formation of CYP450 enzymes. Upon initiation of ustekinumab in patients who are receiving concomitant CYP450 substrates, particularly those with a narrow therapeutic index, monitoring for therapeutic effect (e.g. warfarin) or drug concentration (e.g. for cyclosporine) should be considered and the individual dose of the drug adjusted as needed

IV. ADMINISTRATIVE GUIDELINES

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

B. **Utilize 0.2 micron in-line filter tubing set for administration per Janssen Pharmaceuticals**.

C. Do not co-administer with any other intravenous drug product in the same IV line.

V. NURSING PROCEDURE

A. Supplies may 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. IV Pole
6. IV injection cap
7. IV administration set (flow regulator [ex: dial-a-flow] or gravity) with in-line or add-on 0.22-micron filter
8. Syringes (ex: 30mL-60mL) with needles (ex: 20 G x 1")
9. Sharps container

B. Prescription Items:

1. Ustekinumab vial(s)
2. Bag of sodium chloride 0.9% or 0.45% for dilution 250mL

C. How Supplied: Single dose vial 130mg/26mL (5mg/mL)

D. Storage and Handling: Ustekinumab vials should be stored in refrigerated temperatures 36°F to 46° F (2°C to 8°C). Do not freeze or shake. Keep in original carton.

E. Compatibility: Compatible with 0.9% and 0.45% sodium chloride solution

F. Procedures:

1. Explain the reasoning for visit and use of ustekinumab infusion.
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, PRES, hypersensitivity reactions, nausea, abdominal pain, diarrhea, vomiting, headache, and fatigue.
6. Prepare Product:
    a. Visually inspect ustekinumab vial(s) for integrity prior to preparation. Do not use if visibly opaque particles, discoloration, or foreign particles are observed.
    b. Calculate the dose and number of ustekinumab vials needed for the infusion based on the patient's weight
    c. From the sodium chloride bag, withdraw and discard the same amount of volume of ustekinumab that will be added to the saline bag.

d. Withdraw 26mL from each ustekinumab vial needed and add to the sodium chloride bag. The total volume should be 250mL.

7. Infusion Rates: Infuse over at least 1 hour with an infusion set with a 0.2-micron filter.
8. Monitor patient and vitals periodically throughout the infusion and for at least 30 minutes after end of infusion per CarePathRx Nursing Best Practice Administration Guidelines

VI. CLINICAL MONITORING

A. Prior to therapy:

1. TB screening
2. CBC, Liver function panel, and renal function
3. Ensure patient is up to date on vaccinations

B. During therapy:

1. Monitor for signs and symptoms of infection. Therapy may need interrupted during an active infection.
2. Signs and symptoms of a hypersensitivity reaction
3. Signs or symptoms of malignancies
4. Monitor for PRES including headaches, seizures, confusion, visual disturbances, and imaging changes consistent with PRES a few days to several months after ustekinumab initiation.
5. CBC and CMP periodically throughout therapy

C. Disease progression and therapy efficacy

1. Assess for worsening symptoms including abdominal pain, cramps, changes in stool, changes in weight, and frequency of flares.

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

REFERENCES:

Stelara [package insert]. Horsham, PA. Janssen Pharmaceuticals. 2019.

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

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

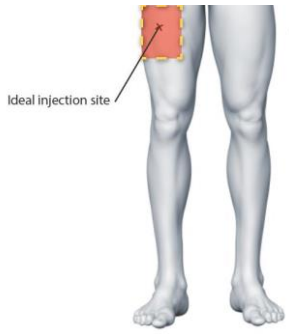
1. **Remove 1 of each item**
    a. 1 -syringe
    b. 1 – brown labeled filter needle (BD Filter Needle)- **for ampule use only**
    c. 1 – black labeled safety needle (Magellan Hypodermic Safety Needle 22G x 1”)
    d. 1 ampule of epinephrine

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.