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.

Sutimlimab-jome (Enjaymo) Clinical Guideline for Home Intravenous Therapy

Section: Clinical Guideline
Compliance: ACHC Infusion Pharmacy
ACHC Standards: N/A
URAC Standards: N/A
Policy ID: CG004
Effective: 12/01/2023
Reviewed:
Revised:
Approved by, Title and Date Approved: Kathleen Patrick, President, 12/1/23

I. BACKGROUND

Sutimlimab-jome (Enjaymo) is an immunoglobulin G subclass 4 (IgG4) monoclonal antibody that inhibits the classical complement pathway. It specifically binds to complement protein component 1s (C1s), a serine protease which cleaves complement component 4 (C4). The inhibition of the classical complement pathway at the level of C1s prevents deposition of complement opsonins on the surface of red blood cells, resulting in inhibition of hemolysis. Sutimlimab is indicated for the treatment of hemolysis in adult patients with an autoimmune disease called cold agglutinin disease (CAD). Patients with CAD may experience low hemoglobin levels requiring transfusions, elevated bilirubin, fatigue, acrocyanosis, and thromboembolism due to the agglutination of red blood cells. By inhibiting the classic complement pathway, sutimlimab prevents the aggregation of the red blood cells. The following outlines the procedures for servicing patients in need of sutimlimab 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 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 sutimlimab must include:
   1. Patient's weight
   2. Drug and dose (including weight-based dosing range)
   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

D. Baseline labs or tests prior to starting therapy

E. Vaccination against encapsulated bacteria at least two weeks prior to treatment.

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. PHARMACOLOGY OVERVIEW

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

A. Indications: Indicated for the treatment of hemolysis in adult patients with cold agglutinin disease (CAD).

B. Dosage: Dosing is based on the patient's weight and the dosing range
   1. 39 kg to <75 kg: 6,500 mg IV once weekly for the first two weeks, and then every two weeks thereafter
   2. 75 kg or more: 7,500 mg IV once weekly for the first two weeks, and then every two weeks thereafter

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

C. Dose Adjustment
   1. If a dose is missed, administer as soon as possible; thereafter resume dosing every two weeks. If the duration after the last dose exceeds 17 days, administer sutimlimab weekly for two weeks, with administration every two weeks thereafter.
   2. No dose adjustments for renal or hepatic impairments
   3. Notify the prescriber if patient's weight changes from a previously prescribed dosing range

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

E. Contraindications: Sutimlimab is contraindicated in patients with a known hypersensitivity to sutimlimab or any of the inactive ingredients

F. Warnings and Precautions:

   1. **Serious infections:** sutimlimab may increase susceptibility to serious infections, including infections caused by encapsulated bacteria such as *Neisseria meningitides*, *Streptococcus pneumoniae*, and *Haemophilus influenza.* Serious infections (bacterial and viral) were reported in 15% (10/66) of patients receiving sutimlimab in the phase 3 studies. These infections included urinary tract infection with sepsis, respiratory tract infection, pneumonia, otomastoiditis, and skin infections. One patient died due to klebsiella pneumonia. Vaccinate patients for encapsulated bacteria according to the most current ACIP recommendations for patients with persistent complement deficiencies. Re-vaccinate patients in accordance with ACIP recommendations. Immunize patients without a history of vaccination against encapsulated bacteria at least two weeks prior to receiving the first dose of sutimlimab. If urgent sutimlimab therapy is indicated in an unvaccinated patient, administer vaccines as soon as possible.

Consider interrupting sutimlimab treatment in patients who are undergoing treatment for a serious infection. Sutimlimab has not been studied in patients with chronic systemic infections such as hepatitis B, hepatitis C, or HIV.

2. **Infusion related reactions**: Sutimlimab is contraindicated in patients with known hypersensitivity to sutimlimab-jome or any of the inactive ingredients. Sutimlimab may result in infusion-related reactions. In the two phase 3 studies, 19 of 66 (29%) patients treated with sutimlimab experienced infusion-related reactions (e.g., shortness of breath, rapid heartbeat, nausea, flushing, headache, hypotension, chest discomfort, pruritus, rash, injection site reaction, and dizziness) were reported in patients from the two clinical studies. One patient permanently discontinued therapy due to an infusion-related reaction. Monitor patients for infusion-related reactions and interrupt if a reaction occurs. Discontinue sutimlimab and institute appropriate supportive measures if signs of hypersensitivity reactions, such as cardiovascular instability or respirator compromise occur.

3. **Risk of autoimmune disease:** Based on its mechanism of action, sutimlimab may potentially increase the risk for developing autoimmune diseases such as systemic lupus erythematosus (SLE). Development of systemic lupus erythematosus (SLE) has been associated with inherited classical complement deficiency. Patients with SLE or autoimmune disease with positive anti-nuclear antibody were excluded from sutimlimab clinical trials. In clinical trials, 3/66 (4.5%) patients developed a relapse or worsening of pre-existing autoimmune disease. Monitor patients being treated with sutimlimab for signs and symptoms and manage medically.

4. **Recurrent hemolysis after sutimlimab discontinuation**: If treatment with sutimlimab is interrupted, closely monitor patients for signs and symptoms of recurrent hemolysis, (e.g. elevated levels of total bilirubin or lactate dehydrogenase (LDH) accompanied by a decrease in hemoglobin, or reappearance of symptoms such as fatigue, dyspnea, palpitations, or hemoglobinuria). Consider restarting sutimlimab if signs and symptoms of hemolysis occur after discontinuation.

5. **Pregnancy and Lactation:** There is no available data on sutimlimab use in pregnant women to evaluate for a drug-associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes. Human immunoglobulin G (IgG) antibodies are known to cross the placental barrier; therefore, sutimlimab may be transmitted from the mother to the developing fetus. In animal reproduction studies, intravenous administration of sutimlimab to pregnant monkeys during organogenesis at doses 2 to 3 times the maximum recommended human doses did not result in adverse effects on pregnancy or offspring development.
There is no data on the presence of sutimlimab in human milk, effects on the breastfed child, or the effects on milk production. Maternal IgG is known to be present in human milk. The effects of local gastrointestinal exposure and limited systemic exposure in the breastfed child to sutimlimab are unknown. No conclusions can be drawn regarding whether sutimlimab is safe for use during breastfeeding. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for sutimlimab and any potential adverse effects on the breastfed child from sutimlimab or from the underlying maternal condition.

G. Pharmacokinetics
   1. Volume of distribution: 5.8 Liters
   2. Elimination half-life: 21 days

H. Adverse Reactions
    1. Common adverse reactions: acrocyanosis (18-21%), peripheral edema (25%), Raynaud's phenomenon (18%), nausea (25%), hypertension (23-25%), arthralgia (25%), dizziness (29%), headache (21-23%), urinary tract infection (38%), cough (25%), rhinitis (18%), bacterial infections (25%), fatigue (33%).
    2. Serious: Infection of skin and/or subcutaneous tissue, hemolysis (recurrent), autoimmune disease, respiratory tract infection (25%), serious infections (15%), infusion reaction (17-29%), and sepsis.

I. Drug Interactions: No drug-drug interactions found. Drug-drug interactions may exist. Consult interaction database for patient specific assessment.

IV. ADMINISTRATIVE GUIDELINES

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

B. **Administer using a line containing a sterile, non-pyrogenic, polyethersulfone (PES) membrane, low protein binding in-line filter (pore size of 0.2 micron**).

C. 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:
    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" with 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) **with in-line or add-on 0.22-micron filter.**
    9. Syringes (50-60mL) with needles (20 G x 1")
    10. Sharps container

B. Prescription items
    1. Sutimlimab vials
    2. Pre-filled 0.9% sodium chloride bag
    3. 50 mL 0.9% sodium chloride stock bag for post-infusion flush

C. How Supplied
    1. Sutimlimab-jome injection is a clear to slightly opalescent, colorless to slightly yellow, preservative-free solution supplied as one 1,100 mg/22 mL (50 mg/mL) single-dose vial per carton. (NDC 80203-347-01)

D. Storage and Handling
    1. Store sutimlimab vials refrigerated at 36°F to 46°F (2°C to 8°C) in the original carton to protect from light. Do not freeze. Do not shake. Discard unused portion.

E. Compatibility
    1. Compatible with 0.9% sodium chloride
    2. No incompatibilities have been observed between sutimlimab infusion solution and infusion bags made of Di-(2-ethylhexyl) phthalate (DEHP) plasticized polyvinyl chloride (PVC), Ethyl Vinyl Acetate(EVA) and polyolefin (PO); administration sets made of DEHP-plasticized PVC, DEHP-free polypropylene (PP) and polyethylene (PE); and vial adapters made of polycarbonate (PC) and acrylonitrile-butadiene-styrene (ABS).

F. Procedures:
    1. Explain the reasoning for visit and use of sutimlimab.
    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 patient on warnings, precautions, and potential side effects including but not limited to: infections, infusion-related reactions, risk of autoimmune disease, acrocyanosis, peripheral edema, nausea, arthralgia, hypertension, dizziness, headache, and fatigue.
    6. Prepare Product
        a. Visually inspect sutimlimab vials prior to mixing for any particulate matter or discoloration. Sutimlimab solution is a clear to slightly opalescent and colorless to slightly yellow solution. Do not administer if discolored or if foreign particulate matter is present.
        b. Withdraw the calculated volume of sutimlimab from the appropriate number of vials based on the prescribed dose. Add the calculated volume to the provided pre-filled 0.9% Sodium Chloride bag for a total volume of 500 mL. Discard any vials with excess drug.
    7. Administer the infusion based on diluted method and dosing range per table below:

Infusion Reference Table for Sutimlimab (Diluted in 0.9% Sodium Chloride)

Body Weight Range	Dose	Number of ENJAYMO Vials Needed	ENJAYMO Volume	Volume of NaCl Diluent	Total Volume	Maximum Infusion Rate
39 kg to less than 70 kg	6,500 mg	6	130 mL	370 mL	500 mL	250 mL/ hour
70 kg to less than 75 kg	6,500 mg	6	130 mL	370 mL	500 mL	500 mL/ hour*
75 kg or greater	7,500 mg	7	150 mL	350 mL	500 mL	500 mL/ hour*

*Patients with cardiopulmonary disease may receive the infusion over 120 minutes.

8. Flush the administration set immediately following completion of the infusion with a sufficient volume (approximately 20 mL) of 0.9% Sodium Chloride.

9. Post infusion monitoring:
    a. Monitor the patient for signs or symptoms of infusion and/or hypersensitivity reactions and vital signs two hours after the first infusion is completed.
    b. Monitor for 1 hour for subsequent infusions.

VI. CLINICAL MONITORING

A. Prior to therapy

1. Assess vaccination status and ensure patients are up-to-date on their vaccinations. Specifically, vaccinations against encapsulated bacteria. Refer to Appendix B for the Advisory Committee on Immunization Practices (ACIP) recommendations for patients with persistent complement deficiencies and patients treated with complement inhibitors.

B. During therapy

1. Monitor for signs and symptoms of infusion related reactions or hypersensitivity reactions including shortness of breath, rapid heartbeat, nausea, flushing, headache, hypotension, chest discomfort, pruritis, rash, injection site reaction, and dizziness
2. Monitor patient for signs and symptoms of infections
3. Monitor for signs and symptoms of new autoimmune disease including SLE including but not limited to fatigue, joint pain, butterfly rash, fever, swollen lymph nodes, chest pain, etc.
4. Therapy efficacy and CAD symptoms:
    a. Total bilirubin reductions
    b. Increased hemoglobin levels
    c. Reduction in number of blood transfusions
    d. Decreased fatigue, dyspnea, heart palpitations, and acrocyanosis
    e. Functional Assessment of Chronic Illness Therapy (FACIT) Fatigue Scale for quality-of-life assessment

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

REFERENCES:

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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 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

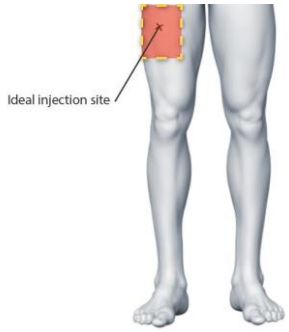
1. **Remove 1 of each item**
    a. 1 -syringe
    b. 1 – brown labeled filter needle (BD Filter Needle)- **for ampul use only**
    c. 1 – black labeled safety needle (Magellan Hypodermic Safety Needle 22G x 1”)
    d. 1 ampul of epinephrine

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.

APPENDIX B: ACIP VACCINE RECOMMENDATIONS

Advisory Committee on Immunization Practices (ACIP) Altered Immunocompetence Guidelines for Immunizations | CDC (www.cdc.gov/vaccines/hcp/acip-recs/general-recs/immunocompetence.html)

Adapted from Table 8-1 Vaccination of persons with primary and secondary immunodeficiencies

Primary Immunodeficiency	Specific Immunodeficiency	Contraindicated vaccine(s)[a]	Risk-specific recommended vaccine(s)*
Complement	Persistent complement, properdin, or factor B deficiency	None	Pneumococcal Meningococcal *Haemophilus influenzae* type b (children 12-59 months of age)
	Taking eculizumab and/or ravulizumab	None	Meningococcal

Other vaccines that are universally or routinely recommended should be given if not contraindicated. An exception is patients with B-cell deficiencies receiving immunoglobulins, who should not receive either live or non-live vaccines, due to safety (live vaccines) and efficacy (live and non-live vaccines) concerns.

Please refer to the most up to date ACIP recommendations for the most current and complete information for vaccinations in persons with persistent complement component deficiencies and patients treated with complement inhibitors.