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.

Alpha-1 Proteinase Inhibitors (Prolastin-C Liquid, Aralast NP, Glassia, and Zemaira) Clinical Guideline for Home Intravenous Therapy

Section: Clinical Guideline
Policy ID: CG045
Effective: 7/7/22
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I. BACKGROUND

Human alpha-1 proteinase inhibitors (Prolastin-C Liquid, Aralast NP, Glassia, and Zemaira) are intravenous agents that augment the deficient alpha 1-antitrypsin, which theoretically is used to correct the imbalance of proteinase inhibitors and the neutrophil elastase in the lungs. Ultimately, it serves to protect the lungs from the damage caused from the deficiency. All drugs in the class share this common purpose and are indicated for adults with confirmed alpha-1-antitrypsin deficiency. The following outlines the procedures for servicing patients in need of outpatient human alpha-1 proteinase inhibitor therapy 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 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. IgA deficiency status
4. Age
5. Other relevant social and/or medical history

C. Physician orders for alpha-1 proteinase inhibitors must include:

1. Patient weight
2. Drug and dose (including weight-based dosage)
3. Route of administration
4. Frequency of administration
5. Emergency medications per protocol
6. Orders for pre-medications, if applicable
7. Line care protocol
8. Routine lab monitoring, if applicable

D. Baseline labs prior to starting therapy including IgA level.

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. PHARMACOLOGIC OVERVIEW

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

A. Indications: Treatment of adult patients with confirmed alpha-1 antitrypsin deficiency

B. Dosing: Dose is 60mg/kg IV infused once weekly for all alpha-1 proteinase products

*Dosing is based off actual body weight. Alpha-1 proteinase inhibitors have not been studied in extremes of body weights.

C. Dose adjustments: No hepatic or renal adjustments

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

E. Contraindications:

1. History of severe systemic reactions or anaphylaxis to alpha-1-proteinase inhibitor products.
2. Immunoglobulin A (IgA) deficient patients with antibodies against IgA

F. Warnings and Precautions:

1. **Hypersensitivity reactions:** Alpha-1 products may contain trace amounts of IgA. Patients with known antibodies to IgA, which can be present in patients with selective or severe IgA deficiency, have a greater risk of developing severe hypersensitivity and anaphylactic reactions. Monitor vital signs continuously and observe the patient carefully throughout the infusion. Discontinue the infusion if hypersensitivity symptoms occur and administer appropriate emergency treatment. Have epinephrine and other appropriate supportive therapy available for the treatment of any acute anaphylactic or anaphylactoid reaction
2. **Transmission of infectious agents:** Because alpha-1 proteinase inhibitors are made from human plasma, it may carry a risk of transmitting infectious agents, such as viruses, the variant Creutzfeldt-Jakob disease (vCJD) and theoretically, the Creutzfeld-Jakob disease (CJD) agent. This also applies to unknown or emerging viruses and other pathogens. The risk of transmitting an infectious agent has been minimized by screening plasma donors for prior exposure to certain viruses, by testing for the presence of certain virus infections and by inactivating and removing certain viruses during the manufacturing process.
3. **Pregnancy and Lactation:** There is no data with alpha-1 product use in pregnant women to inform drug-associated risk. It is not known whether these agents can cause fetal harm when

administered to pregnant women or can affect reproductive capacity. Alpha-1 proteinase inhibitors should only be given to pregnant patients with a clear need for therapy. There is no information regarding the presence of alpha-1 agents in human milk, the effects of the breastfed infant, or the effects on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for alpha-1 treatment and any potential effects on the breastfed infant from alpha-1 agents.

G. Pharmacokinetics:

1. Therapeutic concentration: > 11 micromoles
2. Volume of distribution 3.2-5.6 L
3. Half-life: 4.5-5.9 days

H. Adverse Reactions:

1. Cardiovascular: Chest discomfort (6%), vasodilation (6%)
2. Dermatologic: Flushing, pruritis (1%)
3. Gastrointestinal: Diarrhea, nausea, and vomiting
4. Hepatic: Increased aminotransferase level (11.1%), increased liver enzymes (6%)
5. Musculoskeletal: Joint pain (16%)
6. Neurologic: Asthenia (7.6%), dizziness (6%), headache (up to 20%), somnolence (0.03%)
7. Respiratory: Acute exacerbation of chronic obstructive pulmonary disease (up to 20%), bronchitis (7.6%), cough (up to 24%), rhinitis (6%), sinusitis (up to 15%), upper respiratory infection (up to 15%)
8. Immunologic: Hypersensitivity reaction
9. Other: Fever (6%)

I. Drug Interactions:

1. No formal drug interaction studies have been conducted
2. 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 3 hours of preparation for any alpha 1-proteinase inhibitor product.

B. Filters:

1. Aralast NP: **A 20-micron filter needle** (supplied with drug product) should be used during pooling**.** In line filter is not required during administration.
2. Glassia: Filter the solution through a **5 micron in-line filter** during the infusion
3. Prolastin-C: Filter the solution through a **5-15 micron in-line filter** during the infusion
4. Zemaira**:** Filter the solution through a **5 micron in-line filter** during the infusion

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

V. NURSING PROCEDURE

A. Recommended supplies and procedure below apply to nurse-administered infusions. Patients may be candidates for self-infusion if deemed appropriate by their provider. Nursing 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) with in-line or add-on **5-micron filter** (for Glassia, Prolastin C, and Zemaira)
7. Syringes (50-60mL) with needles (20 G x 1")
8. Vented spike (for Glassia, Prolastin C, and Zemaira)
9. Empty, sterile intravenous solution container or bag for pooling
10. Sharps container
11. Supplies if utilizing a pole mounted ambulatory infusion pump:

    1) Ambulatory pump tubing with **5-micron filter** (for Glassia, Prolastin C, and Zemaira)
    2) Pole mounted ambulatory pump
    3) Batteries for ambulatory pump (Ex: 9 Volt Duracell battery or 4 Double A batteries)
    4) Battery change procedure teaching sheet
    5) Continuous delivery mode teaching sheet
    6) Pump return box

B. Prescription Items:

1. Vials of human alpha-1 proteinase inhibitor
2. Standard flushes per protocol
3. Anaphylaxis kit per protocol

C. How Supplied:

1. Aralast NP:

    1) Available as 0.5 or 1 gram vials of drug
    2) 25mL or 50mL of Sterile Water for Injection diluent respectively
    3) One sterile double-ended transfer needle, and one sterile 20-micron filter needle.

2. Glassia: Supplied in single-dose vials containing the labeled amount of functional active alpha 1-proteinase inhibitor. Supplied as 1 gram/50mL solution, 4grams /200mL solution, and 5grams/250mL solution.

3. Prolastin-C Liquid: supplied in single-dose vials containing the labeled amount of functional active alpha 1-proteinase inhibitor. Supplied as 500 mg/10mL, 1 gram /20mL or 4 grams/80mL solution.

4. Zemaira:

    1) Supplied in single-dose vials containing the labeled amount of functional active alpha 1-proteinase inhibitor. 1 gram, 4 grams, or 5 gram single dose vials of drug
    2) 20 mL, 76 mL, or 95 mL of Sterile Water for Injection diluent respectivel
    3) One filter transfer device for reconstitution.

D. Storage and Handling

1. Aralast NP: Store in the original container at temperature below 25°C (77°F). Do not freeze. Protect from light.

2. Glassia:

    1) Store in the original container in the refrigerator at 2°C to 8°C (36°F to 46°F). Do not freeze.
    2) Product may be stored at a temperature up to 25°C (77°F) for up to 1 month (do not refrigerate once brought to room temperature).

3. Prolastin-C Liquid:

    1) Store in the original container in the refrigerator at 2°C to 8°C (36°F to 46°F). Do not freeze.
    2) Product may be stored at a temperature up to 25°C (77°F) for up to 1 month (do not refrigerate once brought to room temperature).

4. Zemaira: Store in the original container at temperature below 25°C (77°F). Do not freeze. Protect from light.

5. All products: Discard unused medication in vials

E. Compatibility: Alpha 1 proteinase inhibitors have not been studied in other solutions. Aralast NP and Zemaira powders are reconstituted with sterile water for injection.

F. Preparation:

1. Explain the reasoning for visit and use of the human alpha-1 proteinase inhibitor product
2. Don gloves
3. Establish venous access prior to preparation of drug
4. Counsel patient on warnings, precautions, and potential side effects including but not limited to hypersensitivity reactions, chest discomfort, yellow of the skin or eyes, dizziness and headache, and respiratory symptoms
5. Prepare product:

a. **Aralast NP:**

1) Allow product and diluent to come to room temperature.
2) Using aseptic technique and a double ended transfer needle provided, reconstitute the drug with the provided diluent. Let the vial stand until most of the contents are in solution, then gently swirl the product. **Do not shake or invert.**
3) The solution should be colorless to slightly yellow/green. Inspect the vial for particles, but they will ultimately be filtered through the provided 20-micron filter needle.
4) Attach the provided 20-micron filter needle to a luer lock syringe. Draw up the reconstituted product into the syringe. Remove the syringe from the filter needle and attach the syringe a 20G x1" needle. Pool the vial(s) into an empty, sterile solution container.
5) Discard any unused product left in vials.

b. **Glassia:**

1) Allow the product to come to room temperature before administration
2) Inspect the solution for colorless to slightly yellow/green appearance, and particulate matter. Particles will be filtered. Do not use if solution is cloudy.
3) When infusing directly from the vials, use a vented spike. Peel clear plastic hanger from vial label. Hang on IV pole.
4) If pooling into an empty container, use aseptic technique and a vented spike. Pool vial(s) into an empty, sterile container to be infused.
5) Discard any unused product left in vials.
6) Filter the solution during administration using an administration set with a 5 micron filter.

c. Prolastin-C Liquid

1) Allow the product to come to room temperature before administration.
2) Inspect the solution for colorless to slightly yellow/green appearance, and particulate matter. Particles will be filtered. Do not use if solution is cloudy.
3) Vial(s) should be pooled into an empty, sterile container to be infused using aseptic technique and a vented spike.
4) Discard any unused product left in vials.
5) Filter the solution during administration using an administration set with a 5-15 micron filter.

d. **Zemaira:**

1) Allow the product to come to room temperature before administration.
2) Using aseptic technique and the provided Mix2Vial filter set, reconstitute the drug with the provided SWFI diluent. The 1g vial will take ~5 minutes to reconstitute, and the 4 and 5g vial will take ~10 minutes to reconstitute. See package insert for specific Mix2Vial instructions.
3) Inspect the solution for colorless to slightly yellow appearance, and free from visible particles.
4) Vial(s) should be pooled into an empty, sterile container to be infused using aseptic technique and a vented spike.
5) Discard any product left in vials.
6) Filter the solution during administration using an administration set with a 5 micron filter.

G. Infusion rates according to product:

1. **Aralast and Glassia**: Infusion rate not to exceed 0.2 mL/kg/min, as determined by the response and comfort of the patient
2. **Prolastin-C and Zemaira**: infusion rate is recommended to be 0.08mL/kg/min, but is determined by the response and comfort of the patient.

H. Post infusion monitoring: For nurse-administered infusions, monitor patients and vital signs periodically during the infusion and 30 minutes after the infusion has completed.

VI. CLINICAL MONITORING

A. Prior to staring therapy

1. Lab work including immunoglobulin panel for IgA deficiency
2. Baseline CMP and CBC

B. Monitor disease severity including:

1. Progression of COPD or emphysema using pulmonary function tests including but not limited to spirometry
2. Progression of liver disease using hepatic enzyme panels, CT scans or ultrasonography of the liver and abdomen, and objectively measuring jaundice.
3. Monitor for signs and symptoms of infection
4. Monitor for signs and symptoms of hypersensitivity reactions

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

REFERENCES

Aralast NP [package insert]. Lexington, MA: Baxalta U.S. Inc.; May 2025.

Glassia [package insert]. Lexington, MA: Baxalta U.S. Inc.; February 2025.

Prolastin-C Liquid [package insert]. Triangle Park, NC: Grifols Therapeutics LLC; February 2020.

Zemaira [package insert]. Kankakee, IL: CSL Behring LLC; January 2024.

Alpha-1-antitrypsin deficiency. IBM Micromedex Solutions. Truven Health Analytics, Inc. Ann Arbor, MI. Accessed July 7, 2022. http://www.micromedexsolutions.com.

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

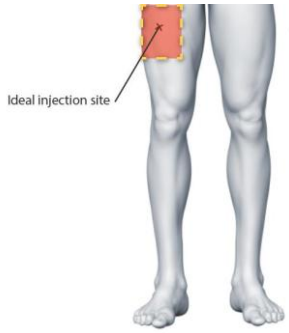
1. **Remove 1 of each item**
    a. 1 -syringe
    b. 1 – brown labeled filter needle (BD Filter Needle)- **for ampule use only**
    c. 1 – black labeled safety needle (Magellan Hypodermic Safety Needle 22G x 1”)
    d. 1 ampule of epinephrine

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.