curative

TITLE:	ALPHA 1-PROTEINASE INHIBITORS POLICY
POLICY #:	MM-PNP-039
VERSION #:	01
DEPARTMENT:	UTILIZATION REVIEW
ORIGINAL EFFECTIVE DATE:	12/20/2023
CURRENT REVISION DATE:	N/A

1. PURPOSE

This policy addresses the medical necessity review of Alpha-1 Proteinase Inhibitors.

2. SCOPE

Medical and Pharmacy UM Departments.

3. DEFINITIONS

3.1. N/A

4. RESPONSIBILITIES

4.1. N/A

5. POLICY

Provides guidelines regarding the medical necessity review of Alpha 1-Proteinase Inhibitors.

Brand Selection for Medically Necessary Indications

As defined in Curative commercial policies, health care services are not medically necessary when they are more costly than alternative services that are at least as likely to produce equivalent therapeutic or diagnostic results. Aralast NP, Glassia, and Zemaira (alpha1-proteinase inhibitor [human]) are more costly to Curative than other medications in the treatment of chronic augmentation and maintenance therapy in adults with clinical evidence of emphysema due to severe hereditary deficiency of alpha1-proteinase inhibitor (alpha1-antitrypsin deficiency). **There is a lack of reliable evidence that Aralst NP, Glassia, and Zemaira are superior to the lower cost alternative, Prolastin-C. Therefore, Curative considers Aralast NP, Glassia, and Zemaira to be medically necessary only for members who have a contraindication, intolerance or ineffective trial to Prolastin-C**.

Note: Requires Precertification:

Precertification of alpha 1-proteinase inhibitors (Aralast NP, Glassia, Prolastin-C, and Zemaira) is required of all Curative participating providers and members in applicable plan designs.

Criteria for Initial Approval

Curative considers alpha 1-proteinase inhibitor (e.g., Aralast NP, Glassia, Prolastin-C, and Zemaira) therapy medically necessary for the treatment of emphysema due to alpha 1-antitrypsin (AAT) deficiency when ***all*** of the following criteria are met:

- The member's pretreatment serum AAT level is less than 11 micromol/L (80 mg/dL by radial immunodiffusion or 50 mg/dL by nephelometry); *and*
    - The member's pretreatment post-bronchodilation forced expiratory volume in 1 second (FEV_1) is greater than or equal to 25% and less than or equal to 80% of the predicted value; *and*
    - The member has a documented PiZZ, PiZ (null), or Pi (null, null) (homozygous) AAT deficiency or other phenotype or genotype associated with serum AAT concentrations of less than 11 micromol/L (80 mg/dL by radial immunodiffusion or 50 mg/dL by nephelometry); *and*
    - The member does not have the PiMZ or PiMS AAT deficiency.

Curative considers all other indications as experimental and investigational (for additional information, see 'Experimental and Investigational' and 'Background' sections).

Continuation of Therapy

Curative considers continuation of alpha 1-proteinase inhibitor (Aralast NP, Glassia, Prolastin-C, and Zemaira) therapy medically necessary for treatment of emphysema due to alpha 1-antitrypsin (AAT) deficiency when the member is experiencing beneficial clinical response from therapy.

Other

Note: If the member is a current smoker, they should be counseled on the harmful effects of smoking on pulmonary conditions and available smoking cessation options.

Dosage and Administration

Aralast NP

- Available as lyophilized powder in single dose vials containing 0.5 gram or 1 gram of functional Alpha1-PI
- Recommended dosage is 60 mg/kg body weight administered once weekly by intravenous infusion
- Administer at a rate not to exceed 0.2 mL/kg body weight/minute, and as determined by the response and comfort of the individual

Source: Baxalta US, 2018

Glassia

- Available for injection: approximately 1 gram of functional alpha1-PI in 50 mL of ready to use solution in a single use vial
- The recommended dosage is 60 mg/kg body weight administered once weekly by intravenous infusion
- Administer at a rate not to exceed 0.2 mL/kg body weight per minute, depending on individual's response and comfort

Source: Takeda Pharmaceuticals, 2022

Prolastin-C and Prolastin-C Liquid

- Prolastin-C is available for injection as approximately 1,000 mg as lyophilized powder in a single-use vial. Reconstitute with sterile water for injection, USP, provided in a separate 20 mL vial.
- Prolastin-C liquid is available for injection as approximately 500 mg (10 mL), 1,000 mg (20 mL) ad 4,000 mg (80 mL) of a solution for injection in single-dose vials.
- The recommended dosage is 60 mg/kg body weight administered once weekly by intravenous infusion.
- Dose ranging studies using efficacy endpoints have not been performed with any Alpha1-PI product, including Prolastin-C and Prolastin-C liquid.
- Administration: 0.08 mL/kg/min as determined by individual's response and comfort.

Source: Grifols Therapeutics, 2020; 2022

Zemaira

- Zemaira is supplied in a single-use vial containing approximately 1000 mg, 4000 mg, or 5000 mg of functionally active A1-PI as a white to off-white lyophilized powder for reconstitution with 20 mL, 76 mL, or 95 mL of Sterile Water for Injection, USP.
- The recommended weekly dose of Zemaira is 60 mg/kg body weight. Dose ranging studies using efficacy endpoints have not been performed with Zemaira or any A1 -PI product.
- Administer at a rate of approximately 0.08 mL/kg/min as determined by the response and comfort of the individual.

Source: CSL Behring, 2022

Experimental and Investigational

Because panacinar emphysema does not develop in some individuals who have AAT deficiency, replacement therapy with AAT inhibitor is of no proven value in affected individuals without clinical evidence of emphysema and is therefore considered experimental and investigational for these individuals.

Curative considers AAT inhibitor experimental and investigational for treatment of the following (not an all-inclusive list):

- Acute respiratory distress syndrome in persons undergoing mechanical ventilation;
- Cystic fibrosis;
- Inflammatory and autoimmune diseases (e.g., acute myocardial infarction, colitis-associated colon cancer, connective tissue/rheumatoid diseases including rheumatoid arthritis, diabetes mellitus, graft-versus-host disease, inflammatory bowel disease);
- Ischemia-reperfusion injury in organ transplantation.

Curative considers alpha-1 antitrypsin deficiency gene therapy experimental and investigational because its effectiveness has not been established.

Curative considers inhaled alpha-1 antitrypsin therapy experimental and investigational because its effectiveness has not been established.

Curative considers PEGylated alpha-1 antitrypsin and recombinant alpha-1 antitrypsin IgG1 Fc-fusion protein experimental and investigational for the treatment of alpha-1 antitrypsin deficiency-associated lung disease.

6. PROCEDURE

N/A

7. TRAINING REQUIREMENT

7.1. All Medical and Pharmacy UM Associates are responsible for reading and comprehending this procedure. Employees are also responsible for contacting management or Privacy and Compliance with any questions or concerns regarding the information contained within this procedure.

8. ENFORCEMENT

Violations of this controlled document will cause the imposition of sanctions in accordance with the Curative sanctions-controlled document. This may include verbal/written warning, suspension, up to termination of employment or volunteer, intern, contractor status with Curative. Additional civil, criminal and equitable remedies may apply.

9. DOCUMENTATION

N/A

10. REFERENCE DOCUMENTS AND MATERIALS

N/A

11. COLLABORATING DEPARTMENTS

N/A

12. DOCUMENT CONTROL

APPROVED BY:		
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(Printed Name)	**(Date)**	**(Signature)**

REVISION HISTORY			
Date	**Author**	**Version**	**Comments**
			Initial Version

APPENDICES

N/A