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Section:	Prescription Drugs	**Effective Date:**	April 1, 2025
Subsection:	Respiratory Agents	**Original Policy Date:**	July 21, 2017
Subject:	Alpha$_1$-Proteinase Inhibitors	**Page:**	1 of 5

Last Review Date: March 7, 2025

Alpha$_1$-Proteinase Inhibitors

Description

Aralast NP, Glassia, **Prolastin-C**, Zemaira

Preferred Alpha$_1$-Proteinase Inhibitor: Prolastin-C

Background
Aralast NP, Glassia, Prolastin-C, and Zemaira are intravenous infusions indicated for individuals with clinically evident emphysema due to severe deficiency of Alpha$_1$-PI, also known as alpha$_1$-antitrypsin (AAT) deficiency. These medications increase antigenic and functional (anti-neutrophil elastase capacity, ANEC) serum levels and antigenic lung epithelial lining fluid levels of Alpha$_1$-PI. Intravenous administration of purified preparations of pooled donor-derived human AAT has been shown to augment levels of AAT and the AAT-related anti-elastase capacity of serum and lung epithelial lining fluid. The current U.S. Food and Drug Administration (FDA)-approved intravenous augmentation therapy dose for chronic administration is 60 mg/kg body weight, administered weekly (1-6).

Regulatory Status
FDA-approved indications: Aralast NP, Glassia, Prolastin-C, and Zemaira are indicated for chronic augmentation therapy in individuals with clinically evident emphysema due to severe congenital deficiency of alpha$_1$-PI (1-4).

The safety of Alpha$_1$-Proteinase Inhibitors in patients with severe renal impairment (creatinine clearance (CrCl) less than 30 mL/min) or end-stage renal disease has not been studied. The

safety of Alpha$_1$-Proteinase Inhibitors in patients with moderate to severe hepatic impairment has not been studied (1-4).

Intravenous augmentation therapy is recommended for individuals with AATD and an FEV1 in the range of 30%-65% predicted (strong recommendation, high quality evidence) (6).

High value is placed on the potential to prolong survival in this group, the finding that intravenous augmentation therapy is associated with lower levels of elastin degradation products in individuals with AATD, and lower rates of loss of CT lung density in individuals with AATD-COPD receiving augmentation therapy. Low value is placed on the cost of this therapy (6).

The safety and effectiveness of Alpha$_1$-Proteinase Inhibitors in pediatric patients have not been established (1-4).

Related policies

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Aralast NP, Glassia, Prolastin-C, and Zemaira may be considered **medically necessary** if the conditions indicated below are met.

Aralast NP, Glassia, Prolastin-C, and Zemaira may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 18 years of age and older

Diagnosis

Patient must have the following:

1. Emphysema
    a. Clinically documented alpha$_1$-antitrypsin (AAT) deficiency

AND ALL of the following for Aralast NP, Glassia, and Zemaira **ONLY**:

1. Patient has a pretreatment serum AAT level less than 11 µM/L (80 mg/dl by radial immunodiffusion or 50 mg/dl by nephelometry)
2. Patient must **NOT** be a current smoker
3. Documented progressive emphysema with **ONE** of the following:
    a. Moderate airflow obstruction is evidenced by forced expiratory volume (FEV_1) of 30-65% of predicted value, prior to initiation of therapy
    b. Individual has a rapid decline in lung function as measured by a change in FEV_1 greater than 120 ml/year
    c. FEV_1 of >65% predicted with bronchiectasis with one or more severe exacerbations resulting in ED visit or hospitalization within the last year
4. Patient **MUST** have tried the preferred product (Prolastin-C), if adjudicated through the pharmacy benefit, unless the patient has a valid medical exception (e.g., inadequate treatment response, intolerance, contraindication)

Prior – Approval *Renewal* Requirements

Age 18 years of age and older

Diagnosis

Patient must have the following:

1. Emphysema

AND ALL of the following for Aralast NP, Glassia, and Zemaira **ONLY**:

1. Patient must **NOT** be a current smoker
2. Clinical evidence of efficacy with **ONE** of the following:
    a. Elevation of AAT levels (above protective threshold)
    b. Reduction in rate of deterioration of lung function with a reduction in FEV_1 rate of decline
3. Patient **MUST** have tried the preferred product (Prolastin-C), if adjudicated through the pharmacy benefit, unless the patient has a valid medical exception (e.g., inadequate treatment response, intolerance, contraindication)

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Duration 3 months

Prior – Approval *Renewal* Limits

Duration 12 months

Rationale

Summary
Aralast NP, Glassia, Prolastin-C, and Zemaira are intravenous infusions indicated for individuals with clinically evident emphysema due to severe deficiency of Alpha$_1$-PI, also known as alpha$_1$-antitrypsin (AAT) deficiency. The safety of Alpha$_1$-Proteinase Inhibitors in patients with severe renal impairment (creatinine clearance less than 30 mL/min), end-stage renal disease or moderate to severe hepatic impairment has not been studied. The safety and effectiveness of Alpha$_1$-Proteinase Inhibitors in pediatric patients have not been established (1-4).

Prior authorization is required to ensure the safe, clinically appropriate, and cost-effective use of Aralast NP, Glassia, Prolastin-C, and Zemaira while maintaining optimal therapeutic outcomes.

References

1. Aralast NP [package insert]. Westlake Village, CA: Baxalta US Inc.; October 2024.
2. Glassia [package insert]. Westlake Village, CA: Baxalta US Inc.; September 2024.
3. Prolastin-C [package insert]. Research Triangle Park, NC: Grifols Therapeutics LLC; May 2020.
4. Zemaira [package insert]. Kankakee, IL: CSL Behring LLC; January 2024.
5. Stoller JK, Rouhani F, Brantly M, et al. Biochemical efficacy and safety of a new pooled human plasma α1-antitrypsin, Respitin. CHEST. 2002;122:66-74.
6. Sandhaus R, Turino G, et al. The Diagnosis and Management of Alpha-1 Antitrypsin Deficiency in the Adult. Journal of the COPD Foundation. Volume 3 Number 3, 2016.

Policy History

Date	Action
July 2017	Addition to PA
September 2017	Annual review and reference update
March 2018	Annual review and reference update
March 2019	Annual review and reference update

March 2020	Annual review and reference update
March 2021	Annual review
March 2022	Annual review
December 2022	Annual review. Revised requirements so Prolastin-C only needs a diagnosis of emphysema and documented AAT deficiency. Added requirement that non-preferred medications must t/f preferred product Prolastin-C. Per SME, added "FEV_1 of >65% predicted with bronchiectasis with one or more severe exacerbations resulting in ED visit or hospitalization within the last year" as evidence of progressive emphysema
March 2023	Annual review
December 2023	Annual review
March 2024	Annual review and reference update
September 2024	Annual editorial review. Per FEP, added "if adjudicated through the pharmacy benefit" to Medex requirement for 2025
December 2024	Annual review
March 2025	Annual review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 7, 2025 and is effective on April 1, 2025.