Policy and Procedure	
PHARMACY PRIOR AUTHORIZATION POLICY AND CRITERIA ORPTCRES006.0625	**RESPIRATORY AGENTS** **ALPHA-1 PROTEINASE INHIBITORS** **Aralast NP®, Glassia®** **Prolastin®-C, Zemaira®** (human alpha-1 proteinase inhibitor)
Effective Date: 8/1/2025	**Review/Revised Date**: 02/11, 06/11, 02/12, 06/13, 06/14, 06/15, 04/16, 05/17, 04/18, 05/19, 04/20, 04/21, 05/22, 04/23, 05/24, 05/25 (JEF)
Original Effective Date: 04/11	**P&T Committee Meeting Date**: 02/11, 06/11, 02/12, 06/13, 06/14, 10/14, 06/15, 06/16 , 06/17, 06/18, 06/19, 06/20, 06/21, 06/22, 06/23, 06/24, 06/25
Approved by: Oregon Region Pharmacy and Therapeutics Committee	

SCOPE:
Providence Health Plan and Providence Health Assurance as applicable (referred to individually as “Company” and collectively as “Companies”).

APPLIES TO:
Commercial
Medicare Part B
Medicaid

POLICY CRITERIA:

COVERED USES:
All Food and Drug Administration (FDA) approved indications not otherwise excluded from the benefit.

REQUIRED MEDICAL INFORMATION:
Documentation of:
1. One of the following:
    a. Serum alpha-1 antitrypsin (AAT) concentrations less than 11 micromol/L (approximately 50 mg/dL by nephelometry or 80mg/dL by immunodiffusion)
    b. Patient has one of the following high-risk phenotypes by protease inhibitor (PI) typing: PI*ZZ, PI*Z(null), PI*(null,null)

AND

2. Diagnosis of emphysema with one of the following:
    a. Forced expiratory volume per one second (FEV-1) of 35 to 65% of predicted volume
    b. Rapid lung function decline as evidence by reduction of FEV-1 of 100 mL/year or greater

AND

3. Documentation that the patient has never smoked or has abstained from smoking for at least the previous six months

Reauthorization requires documentation of positive clinical response to therapy (such as, reduction in exacerbations, reduced progression of emphysema as assessed by computed tomography (CT) densitometry, slowing of FEV-1 decline)

EXCLUSION CRITERIA: N/A

AGE RESTRICTIONS: N/A

PRESCRIBER RESTRICTIONS: N/A

COVERAGE DURATION:
Initial authorization will be approved for six months and reauthorization will be approved for one year.

QUANTITY LIMIT:
60 mg/kg infused every seven days, subject to audit.
Note: Dose may be rounded down to the nearest gram (500 mg for Aralast®) within 10% of calculated dose.

Requests for indications that were approved by the FDA within the previous six (6) months may not have been reviewed by the health plan for safety and effectiveness and inclusion on this policy document. These requests will be reviewed using the New Drug and or Indication Awaiting P&T Review; Prior Authorization Request ORPTCOPS047.

Requests for a non-FDA approved (off-label) indication requires the proposed indication be listed in either the American Hospital Formulary System (AHFS), Drugdex, or the National Comprehensive Cancer Network (NCCN) and is considered subject to evaluation of the prescriber's medical rationale, formulary alternatives, the available published evidence-based research and whether the proposed use is determined to be experimental/investigational.

Coverage for Medicaid is limited to a condition that has been designated a covered line item number by the Oregon Health Services Commission listed on the Prioritized List of Health Care Services.

Coverage decisions are made on the basis of individualized determinations of medical necessity and the experimental or investigational character of the treatment in the individual case.

INTRODUCTION:
Human alpha$_1$-proteinase inhibitors (Aralast NP®, Glassia®, Prolastin®-C, and Zemaira®) contain alpha$_1$-antitrypsin (AAT) protein purified from pooled human

plasma. These products are given intravenously to replace the deficient protein in patients diagnosed of alpha$_1$-proteinase inhibitor (A_1-PI) deficiency, which is a rare genetic disease affecting primary the liver and lung. The recommended dose is 60mg/kg IV once weekly.

Drug availability:
Aralast NP powder 500 mg or 1000 mg vial, Glassia solution 1000 mg/50 mL vial, Prolastin-C powder 1000 mg vial, Prolastin-C solution 1000 mg/20 mL, Zemaira powder 1000 mg vial

FDA APPROVED INDICATIONS:
For chronic augmentation and maintenance therapy in adult patients with emphysema due to congenital deficiency of alpha$_1$-PI.

POSITION STATEMENT:
- Alpha$_1$-proteinase inhibitor (A_1-PI) deficiency, also known as alpha$_1$-antitrypsin (AAT) deficiency, is an autosomal, codominant, hereditary disorder characterized by low serum and lung levels of A_1-PI. Severe forms of the deficiency are frequently associated with slowly progressive, moderate to severe panacinar emphysema that most often manifests in the third to fourth decades of life, resulting in a significantly lower life expectancy. The rate of decline in lung function occurs earlier in smokers. Evidence to support augmentation therapy in current smokers is lacking.
- The *SERPINA1* gene encodes AAT and located on the 14th chromosome. The normal allele is *M* (proteinase [PI] genotype MM is normal). Severe cases of AAT deficiency are most commonly associated with people who are homozygous for the *Z* allele. Heterozygotes of the M allele (e.g., MZ, MS) are expected to produce a enough AAT to prevent developlement of emphasyema. Individuals with the SZ phenotype may be at increased susceptibility for lung disease but evidence is inconclusive.
- Augmentation therapy is not currently recommended for individuals who are heterozygous with serum AAT levels greater than 11 micromol/L or individuals without emphysema. Benefits of augmentation therapy with severe and mild lung disease is not clear.
- In patients with alpha $_1$-antitrypsin deficiency, the cause of the development of emphysema is not well understood; however, it is believed to be due to a chronic biochemical imbalance between neutrophil elastase (an enzyme capable of degrading elastin tissues) and alpha $_1$-PI (the principal inhibitor of neutrophil elastase) that is deficient in alpha $_1$-antitrypsin disease. This imbalance appears to result in alveolar structures being unprotected from chronic exposure to

elastase, which results in the progressive degradation of elastin tissues. Replacement therapy with alpha $_1$-PI reverses the biochemical abnormalities and brings the antineutrophil elastase capacity of the serum into the normal range in direct proportion to the serum concentrations of alpha$_1$-PI.

- Population studies suggest a minimum plasma threshold of 11µM/L (57 mg/dL by nephelometry) below which there is insufficient AAT to protect the lung. Emphysema is most common with ATT levels less than 9 micromol/L. Most patients below this level will have PiZ phenotype. Initiation of augmentation therapy should be considered with levels below the protective threshold in the setting of documented emphysema (reduced forced expiratory volume in 1 second [FEV$_1$]). The effect of augmentation therapy with an Alpha$_1$-PI product on pulmonary exacerbations and on the progression of emphysema in Alpha$_1$-PI deficiency has not been demonstrated in randomized, controlled clinical trials.
- The Global Initiative for Chronic Obstructive Pulmonary Disease 2025 guidelines (GOLD) suggests alpha-1 antitrypsin augmentation therapy in never or ex-smokers with FEV1 of 35 to 60% predicted, based on observational studies. Meanwhile, the guidelines by the COPD Foundation recommend augmentation therapy in patients with AAT deficiency and FEV1 less than or equal to 65%. For patients with lung disease related to AAT deficiency but has FEV1 greater than 65%, a discussion with patient is recommended regarding potential benefits of reducing lung function decline despite high cost and lack of evidence for benefit.
- Clinical data demonstrating the long-term effects of chronic augmentation and maintenance therapy of individuals with Alpha$_1$-PI treatments is not available.
- Alpha1-PI treatments are not indicated as therapy for lung disease in patients in whom severe Alpha$_1$-PI deficiency has not been established.
- Use in patients with immuneglobulin A (IgA) defiency with anitbodies against IgA is contraindicated due to increased risk for hypersensitivity.
- There are no studies to demonstrate that one medication has superiority over other alpha$_1$-PI products for safety or efficacy.

REFERENCES/RESOURCES:

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CODES:

Drug Name	Billing Details	HCPCS Code
Glassia® vial	Injection, alpha 1 proteinase inhibitor (human), (glassia), 10 mg	J0257
Aralast NP® vial Prolastin C® vial Zemaira® vial	Injection, alpha 1 proteinase inhibitor (human), not otherwise specified, 10 mg	J0256