

Subject:	Alpha-1 Proteinase Inhibitor Therapy		
Document #:	ING-CC-0073	Publish Date:	01/01/2019 09/23/2019
Status:	Revised	Last Review Date:	11/16/2018

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Overview

This document addresses the use of alpha-1 proteinase inhibitor therapy for chronic augmentation in adults with emphysema due to congenital alpha-1 proteinase inhibitor deficiency (alpha-1 antitrypsin deficiency). Alpha-1 proteinase inhibitors approved by the Food and Drug Administration include:

- Aralast (alpha-1 proteinase inhibitor)
- Glassia (alpha-1 proteinase inhibitor)
- Prolastin-C (alpha-1 proteinase inhibitor)
- Zemaira (alpha-1 proteinase inhibitor)

Alpha-1 antitrypsin deficiency (AATD) is a hereditary disease characterized by deficient serum and lung concentrations of alpha-1 antitrypsin (AAT). This deficiency creates an imbalance between serine proteases like neutrophil elastase and AAT in the lungs. Neutrophil elastase destroys elastin while AAT protects against elastin degradation. This imbalance leads to destruction of pulmonary connective tissue and development of early-onset emphysema. AATD can also affect the liver cells and cause liver injury, cirrhosis or liver failure.

Severe AATD is highly under recognized and known to affect approximately 100,000 Americans. A diagnosis of AATD relies on laboratory assessment of the individual's serum levels of AAT. AAT can be assessed by radial immunodiffusion, rocket immunoelectrophoresis or nephelometry. The different tests have slightly different normal ranges and the cut-off point for detecting AAT deficiency varies by test.

Chronic augmentation therapy with intravenous alpha-1 proteinase inhibitors is used to manage individuals with congenital AATD and clinically evident emphysema to slow the progression of the disease. The goal of therapy is to correct the imbalance of neutrophil elastase by raising the level of AAT above the protective threshold. Neutrophil elastase levels increase in the lungs in response to irritants such as infection and cigarette smoke. A significant risk factor impacting the decline in lung function is current smoking. Therefore, use of augmentation therapy is recommended only for individuals who are former smokers or non-smokers.

Safety and efficacy data for augmentation therapy in AAT is of poor quality and report no significant differences in outcomes or, in some instances, a decline in lung function. However, the American Thoracic Society/European Respiratory Society (2003) and Canadian Thoracic Society (2012) have released guidance recommending augmentation therapy for individuals with moderate airflow obstruction (FEV₁ of 30-65% of the predicted value) and individuals with a rapid decline of lung function (change in FEV₁ > 120 ml/year). These guidelines did not recommend augmentation therapy for individuals with AATD without emphysema or individuals with mild or severe airway obstruction.

Alpha-1 proteinase inhibitors are derived from pooled human plasma and may contain trace amounts of IgA. Individuals with known antibodies to IgA have a greater risk of developing potentially severe hypersensitivity and anaphylactic reactions. Alpha-1 proteinase inhibitors are contraindicated in individuals with antibodies against IgA due to the risk of severe hypersensitivity.

Clinical Criteria

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Alpha-1 Proteinase Inhibitors (Aralast, Glassia, Prolastin-C, Zemaira)

Requests for alpha-1 proteinase inhibitor therapy may be approved if the following criteria are met:

- I. Individual has a diagnosis of congenital alpha-1 antitrypsin deficiency (alpha-1 proteinase inhibitor deficiency); **AND**
- II. Individual has a confirmed alpha-1 antitrypsin level less than or equal to 11 $\mu\text{mol/L}^{\pm}$ (approximately equivalent to 80 mg/dL measured by radial immunodiffusion or 57 mg/dL measured by nephelometry) (ATS/ERS, 2003; Stoller, 2017); **AND**
- III. Individual is currently a non-smoker (ATS/ERS, 2003; CTS, 2013); **AND**
- IV. Individual has clinically evident emphysema; **AND**
- V. One of the following:
 - A. Individual has moderate airflow obstruction is evidenced by a forced expiratory volume (FEV₁) of 30-65% of predicted value prior to initiation of therapy (ATS/ERS, 2003); **OR**
 - B. Individual has a rapid decline in lung function as measured by a change in FEV₁ greater than 120 ml/year (ATS/ERS, 2003).

Alpha-1 proteinase inhibitor therapy may not be approved for the following:

- I. Individuals with IgA antibodies.

Quantity Limits

Alpha-1 Proteinase Inhibitors (Aralast, Glassia, Prolastin-C, Zemaira) Quantity Limits

Drug	Limit
<u>Aralast (alpha₁-proteinase inhibitor) 500 mg, 1000 mg vial</u>	<u>60 mg/kg once a week</u>
<u>Prolastin (alpha₁-proteinase inhibitor) 500 mg, 1000 mg vial</u>	<u>60 mg/kg once a week</u>
<u>Zemaira (alpha₁-proteinase inhibitor) 1000 mg vial</u>	<u>60 mg/kg once a week</u>
<u>Glassia (alpha₁-proteinase inhibitor) 1000 mg vial</u>	<u>60 mg/kg once a week</u>

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

HCPCS

J0256	Injection, alpha 1-proteinase inhibitor (human), not otherwise specified, 10 mg [Aralast NP, Prolastin-C, Zemaira]
J0257	Injection, alpha 1 proteinase inhibitor (human), (Glassia), 10 mg
S9346	Home infusion therapy, alpha-1-proteinase inhibitor mg [Aralast NP, Prolastin-C, Zemaira, Glassia]

ICD-10 Diagnosis

E88.01	Alpha-1-antitrypsin deficiency
J43.0-J43.9	Emphysema

Document History

Revised: 09/23/2019

Document History:

- 09/23/2019 – Administrative update to add drug specific quantity limits.
- 11/16/2018 – Annual Review: Initial P&T review of Alpha-1 Proteinase Inhibitor Therapy. Remove age criteria. Move alternative values for the alpha-1 antitrypsin level from a note at the end to a parenthetical comment in RN2. Add references for non-label-based criteria elements. Wording updates for clarity and consistency.
- 11/28/2018 – Coding Review: Added HCPCS S9346.

References

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Federal and state laws or requirements, contract language, and Plan utilization management programs or policies may take precedence over the application of this clinical criteria.

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