Medical Policy

Utilization Management and Clinical Medical Policy

Policy Name:	Policy Number:	Scope:	Origination Date:	Effective Date:
Alpha-1 Proteinase Inhibitor Therapy [Aralast, Glassia, Prolastin-C, Zemaira]	**MP-RX-FP-06-23**	☒ **MMM MA** ☒ **MMM MultiHealth**	11/30/2023 **Last Review Date:** **05/06/2026**	**05/06/2026** **Frequently Revision:** **Annual**

Service Category:

- ☐ Anesthesia
- ☐ Surgery
- ☐ Radiology Procedures
- ☐ Pathology and Laboratory Procedures
- ☐ Medicine Services and Procedures
- ☐ Evaluation and Management Services
- ☐ DME/Prosthetics or Supplies
- ☒ Other: Part B Drugs

Service Description:

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

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

Background Information:

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. The 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 including 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) has 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.

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Alpha-1 proteinase inhibitors are derived from pooled human plasma and may contain trace amounts of IgA. Individuals with known antibodies to IgA, which can be present in individuals with selective or severe IgA deficiency, 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.

Approved Indications

A. Apha-1 proteinase inhibitor therapies are indicated for the treatment of chronic augmentation and maintenance therapy in adults with clinically evident emphysema due to severe hereditary deficiency of Alpha1-Proteinase Inhibitor (Alpha1-PI), commonly associated with alpha1-antitrypsin deficiency.

Other Uses

A. None.

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Medical Necessity Guidelines:

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®)

A. Criteria For Initial Approval (*Provider must submit documentation [such as office chart notes, lab results, pathology reports, imaging studies, and any other pertinent clinical information] supporting the patient's diagnosis for the drug and confirming that the patient has met **all** approval criteria.)*

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. Documentation is provided that individual's alpha-1 antitrypsin level less than or equal to 11 µmol/L (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 has clinically evident emphysema (or chronic obstructive pulmonary disease [COPD]); **AND**
iv. Individual is currently a non-smoker (ATS/ERS, 2003); **AND**
v. One of the following:
   A. Documentation is provided that individual has moderate airflow obstruction evidenced by a forced expiratory volume (FEV_1) of 30-65% of predicted value prior to initiation of therapy (ATS/ERS, 2003); **OR**
   B. Documentation is provided that individual has a rapid decline in lung function as measured by a change in FEV_1 greater than 120 ml/year (ATS/ERS, 2003).
vi. Individual meets one of the following:
   A. Individual is not IgA deficient; OR
   B. Individual is IgA deficient and does not have antibodies to IgA.

B. Criteria For Continuation of Therapy

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

i. Documentation is provided that there is clinically significant improvement or stabilization in clinical signs and symptoms of disease (including but not limited to decreased frequency of exacerbations, slowed rate of FEV_1 decline, preservation of CT scan lung density or improvement in symptom burden); **AND**
ii. Individual remains a non-smoker.

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C. Authorization Duration

i. Initial Approval Duration: Up to 6 months
ii. Reauthorization Approval Duration: Up to 6 months

D. Conditions Not Covered

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive):

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

i. May not be approved when the above criteria are not met and for all other indications.

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Limits or Restrictions:

A. Therapeutic Alternatives

The list below includes preferred alternative therapies recommended in the approval criteria and may be subject to prior authorization.

i. N/A

B. Quantity Limitations

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. The chart below includes dosing recommendations as per the FDA-approved prescribing information.

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

Drug	Limit
Aralast (alpha1-proteinase inhibitor) 500 mg, 1000 mg vial	60 mg/kg once a week
Prolastin (alpha1-proteinase inhibitor) 500 mg, 1000 mg vial	60 mg/kg once a week
Zemaira (alpha1-proteinase inhibitor) 1000 mg. 4000 mg, 5000 mg vial	60 mg/kg once a week
Glassia (alpha1-proteinase inhibitor) 1000 mg, 4000 mg, 5000 mg vial	60 mg/kg once a week

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Codes Information:

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

ICD-10 Diagnostic Codes:

Codes	Description
E88.01	Alpha-1-antitrypsin deficiency
J43.0-J43.9	Emphysema
J44.0-J44.9	Other chronic obstructive pulmonary disease

HCPCS Codes:

Codes	Description
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 (e.g., Prolastin); administrative services, professional pharmacy services, care coordination, and all necessary supplies and equipment (drugs and nursing visits coded separately), per diem

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Reference Information:

1. American Thoracic Society (ATS)/European Respiratory Society (ERS) Statement: Standards for the Diagnosis and Management of Individuals with Alpha-1 Antitrypsin Deficiency. Am J Respir Crit Care Med. 2003; 168(7):818-900.
2. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm. Accessed: September 30, 2025.
3. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
4. Hernandez P, Bosse Y, Bush P, et. al. Alpha-1-antitrypsin deficiency targeted testing and augmentation therapy: A Canadian Thoracic Society meta-analysis and clinical practice guideline. Chest. 2025; 167(4):1044.
5. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc. Updated periodically.
6. Marciniuk DD, Hernandez P, Balter M, et al. Alpha-1 antitrypsin deficiency targeted testing and augmentation therapy: a Canadian Thoracic Society clinical practice guideline. Can Respir J. 2012; 19(2):109-116.
7. Stoller JK. Clinical manifestations, diagnosis, and natural history of alpha-1 antitrypsin deficiency. Updated: September 13, 2022. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. Accessed: September 26, 2025.
8. Stoller JK. Treatment of alpha-1 antitrypsin deficiency. Updated: November 4, 2021. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. Accessed: September 26, 2025.
9. Stoller JK, Hupertz V, Aboussouan LS. Alpha-1 Antitrypsin Deficiency. GeneReviews (online). University of Washington, Seattle. Updated: May 21, 2020. Available at: http://www.ncbi.nlm.nih.gov/books/NBK1519/?report=classic. Accessed: September 26, 2025.

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

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Policy History:

Type of Review	Summary of Changes	P&T Approval Date	UM/CMPC Approval Date
Annual Review	Added new vial strengths for Zemaira and Glassia to quantity limits. Coding Reviewed: Added HCPCS S9346 and ICD-10-CM J44.0-J44.9. Wording and formatting changes. Administrative update to incorporate new policy template.	5/1/2026	05/06/2026
Annual Review	Move criteria for antibodies to IgA to initial request section. Coding Reviewed: No changes.	7/17/2025	8/8/2025
Annual Review	Added sections: Approved Indications, Other Uses, Approval Duration, Conditions not covered and Therapeutic Alternatives. Wording and formatting changes. Coding Reviewed: No changes. Clarify clinically evident emphysema. Align may not approve criteria for individuals with IgA antibodies to labeled contraindication. Wording and formatting changes.	11/18/2024	12/17/2024
Policy Inception	Elevance Health's Medical Policy adoption.	N/A	11/30/2023