

Clinical Policy: Alpha₁-Proteinase Inhibitors (Aralast NP, Glassia, Prolastin-C, Zemaira)

Reference Number: LA.PHAR.94

Effective Date:

Last Review Date: 08.22

Line of Business: Medicaid

Coding
Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

The following are alpha₁-proteinase inhibitors requiring prior authorization: alpha₁-proteinase inhibitor, human (Aralast™ NP, Glassia®, Prolastin®-C, Zemaira®).

FDA Approved Indication(s)

Aralast NP, Glassia, Prolastin-C, and Zemaira are indicated for chronic augmentation and maintenance therapy in adults with clinical evidence of emphysema due to severe congenital deficiency of alpha₁-PI (alpha₁-antitrypsin [AAT] deficiency). Alpha₁-PI products increase antigenic and functional (anti-neutrophil elastase capacity) serum levels and antigenic lung epithelial lining fluid levels of alpha₁-PI.

Limitation(s) of use:

- **The effect of augmentation therapy with alpha₁-PI products on pulmonary exacerbations and on the progression of emphysema in alpha₁-PI deficiency has not been conclusively demonstrated in randomized, controlled clinical trials.**
- **Clinical data demonstrating the long-term effects of chronic augmentation and maintenance therapy of individuals with alpha₁-PI products are not available.**
- **Alpha₁-PI products are not indicated as therapy for lung disease in patients in whom severe alpha₁-PI deficiency has not been established.**

Policy/Criteria

Prior Authorization is required. Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of Louisiana Healthcare Connections that Aralast NP, Glassia, Prolastin-C, and Zemaira are medically necessary when the following criteria are met:

I. Initial Approval Criteria

A. Alpha₁-Antitrypsin Deficiency (must meet all):

1. **Diagnosis of severe congenital AAT deficiency;**
2. **Prescribed by or in consultation with a pulmonologist;**
3. **Age ≥ 18 years;**
4. **Member meets one of the following (a or b):**

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- a. Documentation of plasma AAT level < 11 micromol/L (approximately 50 mg/dL using nephelometry or 80 mg/dL by radial immunodiffusion);
- b. If AAT level >11 micromol/L, member has one of the high-risk phenotypes (i.e. PiZZ, PiZnull, Pi(null, null), or one of a few rare phenotypes [e.g. Pi(Malton, Malton)]);
5. Member demonstrates clinical evidence of emphysema (a or b):
 - a. Forced expiratory volume in one second (FEV₁) from ≥ 30% to ≤ 65% of predicted, post-bronchodilator;
 - b. FEV₁ from > 65% to < 80% of predicted, post-bronchodilator, and a rapid decline in lung function showing a change in FEV₁ > 100 mL/year;
6. Member is not an active smoker as evidenced by recent (within the last 30 days) negative nicotine metabolite (i.e., cotinine) test;
7. Dose does not exceed 60 mg/kg per week.

Approval duration:

Medicaid – 6 months

B. Other diagnoses/indications

1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): LA.PMN.53 for Medicaid.

II. Continued Therapy

A. Alpha₁-Antitrypsin Deficiency (must meet all):

1. Currently receiving medication via Louisiana Healthcare Connections benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed 60 mg/kg per week.

Approval duration:

Medicaid– 12 months

B. Other diagnoses/indications (must meet 1 or 2):

1. Currently receiving medication via Louisiana Healthcare Connections benefit and documentation supports positive response to therapy.
Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): LA.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

- A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies –LA.PMN.53 for Medicaid or evidence of coverage documents;
- B. Immunoglobulin A (IgA) deficiency (IgA level less than 15 mg/dL) with known antibody against IgA.

Alpha₁-Proteinase InhibitorsIV. Appendices/General InformationAppendix A: Abbreviation/Acronym KeyAAT: alpha1-antitrypsinAlpha₁-PI: alpha1-proteinase inhibitorsCOPD: chronic obstructive pulmonary diseaseFDA: Food and Drug AdministrationFEV₁: forced expiratory volume in one secondAppendix B: Therapeutic AlternativesNot applicableAppendix C: Contraindications/Boxed Warnings

- Contraindication(s): use in IgA deficient patients with known antibodies against IgA and/or a history of anaphylaxis or other severe systemic reaction to alpha₁-PI, due to the risk of severe hypersensitivity, including anaphylaxis.
- Boxed warning(s): none reported

Appendix D: General Information

- The American Thoracic Society (ATS) and the European Respiratory Society (ERS) state that alpha₁-proteinase inhibitor therapy does not confer benefit in, and is not recommended for, patients who have alpha₁-proteinase-associated liver disease.
- The 2016 COPD Foundation's clinical practice guidelines for AAT deficiency in the adult recommend intravenous augmentation therapy for individuals with FEV₁ less than 30% predicted with a weak recommendation with a low quality of evidence, and low value placed on the cost of this therapy. The 2003 ATS-ERS guidelines mirror the COPD Foundation in that evidence of benefit from augmentation therapy is weak in those with severe airflow obstruction.
- Aralast NP, Glassia, Prolastin-C, Zemaira: Safety and effectiveness in the pediatric population have not been established
- Smoking is an important risk factor for the development of emphysema in patients with AAT deficiency. Both the 2003 ATS and 2016 COPD Foundation AAT guidelines state that smoking cessation is important in this patient population.
- The goal of AAT augmentation is to slow the progression of emphysema/lung function decline. Lung function can be measured with FEV₁, which is most important predictor of survival of patients with emphysema due to AAT deficiency per the 2003 ATS AAT guidelines. Improvement, maintenance, or stabilization in FEV₁ rate of decline is therefore an acceptable example of positive response to therapy.

V. Dosage and Administration

<u>Indication</u>	<u>Dosing Regimen</u>	<u>Maximum Dose</u>
<u>Emphysema due to AAT deficiency</u>	<u>60 mg/kg IV once weekly</u>	<u>60 mg/kg/week</u>

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VI. Product Availability

<u>Drug Name</u>	<u>Availability</u>
<u>Alpha₁-proteinase inhibitor, human (Aralast NP)</u>	<u>Single-use vial: 500 mg, 1,000 mg</u>
<u>Alpha₁-proteinase inhibitor, human (Glassia)</u>	<u>Single-use vial: 1,000 mg/50 mL</u>
<u>Alpha₁-proteinase inhibitor, human (Prolastin-C)</u>	<u>Single-use vial: 1,000 mg (powder)</u>
	<u>Single-use vial: 500 mg/10 mL, 1,000 mg/20 mL, 4,000 mg/80 mL (liquid)</u>
<u>Alpha₁-proteinase inhibitor, human (Zemaira)</u>	<u>Single-use vial: 1,000 mg, 4,000 mg, 5,000 mg</u>

VII. References

1. Aralast NP Prescribing Information. Westlake Village, CA: Baxter Healthcare Corporation; December 2018. Available at: http://www.shirecontent.com/PI/PDFs/ARALASTNP_USA_ENG.pdf. Accessed September 14, 2021.
2. Glassia Prescribing Information. Negev, Israel: Kamada, Ltd.; June 2017. Available at: <http://www.liquidglassia.com>. Accessed September 14, 2021.
3. Prolastin-C Powder Prescribing Information. Research Triangle Park, NC: Grifols Therapeutics, Inc.; June 2018. Available at: <https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=91edab72-c889-470e-8315-1798b5548dca>. Accessed September 14, 2021.
4. Prolastin-C Liquid Prescribing Information. Research Triangle Park, NC: Grifols Therapeutics, Inc.; May 2020. Available at: <http://www.prolastin.com>. Accessed September 14, 2021.
5. Zemaira Prescribing Information. Kankakee, IL: CSL Behring LLC; April 2019. Available at: <http://www.zemaira.com>. Accessed September 14, 2021.
6. American Thoracic Society/European Respiratory Society 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.
7. Sandhaus RA, Turino G, and Brantly ML, et al. The diagnosis and management of alpha-1 antitrypsin deficiency in the adult. *Journal of COPD Foundation*. 2016;3(3):668-682.
8. Cazzola M, MacNee W, Martinez FJ, et al.; American Thoracic Society; European Respiratory Society Task Force on outcomes of COPD. Outcomes for COPD pharmacological trials: from lung function to biomarkers. *Eur Respir J*. 2008;31:416–469.
9. Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease (2021 report). Available at: <http://www.goldcopd.org>. Accessed September 14, 2021.

Coding Implications

Alpha₁-Proteinase Inhibitors

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

<u>HCPCS Codes</u>	<u>Description</u>
<u>J0256</u>	<u>Injection, alpha 1 proteinase inhibitor (human), not otherwise specified, 10 mg</u>
<u>J0257</u>	<u>Injection, alpha 1 proteinase inhibitor (human), (Glassia), 10 mg</u>

<u>Reviews, Revisions, and Approvals</u>	<u>Date</u>	<u>LDH Approval Date</u>
<u>Converted corporate to local policy.</u>	<u>09.22</u>	

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. LHCC makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable LHCC administrative policies and procedures.

This clinical policy is effective as of the date determined by LHCC. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. LHCC retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

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This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

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