# Clinical Policy: Alpha$_1$-Proteinase Inhibitors (Aralast NP, Glassia, Prolastin-C, Zemaira)

Reference Number: CP.PHAR.94
Effective Date: 03.01.12
Last Review Date: 02.23
Line of Business: Commercial, HIM*, Medicaid

Coding Implications
Revision Log

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

## Description

The following are alpha$_1$-proteinase inhibitors requiring prior authorization: alpha$_1$-proteinase inhibitor, human (Aralast™ NP, Glassia®, Prolastin®-C, Zemaira®).

**For Health Insurance Marketplace (HIM),* *if request is through pharmacy benefit, Glassia is non-formulary and should not be approved using these criteria; refer to the formulary exception policy, HIM.PA.103.*

## 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 alpha$_1$-PI (alpha$_1$-antitrypsin [AAT] deficiency). Alpha$_1$-PI products increase antigenic and functional (anti-neutrophil elastase capacity) serum levels and antigenic lung epithelial lining fluid levels of alpha$_1$-PI.

Limitation(s) of use:

- The effect of augmentation therapy with alpha$_1$-PI products on pulmonary exacerbations and on the progression of emphysema in alpha$_1$-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 alpha$_1$-PI products are not available.
- Alpha$_1$-PI products are not indicated as therapy for lung disease in patients in whom severe alpha$_1$-PI deficiency has not been established.

## Policy/Criteria

*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 health plans affiliated with Centene Corporation® that Aralast NP, Glassia, Prolastin-C, and Zemaira are **medically necessary** when the following criteria are met:

**I. Initial Approval Criteria**

**A. Alpha$_1$-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):
   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 ($FEV_1$) from ≥ 30% to ≤ 65% of predicted, post-bronchodilator;
   b. $FEV_1$ from > 65% to < 80% of predicted, post-bronchodilator, and a rapid decline in lung function showing a change in $FEV_1$ > 100 mL per 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
**HIM –** 6 months for Aralast NP, Prolastin-C, Zemaira (*refer to HIM.PA.103 for Glassia*)
**Commercial –** 6 months or to the member's renewal date, whichever is longer

**B. Other diagnoses/indications** (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

## II. Continued Therapy

**A. Alpha$_1$-Antitrypsin Deficiency** (must meet all)**:**
1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
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
**HIM –** 12 months for Aralast NP, Prolastin-C, Zemaira (*refer to HIM.PA.103 for Glassia*)
**Commercial –** 6 months or to the member's renewal date, whichever is longer

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

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.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 – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.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.

## IV. Appendices/General Information

*Appendix A: Abbreviation/Acronym Key*

AAT: alpha1-antitrypsin
alpha$_1$-PI: alpha$_1$-proteinase inhibitors
COPD: chronic obstructive pulmonary disease
FDA: Food and Drug Administration
$FEV_1$: forced expiratory volume in one second
IgA: immunoglobulin A

*Appendix B: Therapeutic Alternatives*

Not applicable

*Appendix 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 alpha$_1$-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 alpha$_1$-proteinase inhibitor therapy does not confer benefit in, and is not recommended for, patients who have alpha$_1$-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 $FEV_1$ 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 $FEV_1$, 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 $FEV_1$ rate of decline is therefore an acceptable example of positive response to therapy.

## V. Dosage and Administration

| Indication | Dosing Regimen | Maximum Dose |
|---|---|---|
| Emphysema due to AAT deficiency | 60 mg/kg IV once weekly | 60 mg/kg/week |

## VI. Product Availability

| Drug Name | Availability |
|---|---|
| Alpha$_1$-proteinase inhibitor, human (Aralast NP) | Single-use vial: 500 mg, 1,000 mg |
| Alpha$_1$-proteinase inhibitor, human (Glassia) | Single-use vial: 1,000 mg/50 mL |
| Alpha$_1$-proteinase inhibitor, human (Prolastin-C) | Single-use vial: 1,000 mg (powder) |
| | Single-use vial: 500 mg/10 mL, 1,000 mg/20 mL, 4,000 mg/80 mL (liquid) |
| Alpha$_1$-proteinase inhibitor, human (Zemaira) | Single-use vial: 1,000 mg, 4,000 mg, 5,000 mg |

## 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 November 3, 2022.
2. Glassia Prescribing Information. Negev, Israel: Kamada, Ltd.; March 2022. Available at: http://www.liquidglassia.com. Accessed November 3, 2022.
3. Prolastin-C Powder Prescribing Information. Research Triangle Park, NC: Grifols Therapeutics, Inc.; January 2022. Available at: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=91edab72-c889-470e-8315-1798b5548dca. Accessed November 3, 2022.
4. Prolastin-C Liquid Prescribing Information. Research Triangle Park, NC: Grifols Therapeutics, Inc.; May 2020. Available at: http://www.prolastin.com. Accessed November 3, 2022.
5. Zemaira Prescribing Information. Kankakee, IL: CSL Behring LLC; September 2022. Available at: http://www.zemaira.com. Accessed November 3, 2022.
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 (2022 report). Available at: http://www.goldcopd.org. Accessed November 3, 2022.

## Coding Implications

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.

| HCPCS Codes | Description |
|---|---|
| J0256 | Injection, alpha 1 proteinase inhibitor (human), not otherwise specified, 10 mg |
| J0257 | Injection, alpha 1 proteinase inhibitor (human), (Glassia), 10 mg |

| Reviews, Revisions, and Approvals | Date | P&T Approval Date |
|---|---|---|
| 1Q 2019 annual review: per 2018 GOLD and 2003 ATS guidelines, corrected $FEV_1$ range to include 65% without requiring demonstration of rapid decline in lung function in $FEV_1$ of > 100 mL/year; added Aralast NP 500 mg and Prolastin-C Liquid as non-formulary for HIM; revised HIM continued approval duration to | 10.30.18 | 02.19 |

| Reviews, Revisions, and Approvals | Date | P&T Approval Date |
|---|---|---|
| align with Medicaid; revised Commercial approval duration to 6 months or member's renewal whichever is longer; references reviewed and updated. | | |
| No significant changes: new 4g and 5g formulations for Zemaira added. | 04.30.19 | |
| 1Q 2020 annual review: no significant changes; removed HIM NF disclaimer statements; references reviewed and updated. | 11.26.19 | 02.20 |
| Added requirement that member is not an active smoker as supported by both ATS and COPD Foundation AAT guidelines. | 04.14.20 | 05.20 |
| 1Q 2021 annual review: no significant changes; references to HIM.PHAR.21 revised to HIM.PA.154; references reviewed and updated. | 10.20.20 | 02.21 |
| 1Q 2022 annual review: no significant changes; for HIM, added language referring requests for Glassia (NF) to the formulary exception policy; added 500 mg/10 mL and 4,000 mg/80 mL Prolastin-C vials; references reviewed and updated. | 09.14.21 | 02.22 |
| Template changes applied to other diagnoses/indications and continued therapy section. | 10.12.22 | |
| 1Q 2023 annual review: no significant changes; references reviewed and updated. | 11.03.22 | 02.23 |

**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. The Health Plan 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. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

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 Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. 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. The Health Plan 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.

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.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

**Note:**
**For Medicaid members**, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.