

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

Reference Number: CP.PHAR.94

Effective Date: 03.01.12

Last Review Date: 02.19

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

**For Health Insurance Marketplace (HIM), if request is for the pharmacy benefit, Aralast NP 500 mg, Glassia, Prolastin-C Liquid are non-formulary and cannot 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 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

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. 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):
 - a. Documentation of plasma AAT level < 11 micromol/L (approximately 50 mg/dL using nephelometry or 80 mg/dL by radial immunodiffusion);
 - b. If member has an AAT level >11 umol/L, then the member must have 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. 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. Dose does not exceed 60 mg/kg/week.

Approval duration:

Medicaid – 6 months

HIM – 6 months for Aralast NP 1,000 mg, Prolastin-C powder or Zemaira (*refer to HIM.PA.103 for Aralast NP 500 mg, Glassia, and Prolastin-C Liquid*)

Commercial – 6 months or to the member’s renewal date, whichever is longer

B. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

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

1. Currently receiving medication via Centene 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/week.

Approval duration:

Medicaid – 12 months

HIM – 12 months for Aralast NP 1,000 mg, Prolastin-C powder or Zemaira (*refer to HIM.PA.103 for Aralast NP 500 mg, Glassia, and Prolastin-C Liquid*)

Commercial – 6 months or to the member’s renewal date, whichever is longer

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

1. Currently receiving medication via Centene 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 for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PHAR.21 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.PHAR.21 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: alpha 1-antitrypsin	FDA: Food and Drug Administration
Alpha ₁ -PI: alpha ₁ -proteinase inhibitors	FEV ₁ : forced expiratory volume in one second
COPD: chronic obstructive pulmonary disease	

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 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

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

Drug Name	Availability
Alpha ₁ -proteinase inhibitor, human (Prolastin-C)	Single-use vial: 1,000 mg (Powder)
Alpha ₁ -proteinase inhibitor, human (Prolastin-C)	Single-use vial: 1,000 mg/20 mL (Liquid)
Alpha ₁ -proteinase inhibitor, human (Zemaira)	Single-use vial: 1,000 mg

VII. References

1. Aralast NP Prescribing Information. Westlake Village, CA: Baxter Healthcare Corporation; September 2015. Available at: http://www.shirecontent.com/PI/PDFs/ARALASTNP_USA_ENG.pdf. Accessed October 30, 2018.
2. Glassia Prescribing Information. Negev, Israel: Kamada, Ltd.; June 2017. Available at: <http://www.liquidglassia.com>. Accessed October 30, 2018.
3. Prolastin-C Powder Prescribing Information. Research Triangle Park, NC: Grifols Therapeutics, Inc.; August 2016. Available at: <http://www.prolastin.com>. Accessed October 30, 2018.
4. Prolastin-C Liquid Prescribing Information. Research Triangle Park, NC: Grifols Therapeutics, Inc.; September 2017. Available at: <https://www.prolastin.com/documents/45403777/0/prolastinpi/b436e646-0787-4aad-a3d5-b5e004cc92c6>. Accessed October 30, 2018.
5. Zemaira Prescribing Information. Kankakee, IL: CSL Behring LLC; September 2015. Available at: <http://www.zemaira.com>. Accessed October 30, 2018.
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 (2018 Report). Available at: https://goldcopd.org/wp-content/uploads/2017/11/GOLD-2018-v6.0-FINAL-revised-20-Nov_WMS.pdf. Accessed October 30, 2018.

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
References reviewed and updated	02.15	03.15
Corrected FEV ₁ range from 35 to 65% to 30 to 65% based on Table 9 in the 2003 ATS/ERS AAT guidelines	08.15	
Policy converted to new template. Criteria: added max dose and attestation that member is receiving additional supportive measures per COPD guidelines.	02.16	03.16
Initial criteria: Age removed; conditions representing potential contraindications to therapy are removed.	02.17	03.17
1Q18 annual review: Combined existing policies for Medicaid and commercial business; HIM added; Medicaid: removed requirement for supportive measures (avoidance of cigarette smoking and vaccinations) due to lack of actionability and objectivity; protective threshold value per nephelometry changed from 57 mg/dL to 50 mg/dL per American Thoracic Society 2003 guidelines; added “If the member has an AAT level >11 umol/L, then the member must have 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)]” to allow treatment before clinical deterioration due to definite diagnosis; added prescriber requirement due to the complexity of disease diagnosis and management; Changed minimally significant change in FEV from 120 mL to 100 mL per ATC guidelines and specialist feedback; references reviewed and updated.	12.05.17	02.18
No significant changes: new Prolastin-C liquid formulation added.	07.13.18	
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 align with Medicaid; revised Commercial approval duration to 6 months or member’s renewal whichever is longer; references reviewed and updated.	10.30.18	02.19

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.

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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.

For Health Insurance Marketplace members, when applicable, this policy applies only when the prescribed agent is on your health plan approved formulary. Request for non-formulary drugs must be reviewed using the non-formulary policy; HIM.PA.103.

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