Clinical Policy: Alpha-1 Proteinase Inhibitors (Aralast NP, Glassia, Prolastin-C, Zemaira)

Reference Number: PA.CP.PHAR.94
Effective Date: 01/2018
Last Review Date: 01/2026

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 (*Aralast NP, Prolastin-C, Zemaira*) or individuals (*Glassia only*)

- with clinical evidence of emphysema (Zemaira only)
- with clinical evidence of emphysema due to severe congenital deficiency of alpha$_1$-PI (alpha$_1$-antitrypsin [AAT] deficiency) (*Aralast NP*)
- with clinical evidence of emphysema due to severe hereditary deficiency of alpha$_1$-PI (AAT deficiency) (*Glassia and Prolastin-C)*

Aralast NP, Prolastin-C, and Zemaira 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
It is the policy of PA Health & Wellness 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/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/week.

Approval Duration: 12 months

B. Acute Graft-Versus-Host Disease (off-label) (must meet all)**:**
1. Diagnosis of acute graft-versus-host disease (GVHD);
2. Prescribed by or in consultation with an oncologist, hematologist, or bone marrow transplant specialist;
3. Age ≥ 18 years;
4. Disease is steroid-refractory as evidenced by any of the following (a, b, or c):
   a. Progression of acute GVHD within 3 to 5 days of therapy onset with ≥ 2 mg/kg per day of prednisone or dose equivalent corticosteroid (*see Appendix B and E*);
   b. Failure to improve within 5 to 7 days of treatment initiation with ≥ 2 mg/kg per day of prednisone or dose equivalent corticosteroid (*see Appendix B and E*);
   c. Incomplete response after > 28 days of immunosuppressive treatment including ≥ 2 mg/kg per day of prednisone or dose equivalent corticosteroid (*see Appendix B and E*);
5. Prescribed in combination with systemic corticosteroids;
6. Request meets one of the following (a or b):
   a. Dose does not exceed 60 mg/kg per day administered twice per week for up to a total of 8 doses;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 4 weeks

C. Other diagnoses/indications: Refer to PA.CP.PMN.53

II. Continued Approval

A. Alpha-1 Antitrypsin Deficiency (must meet all)**:**
1. Currently receiving medication via of PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies;
2. Documentation supports positive response to therapy;
3. If request is for a dose increase, new dose does not exceed 60 mg/kg per week.

Approval Duration: 12 months

B. Acute Graft-Versus-Host Disease (off-label)
1. Re-authorization is not permitted. Members must meet the initial approval criteria.

Approval duration: Not applicable

C. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via of PA Health & Wellness benefit and documentation supports positive response to therapy; or
2. Refer to PA.CP.PMN.53

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 – PA.CP.PMN.53;

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: alpha1-proteinase inhibitors
COPD: chronic obstructive pulmonary disease
FDA: Food and Drug Administration
FEV_1: forced expiratory volume in one second
GVHD: graft-versus-host disease
IgA: immunoglobulin A

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Examples of corticosteroids for acute GVHD		
betamethasone, dexamethasone, prednisone, prednisolone, methylprednisone*	Dose recommendations per NCCN based on organ involvement: Upper GI only: 0.5-1 mg/kg/day methylprednisolone (or prednisone dose equivalent) Skin/lower GI/liver: 1-2 mg/kg/day methylprednisolone (or prednisone dose equivalent)	Corticosteroid dosage must be individualized and is highly variable depending on the nature and severity of the disease, route of treatment, and on patient response

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.
**Off-label*

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 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 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.
- Acute GVHD refers to an allogeneic inflammatory response occurring in three organs: the skin, the liver, and the gastrointestinal tract. A grading system is used to assess the severity of disease based on clinical manifestations and the extent of organ involvement. There are a number of different grading systems available (e.g., Glucksberg, modified Glucksberg, Keystone, International Bone Marrow Transplantation Registry [IBMTR], Mount Sinai Acute GvHD International Consortium [MAGIC]), none of which has been shown to be superior in predicting survival. While there are no standardized definitions for each grade across these systems, all consider grade I disease to involve only the skin. Grade II, III, and IV disease go beyond the skin and additionally involve the liver and/or gastrointestinal tract.

Appendix E: Equivalent Corticosteroid Dosages

Acute Steroid-Refractory GVHD: Equivalent Corticosteroid Dosages	
Prednisolone	5 mg PO
Prednisone	5 mg PO
Methylprednisolone	4 mg PO
Dexamethasone	0.75 mg PO
Betamethasone	0.75 mg PO

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; May 2025. Available at: http://www.shirecontent.com/PI/PDFs/ARALASTNP_USA_ENG.pdf. Accessed October 17, 2025.
2. Glassia Prescribing Information. Negev, Israel: Kamada, Ltd.; February 2025. Available at: https://www.glassialiquid.com/hcp. Accessed October 17, 2025.
3. Prolastin-C Powder Prescribing Information. Research Triangle Park, NC: Grifols Therapeutics, Inc.; February 2022. Available at: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=91edab72-c889-470e-8315-1798b5548dca. Accessed October 17, 2025.
4. Prolastin-C Liquid Prescribing Information. Research Triangle Park, NC: Grifols Therapeutics, Inc.; May 2020. Available at: https://www.prolastin.com/en/patients. Accessed October 17, 2025.
5. Zemaira Prescribing Information. Kankakee, IL: CSL Behring LLC; January 2024. Available at: https://www.zemaira.com/prescribing-information. Accessed October 17, 2025.
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 (2026 report). Available at: https://goldcopd.org/2023-gold-report-2/. Accessed November 25, 2025.
10. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed November 20, 2025.
11. National Comprehensive Cancer Network. Hematopoietic Cell Transplantation Version 3.2025. Available at https://www.nccn.org/professionals/physician_gls/pdf/hct.pdf. Accessed November 20, 2025.

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
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.	
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; references reviewed and updated.	01/2019
1Q 2020 annual review: new 4g and 5g formulations for Zemaira added; references reviewed and updated.	01/2020
1Q 2021 annual review: references reviewed and updated.	01/2021
1Q 2022 annual review: Added requirement that member is not an active smoker as supported by both ATS and COPD Foundation AAT guidelines; added 500 mg/10 mL and 4,000 mg/80 mL Prolastin-C vials; references reviewed and updated.	01/2022
1Q 2023 annual review: no significant changes; references reviewed and updated.	01/2023
1Q 2024 annual review: updated FDA approved indications section to align with prescriber information for Aralast NP, Glassia, Prolastin-C, and Zemaira; references reviewed and updated.	01/2024
1Q 2025 annual review: no significant changes; references reviewed and updated.	01/2025
1Q 2026 annual review: added off-label indication of steroid-refractory acute GVHD per NCCN; extended initial approval duration from 6 to 12 months for these maintenance medications for a chronic condition; references reviewed and updated.	01/2026