

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

Reference Number: LA.PHAR.94

Effective Date: 10.30.22

Last Review Date: ~~02.18.2602-11-25~~

Line of Business: Medicaid

[Coding Implications](#)
[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

****Please note: This policy is for medical benefit****

Description

The following are alpha₁-proteinase inhibitors requiring prior authorization: alpha₁-proteinase inhibitor, human (AralastTM 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 alpha₁-PI (alpha₁-antitrypsin [AAT] deficiency) (*Aralast NP*)
- with clinical evidence of emphysema due to severe hereditary deficiency of alpha₁-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 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 Louisiana Healthcare Connections that Aralast NP, Glassia, Prolastin-C, and Zemaira are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

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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 \geq 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 (FEV₁) from \geq 30% to \leq 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 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: ~~6~~12 months

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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 \geq 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 \geq 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 \geq 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 \geq 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).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 4 weeks

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B-C. 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 LA.PMN.255

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- 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 LA.PMN.53

II. Continued Therapy

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

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

Approval duration: 12 months

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

- 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 LA.PMN.255
- 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 LA.PMN.53

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

- 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 policy LA.PMN.53
- 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	<u>GVHD: graft-versus-host disease</u>
	IgA: immunoglobulin A

Appendix B: Therapeutic Alternatives

Not applicable

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.

<u>Drug Name</u>	<u>Dosing Regimen</u>	<u>Dose Limit/ Maximum Dose</u>
<u>Examples of corticosteroids for acute GVHD</u>		
<u>betamethasone, dexamethasone, prednisone.</u>	<u>Dose recommendations per NCCN based on organ involvement:</u>	<u>Corticosteroid dosage must be individualized and is highly variable depending on the nature and severity of</u>

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Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
prednisolone, methylprednisone*	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)	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 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.
- 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.

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Grade II, III, and IV disease go beyond the skin and additionally involve the liver and/or gastrointestinal tract.

Appendix E: Equivalent Corticosteroid Dosages

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

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; ~~March 2023~~ May 2025. Available at: https://www.shirecontent.com/PI/PDFs/ARALASTNP_USA_ENG.pdf. Accessed ~~November 14, 2023~~ October 17, 2025.
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3. Prolastin-C Powder Prescribing Information. Research Triangle Park, NC: Grifols Therapeutics, Inc.; ~~January~~ February 2022. Available at: <https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=91edab72-c889-470e-8315-1798b5548dca>. Accessed ~~November 14, 2023~~ October 17, 2025.
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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.

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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	LDH Approval Date
Converted corporate to local policy	09.22	10.30.22
Template changes applied to other diagnoses/indications and continued therapy section. References reviewed and updated. Added blurb this policy is for medical benefit only.	06.27.23	10.05.23
Annual review: updated FDA approved indications section to align with prescriber information for Aralast NP, Glassia, ProLastin-C, and Zemaira; references reviewed and updated.	05.09.24	7.29.24
Annual review: no significant changes; references reviewed and updated.	2.11.25	<u>05.19.25</u>
<u>Annual review: added off-label indication of steroid-refractory acute GVHD per NCCN; extended initial approval duration from 6 to 12 months for these medications for a chronic condition; references reviewed and updated.</u>	<u>02.18.26</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

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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.

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