Clinical Policy Title:	alpha$_1$-proteinase inhibitor (human)
Policy Number:	RxA.015
Drug(s) Applied:	Aralast NP®, Glassia®, Prolastin®-C, Zemaira®
Original Policy Date:	02/07/2020
Last Review Date:	01/17/2022
Line of Business Policy Applies to:	All lines of business

Background

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, ANEC) 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 Alpha1-PI products are not available.
- Alpha1-PI products are not indicated as therapy for lung disease in patients in whom severe alpha$_1$-PI deficiency has not been established.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
alpha$_1$-proteinase inhibitor (human) (Aralast NP®, Glassia®, Prolastin®-C, Zemaira®)	Emphysema due to AAT deficiency	60 mg/kg intravenous once weekly	60 mg/kg/week

Dosage Forms

- alpha$_1$-proteinase inhibitor, human (Aralast NP®): Single-use vial: 500 mg, 1,000 mg (lyophilized powder)
- alpha1-proteinase inhibitor, human (Glassia®): Single-use vial: 1,000 mg/50 mL
- alpha1-proteinase inhibitor, human (Prolastin®-C): Single-use vial: 1,000 mg (lyophilized powder)
- alpha1-proteinase inhibitor, human (Prolastin®-C): Single-use vial: 1,000 mg/20 mL
- alpha1-proteinase inhibitor, human (Zemaira®): Single-use vial: 1,000 mg

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the

terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

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 member has an AAT level >11 umol/L, then the member must have one of the high-risk phenotypes (i.e. PiZZ, PiZ(null), 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 (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
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

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

1. Member is currently receiving medication that has been authorized by RxAdvance or the member has met initial approval criteria listed in this policy;
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
Commercial: 6 months
Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
AAT: alpha1-antitrypsin
Alpha$_1$-PI: alpha$_1$-proteinase inhibitors
COPD: chronic obstructive pulmonary disease
ANEC: anti-neutrophil elastase capacity

APPENDIX B: Therapeutic Alternatives
Not Applicable

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):

- Use in IgA deficient patients with known antibodies against IgA, due to the risk of severe hypersensitivity, including anaphylaxis.
- History of anaphylaxis or other severe systemic reaction to alpha1-PI.

- 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 adults 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 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.

References

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Review/Revision History	Review/Revision Date	P&T Approval Date
Policy established.	01/2020	02/07/2020
Formatting and references updated	05/07/2020	05/20/2020
Policy was reviewed: 1. Policy title table was updated: Clinical Policy Title was updated to 'alpha1-proteinase inhibitor (human)', Drug(s) Applied was updated to 'Aralast NP®, Glassia®, Prolastin®-C, Zemaira®', Line of business policy applies was updated to All lines of business. 2. Dosing information: Drug name was updated to 'alpha1-proteinase inhibitor (human) (Aralast NP®, Glassia®, Prolastin®-C, Zemaira®)'. 3. Dosage forms were updated. 4. Initial approval criteria IA.6. was added as 'Member is not an active smoker as evidenced by...' 5. Continued therapy approval criteria II.A.1 was rephrased to "Currently receiving medication that has been authorized by RxAdvance…". 6. Commercial approval duration was updated to 6 months, from "6 months or to the member's renewal date, whichever is longer." HIM was removed for both initial and continued therapy approval criteria. 7. Appendix A: ANEC was added. 8. Appendix D was added. 9. References were updated.	01/13/2021	03/09/2021
Policy was reviewed: 1. Statement about provider sample ''The provision of provider samples does not guarantee coverage…" was added to Clinical Policy. 2. Continued Therapy Approval Criteria II.A.1 was rephrased to "Member is currently receiving medication that has been authorized by RxAdvance...".	11/19/2021	01/17/2022

3. References were reviewed and updated.		