envolve Pharmacy Solutions

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

Reference Number: ERX.SPA.87
Effective Date: 03.01.14
Last Review Date: 02.18 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: 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 with clinical evidence of emphysema due to severe congenital deficiency of alpha1-PI (alpha-1 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-P1 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 (which may include office chart notes and lab results) supporting that member has met all approval criteria

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ 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. Age ≥ 18 years;
3. 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 micromol/L, then the 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)]);
4. Prescribed by or in consultation with a pulmonologist;
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. Dose does not exceed 60 mg/kg/week.

Approval duration: 6 months

B. Other diagnoses/indications

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. Alpha-1 Antitrypsin Deficiency (must meet all)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions 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: 12 months

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

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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 policy – ERX.PA.01 or evidence of coverage documents;

B. Immunoglobulin A (IgA) deficiency (IgA level less than 15mg/dL) with known antibody against IgA.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

AAT: alpha-1 antitrypsin
Alpha-1 PI: alpha-1 proteinase inhibitors
COPD: chronic obstructive pulmonary disease
FDA: Food and Drug Administration
FEV1: forced expiratory volume in one second

Appendix B: Therapeutic Alternatives

N/A

Appendix C: General Information

- Augmentation therapy by boosting AAT levels is not a cure, will not reverse lung damage that has already occurred, and has not yet been proven to retard the progression of emphysema.
- Clinical data demonstrating the long-term effects of chronic augmentation or replacement therapy of individuals with alpha-1 proteinase inhibitor are not available.
- IgA may be present in alpha 1-proteinase inhibitors and patients may experience severe reactions, including anaphylaxis.
- 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.
- Aralast NP, Glassia, Prolastin-C, Zemaira: Safety and effectiveness in the pediatric population have not been established
- Aralast, Glassia, Prolastin, and Zemaira increase antigenic and functional (anti-neutrophil elastase capacity [ANEC]) serum levels and antigenic lung epithelial lining fluid levels of alpha 1-proteinase inhibitor.
- The effect of augmentation therapy with any alpha 1-proteinase inhibitor on pulmonary exacerbations and on the progression of emphysema in alpha1-antitrypsin deficiency has not been conclusively demonstrated in randomized, controlled clinical trials

V. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
alpha1-proteinase inhibitor, human (Aralast NP)	Emphysema due to AAT deficiency	60 mg/kg IV once weekly	60 mg/kg/week
alpha1-proteinase inhibitor, human (Glassia)			
alpha1-proteinase inhibitor, human (Prolastin-C)			
alpha1-proteinase inhibitor, human (Zemaira)			

VI. Product Availability

Drug Name	Availability
alpha1-proteinase inhibitor, human (Aralast NP)	Single-use vial: 500 mg, 1000 mg
alpha1-proteinase inhibitor, human (Glassia)	Single-use vial: 1000 mg/50 mL
alpha1-proteinase inhibitor, human (Prolastin-C)	Single-use vial: 1000 mg
alpha1-proteinase inhibitor, human (Zemaira)	Single-use vial: 1000 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 November 20, 2017.
2. Glassia Prescribing Information. Negev, Israel: Kamada, Ltd.; June 2016. Available at http://www.liquidglassia.com. Accessed November 20, 2017.
3. Prolastin-C Prescribing Information. Research Triangle Park, NC: Grifols Therapeutics, Inc.; August 2016. Available at http://www.prolastin.com. Accessed November 20, 2017.
4. Zemaira Prescribing Information. Kankakee, IL: CSL Behring LLC; September 2015. Available at http://www.zemaira.com. Accessed November 20, 2017.
5. 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.
6. 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.
7. 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.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	02.14	03.14
Policy converted to new template. Modified initial approval duration from 12 months to 6 months. Corrected FEV1 range from 35 to 65% to 30 to 65% based on Table 9 in the 2003 ATS/ERS AAT guidelines. Added max dose criteria and attestation that member is receiving additional supportive measures per COPD guidelines.	07.16	09.16
Converted to new template. Clarified criteria surrounding supportive measures into 2 different subbullets.	06.17	08.17
1Q18 annual review: 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;	12.05.17	02.18

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Added "If the member has an AAT level >11 umol/L, then the 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)]" 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		

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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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.

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