



**INLAND EMPIRE HEALTH PLAN**

This policy has been developed through review of medical literature, consideration of medical necessity, generally accepted medical practice standards, and approved by the IEHP Pharmacy and Therapeutic Subcommittee.

**Drug:** Zemaira, Aralast, Prolastin, Glassia (alpha-1 proteinase inhibitor, human)

**Class:** Blood Modifier Agent

**Formulary medication:** N/A

**Effective date:** November 16, 2011

**Policy/Criteria:**

Zemaira, Aralast, Prolastin, Glassia may be medically necessary in patients with:

- I. Must have documented Alpha-1-antitrypsin deficiency:
  - a. Alpha<sub>1</sub>-antitrypsin (AAT) level  $\leq 11 \mu\text{mol/L}$  (80mg/dl if measured by radial immunodiffusion or 0.8 g/L /dl if measured by nephelometry); **OR**
  - b. If the patient has an AAT level  $> 11 \mu\text{mol/L}$ , then the patient must have one of the increased-risk phenotypes (PiZZ, PiZnull, Pi(null, null), PiMZ, PiSZ), determined by a phenotyping lab test;

**AND**

- II. Must have clinically evident emphysema:
  - a. Forced expiratory volume in one second (FEV<sub>1</sub>) of 30–65% of predicted value; **OR**
  - b. A rapid decline in lung function defined as a change in FEV<sub>1</sub> of  $>120\text{ml/year}$ ;

**AND**

- III. Must be a Non-smoker

**Duration of approval:** 6 months. Continuation of therapy will be assessed based on improvement of pulmonary function tests and clinical benefit documented in chart notes.

**Clinical Justification:**

**FDA Approved Indication:** Chronic replacement therapy in patients with congenital deficiency of alpha-1 antitrypsin (alpha-1 proteinase inhibitor) and clinically evident emphysema

**Dosage:** 60 mg/kg IV infusion ONCE weekly

Alpha<sub>1</sub>-proteinase inhibitor (A1PI) or alpha<sub>1</sub> antitrypsin (AAT) deficiency is a chronic hereditary disorder. Augmentation therapy with A1PI is indicated only in patients with severe congenital A1PI deficiencies who have clinically evident emphysema. Population studies indicate a minimum plasma threshold of  $11 \mu\text{mol/L}$ , below which there is insufficient A1PI to protect the lung, leading to a risk of developing progressive, severe emphysema. The American Thoracic Society and the European Respiratory Society (ATS/ERS) issued standards for the diagnosis and management of individuals with

AATD in 2003. These standards recommend augmentation therapy with A1PI (human) for patients with AAT level  $\leq 11 \mu\text{mol/L}$  and with obstructive lung disease defined by a forced expiratory volume in one second ( $\text{FEV}_1$ ) of 30–65% of predicted or a rapid decline in lung function defined as a change in  $\text{FEV}_1$  of  $> 120 \text{ ml/year}$ . A1PI protects lung tissues by preventing neutrophil elastase from breaking down elastin, the protein that contributes to the elasticity of the lungs. The goal of therapy is to protect lung function by correcting the imbalance between levels of neutrophil elastase and protease inhibitors. Certain phenotypes are also associated with increased risk for development of emphysema. Clinical and biochemical studies demonstrate that the administration of A1PI can reverse the biochemical abnormalities in blood and lung fluid that characterize the disease. However, the clinical efficacy of A1PI augmentation therapy in improving lung function has not been established. Long term controlled trials to evaluate the effect of chronic replacement with A1PI on the development or progression of emphysema in patients with congenital alpha1 antitrypsin deficiency have not been performed. In an observational study that conducted multivariate analysis based on data from the NHLBI Registry, the mortality rate was lower in those receiving augmentation therapy as compared with those not receiving therapy.

Zemaira, Aralast, Prolastin, and Glassia are derived from human plasma, and therefore the risk of transmission of infectious agents, including viruses and the Creutzfeldt-Jakob disease (CJD) agent. Zemaira, Aralast, Prolastin, and Glassia should not be administered in patients with selective IgA deficiencies who have known antibodies against IgA due to the possibility of severe allergic reactions, including anaphylaxis. These agents have similar safety profiles with adverse effects (fever, light-headedness, dizziness, cough, infusion site reactions, headache, somnolence) generally occurring in less than 2% of patients. Due to the similar safety profile and efficacy data among the A1PI human products, determination of appropriate therapy may be based on patient specific factors (i.e. physician determination, availability, infusion duration).

Drug	AWP/unit	AWP/vial	Cost/Month
Zemaira 1000mg	0.50/mg	\$500	\$10,000.00
Prolastin 1000mg	0.48/mg	\$480	\$9,600.00
Aralast NP 1000mg	0.53/mg	\$530	\$10,600.00
Glassia 1000mg	0.55/mg	\$550	\$11,000.00

\*Cost calculated based on average body weight 70kg.

Phenotype – Risk for Emphysema	A1PI Plasma Level ( $\mu\text{mol/L}$ )
<b>MZ - Possible mild increase</b>	12 – 35
<b>SZ - Mild increase</b>	8 – 19
<b>ZZ - High risk (80-100%)</b>	2.5
<b>Null/Null - High risk (100% by age 30)</b>	0

## References:

1. Campos MA, Wanner A, Zhang G, Sandhaus RA. Trends in the diagnosis of symptomatic patients with alpha1-antitrypsin deficiency between 1968 and 2003. *Chest*. Sep 2005;128(3):1179-86
2. Characteristics of alpha-1 antitrypsin phenotypes (originally published in *American Review of Respiratory Disease* 1989; 140:1494).
3. DrugDex Drug Database. Thompson Micromedex Web site. Available at: <http://www.thomsonhc.com>. Accessed September 6, 2011.
4. Martin, Lawrence, Alpha-1 Anti-trypsin Deficiency: What is it and how is it treated? Lakeside Press, 2009

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 Oct 1;168(7):818-900.
6. Product Information: Zemaira(R) IV powder for solution, Alpha1-Proteinase Inhibitor (Human) IV powder for solution. CSL Behring LLC, Kankakee, IL, 2007.
7. Pierce JA: Antitrypsin and emphysema: perspective and prospects. JAMA 1988; 259(19):2890-5.
8. GOLD COPD Guideline. Updated 2010. Accessed at [www.goldcopd.org](http://www.goldcopd.org) on September 13, 2011.
9. Rovner et al. Treatment of alpha-1 antitrypsin deficiency. In: UpToDate, Hollingsworth, H (ED), UpToDate, Waltham, MA, 2011.