BENEFIT DESCRIPTION AND LIMITATIONS OF COVERAGE

ITEM: Prolastin®, Aralast NP™, Zemaira™, Glassia (alpha_1_-proteinase inhibitors infusions)

PRODUCT LINES: Commercial HMO/PPO/CDHP

COVERED UNDER: HMO: Rx (self-administered); Medical (provider setting)  
PPO/CDHP: Rx

DESCRIPTION: Alpha1-PI functions in the lungs to inhibit serine proteases such as neutrophil elastase (NE), which is capable of degrading protein components of the alveolar walls and is chronically present in the lung. In the healthy lung, alpha1-PI is thought to provide more than 90% of the anti-NE protection in the lower respiratory tract. [Facts and Comparisons Online, 7/7/2010]

CPT/HCPCS Code: J0256

Company Supplying: Talecris Biotherapeutics, Baxter, Aventis Behring, Kamada

Setting: Intravenous (IV)

Coverage Criteria: Express Scripts, Inc. monograph dated 10/21/2009

Approval Period: 12 months

Recommended Authorization Criteria

Coverage of alpha_1_-proteinase inhibitor (Prolastin, Aralast NP, Zemaira, Glassia) is recommended for those who meet the following criteria:

FDA-Approved Indications

1. Alpha_1_-antitrypsin deficiency with emphysema (or COPD). Approve in patients with baseline (pretreatment) alpha_1_-antitrypsin serum concentration < 80 mg/dL or 11 µM (11 µmol/L). These products are FDA-approved for chronic augmentation and maintenance therapy of individuals having congenital deficiency of alpha_1_-proteinase inhibitor (AAT deficiency) with clinically demonstrable panacinar emphysema. Patients with endogenous levels < 80 mg/dL (or 11 µM) have been noted to have an increase risk for the development of emphysema. Maintenance of AAT levels > 80 mg/dL (> 11 µM) was determined to be the serum concentration necessary to provide adequate anti-elastase activity per epidemiologic studies for most patients with AAT deficiency.

Alpha1-PI deficiency is an autosomal, codominant, hereditary disorder characterized by low serum and lung levels of alpha1-PI. Severe forms of the deficiency are frequently associated with slowly progressive, moderate to severe panacinar emphysema that most often manifests in the third to fourth decades of life, resulting in a significantly lower life expectancy. Individuals with alpha1-PI deficiency have little protection against NE released by a chronic, low-level of neutrophils in their lower respiratory tract, resulting in a protease:protease inhibitor imbalance in the lung. The emphysema associated with alpha1-PI deficiency is typically worse in the lower lung zones. It is believed to develop because there are insufficient amounts of alpha1-PI in the lower respiratory tract to
inhibit NE. This imbalance allows unopposed destruction of the connective tissue framework of the lung parenchyma. [Facts and Comparisons Online, 7/7/2010]

Other Uses with Supportive Evidence

2. **AAT deficiency-associated panniculitis.** Approve. Many case reports are available for the treatment of this rare complication. The ATS/ERS standards for the diagnosis and management of individuals with AAT deficiency state the panniculitis is an uncommon but well-recognized complication of AAT deficiency. Although no controlled trials provide a clear treatment recommendation, augmentation therapy with purified human AAT or fresh frozen plasma to restore plasma and local tissue levels of AAT appears rational, safe, and effective.

Diagnoses other than alpha₁-antitrypsin deficiency with emphysema that are not addressed in the exclusions below will be evaluated by a pharmacist and/or a physician on a case-by-case basis to determine a coverage recommendation for the client.

Exclusions

Coverage of alpha₁-proteinase inhibitor is *not* recommended in the following circumstances:

1. **Cystic fibrosis.** The use of alpha₁-proteinase inhibitor is considered investigational due to the lack of literature available regarding use of the agent for this disease state and many studies utilized an investigational aerosolized delivery mechanism. Studies have investigated use of aerosolized alpha₁ antitrypsin in cystic fibrosis.

2. **Chronic obstructive pulmonary disease (COPD) without alpha₁-antitrypsin deficiency.** The Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines for the diagnosis management and prevention of COPD, updated in 2007, state that young patients with severe hereditary alpha₁ antitrypsin deficiency and established emphysema may be candidates for alpha₁ antitrypsin augmentation therapy. However, this therapy is very expensive, is not available in most countries, and is not recommended for COPD that is unrelated to alpha₁ antitrypsin deficiency. In 2004 the American Thoracic Society (ATS) and the European Respiratory Society (ERS) published standards for the diagnosis and treatment of patients with COPD, which do not mention alpha₁-antitrypsin augmentation therapy as a therapeutic alternative in patients with this disease state. The ATS/ERS standards for the diagnosis and management of individuals with AAT deficiency, published in 2003, do not specifically address COPD in the absence of AAT deficiency and refer to COPD guidelines as applicable in those with pulmonary disease associated with AAT deficiency. Certain phenotypes of AAT deficiency are associated with an increased risk of COPD.

3. **Alpha₁-antitrypsin deficiency without lung disease, even if deficiency-induced hepatic disease is present.** The ATS/ERS standards for the diagnosis and management of individuals with AAT deficiency, published in 2003, states that the pathophysiology of liver disease in AAT deficiency is different from that of lung disease and use of alpha₁-proteinase inhibitor for these patients is not discussed. There is an absence of information that suggests that alpha₁-proteinase inhibitor is useful in patients with AAT deficiency-related liver disease.

4. **Bronchiectasis (without alpha₁-antitrypsin deficiency).** Studies have not demonstrated alpha₁ proteinase inhibitor to be effective for this condition. The ATS/ERS standards for the diagnosis and management of individuals with AAT deficiency, published in 2003, states that despite the well recognized association between AAT
deficiency and the early development of emphysema, only a limited number of studies have assessed the association between AAT deficiency and bronchiectasis. Studies suggest that bronchiectasis is more a result of emphysematous changes in the parenchyma than of AAT deficiency.

Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.