Aetna considers alpha 1-antitrypsin (AAT) inhibitor therapy (e.g., Aralast NP, Glassia, Prolastin-C, and Zemaira) medically necessary for selected adult members with emphysema due to AAT deficiency when all of the following criteria are met:

1. Member has a low serum concentration of AAT less than 80 mg/dL or less than 11 uM/L or less than 0.8 g/L (35% of normal), which is considered the threshold thought to protect against emphysema; and
2. Member has PiZZ, PiZ(null) or Pi(null, null) phenotype (homozygous) AAT deficiency or other phenotypes associated with serum AAT concentrations of less than 80 mg per deciliter (mg/dL). (AAT inhibitor is considered not medically necessary for use in individuals with the PiMZ or PiMS phenotypes of AAT deficiency because these individuals appear to be at small risk of developing panacinar emphysema); and
3. Member has progressive panacinar emphysema with a documented rate of decline in forced expiratory volume in 1 second (FEV1); and
4. Member is a non-smoker;

Because panacinar emphysema does not develop in some individuals who have AAT deficiency, replacement therapy with AAT inhibitor is of no proven value in affected individuals without clinical evidence of emphysema and is therefore considered experimental and investigational for these individuals.

Aetna considers AAT inhibitor experimental and investigational for treatment of cystic fibrosis. Aetna considers AAT inhibitor therapy experimental and investigational when criteria are not met.

Aetna considers repeat doses of AAT inhibitor therapy medically necessary for members who met the requirements for AAT inhibitor at therapy initiation and who demonstrate a substantial reduction in rate of deterioration of lung function.

Background

Alpha 1-antitrypsin is an antiprotease found in human plasma that inhibits the neutrophil
elastase enzyme from degrading elastin tissues in the lung. Alpha-1-antitrypsin (AAT) deficiency is a hereditary disorder associated with the early onset of severe pulmonary emphysema in adults. Although alpha 1-antitrypsin inhibitor therapy (Prolastin, Aralast) has not been shown to prevent or reverse emphysema in these patients affected by AAT deficiency, there is reason to believe that maintenance of antitrypsin serum levels may be compatible with retardation of the progression of emphysema.

Once initiated, therapy will usually be continued for the remainder of the patient's life. Recipients of alpha 1-antitrypsin inhibitor therapy should be immunized against hepatitis B. It is also recommended that this medication not be used in patients with immunoglobulin antibody IgA deficiency that is known to have antibodies against IgA (anti-IgA antibody). These patients may experience severe reactions, including anaphylaxis to IgA, which may be present in human alpha 1-antitrypsin inhibitor.

Abboud and colleagues (2005) stated that AAT replacement therapy has not yet been proven to be clinically effective in reducing the progression of disease in AAT-deficient patients. There was a suggestion of a slower progression of emphysema by computed tomography scan in a small randomized trial. Two non-randomized studies comparing AAT-deficient patients already receiving replacement therapy with those not receiving it, and a retrospective study evaluating a decline in FEV1 before and after replacement therapy, suggested a possible benefit for selected patients. Because of the lack of definitive proof of the clinical effectiveness of AAT replacement therapy and its cost, these investigators recommended reserving AAT replacement therapy for deficient patients with impaired FEV1 (35 to 65 % of predicted value), who have quit smoking and are on optimal medical therapy but continue to show a rapid decline in FEV1 after a period of observation of at least 18 months.

An assessment by the Canadian Agency for Drugs and Technologies in Health (Chen et al, 2007) concluded that evidence showing health improvement from alpha-1 antitrypsin inhibitor therapy is inconclusive. The assessment found that, in controlled trials, augmentation therapy has not shown reduced lung function impairment in patients with AAT deficiency and chronic obstructive pulmonary disease (COPD), compared with normal care. Conversely, the assessment reported that in observational studies, alpha-1 antitrypsin inhibitor therapy is associated with outcomes suggestive of therapeutic benefit in patients with severe AAT deficiency and moderate airflow obstruction. The assessment found that severe adverse events from treatment have been reported in approximately 1 % of study populations.

The assessment concluded that use of alpha-1 antitrypsin inhibitor therapy in patients without COPD is experimental (Chen et al, 2007). The assessment found no evidence evaluating the use of alpha-1 antitrypsin inhibitor therapy in patients with AAT deficiency and no lung function impairment.

On July 1, 2010, Kamada, Ltd., (Beit Kama, Israel) received approval from the Food and Drug Administration for manufacturing Glassia (alpha-1-proteinase inhibitor [human]), which is an intravenously administered biologic product indicated for chronic augmentation and maintenance therapy in individuals with emphysema due to congenital deficiency of alpha-1-proteinase inhibitor, also known as AAT deficiency.

Appendix

Note: Prolastin-C is a more purified and concentrated form of alpha1-antitrypsin (AAT) that may be infused over a shorter period of time than Prolastin (15 minutes on average).

Aralast NP is a similar product to Aralast (now off the market), containing the same active
components of plasma alpha1-proteinase inhibitor with identical formulations. However, Aralast NP should be stored at room temperature, not to exceed 25°C (77°F). Refrigeration is not needed.

CPT Codes / HCPCS Codes / ICD-9 Codes

Other CPT codes related to the CPB:

82103

82104

HCPCS codes covered if selection criteria are met:

J0256 Injection, alpha 1-proteinase inhibitor (human), not otherwise specified, 10 mg [Aralast NP Prolastin-C]

J0257 Injection, alpha 1 - proteinase inhibitor (human), (glassia), 10 mg

S9346 Home infusion therapy, alpha-1-proteinase inhibitor (e.g., Prolastin); administrative services, professional pharmacy services, care coordination, and all necessary supplies and equipment (drugs and nursing visits coded separately), per diem

ICD-9 codes covered if selection criteria are met:

492.8 Other emphysema [panacinar emphysema] [due to alpha-1-antitrypsin deficiency]

ICD-9 codes not covered for indications listed in the CPB:

305.1 Tobacco use disorder [member must be nonsmoker]

Other ICD-9 codes related to the CPB:

273.4 Alpha-1-antitrypsin deficiency [AAT deficiency] [*note when billed alone, indicates no clinical evidence of emphysema]

The above policy is based on the following references:


25. Chen S, Farahati F, Marciniuk D, et al. Human a1-proteinase inhibitor for patients...
with α1-antitrypsin deficiency. Technology Report No. 74. Ottawa, ON: Canadian Agency for Drugs and Technologies in Health (CADTH); 2007.


