Respiratory Agents – MISC :
Alpha-Proteinase Inhibitor (Human)

WA.PHAR.68 Respiratory Agents- Misc: Alpha-Proteinase Inhibitor (Human) Effective Date: July 1, 2019

Background:

Deficiency of alpha1-proteinase inhibitor (A1-PI), also known as alpha1-antitrypsin deficiency, is characterized by reduced levels of A1-PI in the blood and lungs. A1-PI deficiency is an autosomal, co-dominant, hereditary disorder. Patients with severe A1-PI deficiency have increased levels of neutrophil and neutrophil elastase levels in lung epithelial lining fluid that results in destruction of the connective tissue framework of the lung parenchyma. A1-PI (human) therapy augments the level of the deficient protein and theoretically corrects the imbalance between neutrophil elastase and protease inhibitors, which may protect the lower respiratory tract.

Medical necessity:

Drug	Medical Necessity
Zemaira Aralast Glassia Prolastin-C	Treatment of an FDA approved indication for augmentation and maintenance therapy of patients 18 years of age or older with severe hereditary deficiency of alpha1-antitrypsin (AAT) with clinical evidence of emphysema

Clinical policy:

Clinical Criteria (Initial Approval)
Alpha-1-proteinase inhibitors (human) may be considered medically necessary when **ALL** of the following are met: 1. An FDA approved indication for augmentation and maintenance therapy of patients 18 years of age or older with severe hereditary deficiency of alpha1-antitrypsin (AAT) with clinical evidence of emphysema; 2. Diagnosis confirmed by ALL of the following: a. Genetic confirmation of PiZZ, PiZ(null), or Pi(null, null) phenotype alpha1-antitrypsin deficiency (AATD) or other alleles determined to increase risk of AATD; b. **ONE** of the following lab values testing for ATT: i. test levels of AAT: less than 11 µmol/L; ii. immunoturbidimetry: less than or equal to 57 mg/dL iii. nephelometry: less than or equal to 57 mg/dL; iv. radial immunodiffusion: less than or equal to 80 mg/dL; c. Documented emphysema with airflow obstruction; 3. Prescriber must document that member's forced expiratory volume in one second (FEV1) is less than or equal to 65% predicted; 4. The prescriber must verify that patient is a non-smoker or initiating smoking cessation; 5. The prescriber must verify the patient does not have antibodies to IgA; 6. The diagnosis was established by, or in consultation with, a specialist in pulmonology;

7. The patient's recent weight must be provided in order to authorize the appropriate amount of drug required according to package labeling;
    a. Dose limit: 60 mg/kg every week

If ALL criteria are met, the request will be approved for 6 months

Criteria (Reauthorization)

Alpha-1-proteinase inhibitors (human) may be considered for reauthorization when **ALL** of the following are met:

1. Documentation of a positive clinical response from pretreatment baseline to alpha1-proteinase inhibitor treatment;
2. The prescriber must verify that patient is a non-smoker or initiating smoking cessation;
3. The patient's recent weight must be provided in order to authorize the appropriate amount of drug required according to package labeling;
    a. Dose limit: 60 mg/kg every week

If ALL criteria are met, the request will be approved for 12 months

Preferred therapies:

Drug Name	Preferred For:
Zemaira **Aralast** **Glassia** **Prolastin-C**	Treatment of an FDA approved indication for augmentation and maintenance therapy of patients 18 years of age or older with severe hereditary deficiency of alpha1-antitrypsin (AAT) with clinical evidence of emphysema

Dosage and quantity limits:

Drug Name	Dose and Quantity Limits
Zemaira **Aralast** **Glassia** **Prolastin-C**	60 mg/kg weekly

Coding:

HCPCS Code	Description
J0257	Injection, alpha 1 proteinase inhibitor – (human), 10 mg [Glassia]
J0256	Injection, alpha 1 - proteinase inhibitor - (human), not otherwise specified, 10 mg [Aralast NP, Prolastin-C, Zemaira]
ICD-10 codes	**Description**
E88.01	Alpha-1-antitrypsin deficiency

Table:

Product	Aralast NP	Glassia	Prolastin-C	Zemaira
Dosage form	powder for solution	premixed solution	powder for solution	powder for solution
Concentration	1 gm/50 mL	1 gm/50 mL	1 gm/20 mL	1 gm/20 mL
Rate of infusion (mL/kg/minute)	0.08	0.04	0.08	0.08
Usual infusion time	30-40 minutes	60-80 minutes	15 minutes	15 minutes
Stability after mixing	3 hours	Premixed	3 hours	3 hours

Evidence review:

Several randomized, controlled trials have established the safety and efficacy of AAT augmentation to treat certain patients with AATD. Chapman et al. published a meta-analysis in 2009 which demonstrated slower FEV1 decline rate in patients treated with AAT therapy in 5 trials (13.4 mL/year absolute difference; CI 1.5-25.3 mL/year). Patients with moderate lung obstruction, defined as baseline FEV1 value between 30 and 65% of predicted, were observed to have a significantly greater benefit in FEV1 rate decline compared to the overall group (17.9 mL/year absolute difference; CI 9.6-26.1 mL/year). The meta-analysis showed similar trends in patient groups with mild and severe obstruction, however these results were not statistically significant.

Patients with severe ATTD that were treated with alpha 1 proteinase inhibitor demonstrated slower emphysema progression compared to patients treated with placebo in the initial RAPID-RCT trial published by McElvaney et al. in 2015. This trial was extended with an open-label extension period (RAPID-OLE) in 2017 to test the long-term treatment effects. Patients were divided into the early-start group (treatment group during RAPID-RCT) and the delayed-start group (placebo group during RAPID-RCT). The rate of lung density loss was lower in the early-start group (-1.51 g/L per year at total lung capacity; SE 0.25) than the delayed-start group (-2.26 g/L per year at total lung capacity; SE 0.26) between day one and month 24. The rate of lung density loss was lower in the delayed-start patients (-2.26 g/L per year to -1.26 g/L per year) from month 24 to month 48. During this time period, there was no significant difference in the rate in the early-start group. Overall, these results demonstrate the importance of starting treatment early as the lung density lost is never recovered. The sustainability of the treatment effect was also shown in the early-start group that continued to have a low lung density loss rate after 4 years of treatment.

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History

Date	Action and Summary of Changes
05.03.2019	New Policy