Medication Policy Manual

Policy No: dru382

Date of Origin: December 12, 2014

Committee Approval Date: December 16, 2016

Next Review Date: December 2017

Effective Date: January 1, 2017

IMPORTANT REMINDER

This Medication Policy has been developed through consideration of medical necessity, generally accepted standards of medical practice, and review of medical literature and government approval status.

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

The purpose of medication policy is to provide a guide to coverage. Medication Policy is not intended to dictate to providers how to practice medicine. Providers are expected to exercise their medical judgment in providing the most appropriate care.

Description

Alpha-1 proteinase inhibitors (available as Aralast NP, Glassia, Prolastin-C and Zemaira) are preparations containing alpha-1 antitrypsin (A1AT), a naturally occurring enzyme purified from human blood. They are used in the treatment of alpha-1 antitrypsin deficiency (AATD), a rare genetic disorder that can lead to disease of the lungs (emphysema), and administered by intravenous infusion.
Policy/Criteria

I. Most contracts require prior authorization approval of alpha-1 proteinase inhibitor (Aralast NP, Glassia, Prolastin-C, Zemaira), prior to coverage. Alpha-1 proteinase inhibitor may be considered medically necessary when criteria A and B below are met.
   A. A confirmed diagnosis of outflow obstruction (emphysema) due to alpha-1 antitrypsin deficiency (AATD).
   AND
   B. The diagnosis was established by, or in consultation with, a specialist in pulmonology.

II. Administration, Quantity Limitations, and Authorization Period
   A. OmedaRx does not consider alpha-1 proteinase inhibitor to be a self-administered medication.
   B. When prior authorization is approved, alpha-1 proteinase inhibitor doses up to 60 mg/kg every week may be authorized.
   C. Authorization may be reviewed at least annually to confirm that current medical necessity criteria are met and that the medication is effective.

III. Use of an alpha-1 proteinase inhibitor is considered investigational when used for all other conditions, including but not limited to:
   A. AATD without airflow obstruction (without emphysema), such as AATD-related liver disease or other AATD-related complications.
   B. Use in combination with other alpha1-PI products

Position Statement
- All alpha-1 proteinase inhibitor (alpha1-PI) products (Aralast NP, Glassia, Prolastin-C, and Zemaira) appear to be similar in biologic activity for slowing progression of emphysema in patients with alpha-1 antitrypsin deficiency (AATD).
- Although the overall net health benefit of alpha1-PI therapy is uncertain, treatment options for patients with moderate to severe emphysema are limited to symptomatic management, aside from lung transplantation.
- There is no evidence of clinically meaningful differences in safety or efficacy between alpha1-PI products. They vary in their reconstitution, time of infusion and storage, and have slight differences in protein composition and chemical structures; however, these differences have not been linked to specific clinical outcomes.
- Consensus guidelines recommend use of alpha1-PI replacement therapy (“augmentation therapy”) for treatment of patients with airflow obstruction from AATD but do not differentiate between products. Patients with heterozygous phenotypes should not be treated with alpha1-PIs if the AAT level exceeds 11 micromol/L.
- All alpha1-PIs are approved for 60 mg/kg once a week dosing.
**Background** [1,2]

- Emphysema, from any cause, is a progressive, non-curable disease, leading to decline in lung function (FEV₁), exacerbation of symptoms, decline in ability to function and death.
- Alpha-1 antitrypsin deficiency (AATD) is a rare inherited genetic disorder, but leads to emphysema in approximately 40,000-60,000 Americans (2-3% of all emphysema patients).
- Smoking increases the risk of emphysema in patients with AATD.
- Deficient alpha-1 antitrypsin levels (A1AT) levels can lead to uninhibited lung and liver tissue breakdown from elastase and manifestations of emphysema, as well as hepatic cirrhosis.
- The ideal A1AT level with alpha1-PI repletion is uncertain. A1AT levels alone do not predict disease, as patients with very low A1AT levels can have normal lung function.
- There are four alpha1-PI products (Aralast NP, Glassia, Prolastin-C, and Zemaira) available for repletion of A1AT levels (“augmentation therapy”), with a goal of slowing disease progression. [1,2]

**Clinical Efficacy**

- Alpha1-PIs replete A1AT levels, a surrogate endpoint and the basis for their FDA approval; however, their effect on attenuation of emphysema progression with clinically meaningful efficacy endpoints (e.g. survival, quality of life) is uncertain. [3]
- Augmentation therapy with alpha1-PIs has not yet been proven to provide benefit in reversing or decreasing outflow obstruction (emphysema) associated with AATD. [4]
- There is no evidence that there is any difference in efficacy between the alpha1-PI products.
- Although there is low certainty in the evidence that alpha1-PI therapy improves health outcomes in patients with emphysema due to AATD, the products in the class appear to be similar in biologic activity.
- Despite the insufficient evidence for health outcomes with alpha1-PIs, treatment options for patients with moderate to severe emphysema are limited to symptomatic management, aside from lung transplantation. [4,5]
- There is no evidence to support the use of doses greater than 60 units/kg weekly. One small, short-term (8-week), safety and pharmacokinetic trial of higher doses of alpha1-PI (Prolastin C) in patients with AATD resulted in higher steady state levels of alpha-1 PI concentrations. However, the effect of these higher alpha-1 PI concentrations on long-term emphysema disease progression is unknown. [6]
- Treatment guidelines recommended use of augmentation therapy with alpha1-PIs for patients with airflow obstruction from AATD but do not differentiate between products. Patients should be confirmed nonsmokers or ex-smokers and plasma AAT levels less than 11 mMol/L. Patients with a heterozygous phenotype and AAT levels that exceed 11 mMol/L should not be treated with alpha1-PI augmentation therapy. [5]
- There is no evidence that augmentation therapy with alpha1-PIs are effective for treatment of AATD-related liver disease, including, hepatic cirrhosis. Guidelines recommend against the use of alpha1-PIs for AATD-related liver or other AATD-related diseases.
Safety
- Adverse events with alpha1-PIs are generally mild including headache and malaise. [7]
- There is no conclusive evidence of difference in safety or immunogenicity between alpha1-PIs. [8]

Dosing and Administration [7]
- All alpha1-PIs are dosed once weekly, via intravenous infusion.
- Alpha1-PI (Glassia) is the only liquid preparation, but has a longer infusion time versus other alpha1-PI products (60-80 minutes versus 15-30 minutes) (See Appendix 1).

Cross References
None

Codes

<table>
<thead>
<tr>
<th>Codes</th>
<th>Number</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>HCPCS</td>
<td>J0257</td>
<td>Glassia, Alpha 1-proteinase inhibitor, human 10 mg IV, liquid</td>
</tr>
<tr>
<td>HCPCS</td>
<td>J0256</td>
<td>Aralast NP, Prolastin-C, Zemaira, Alpha 1-proteinase inhibitor, human 10 mg IV, powder</td>
</tr>
</tbody>
</table>

Appendix 1. Alpha-1 Proteinase Inhibitor Product Characteristics [7]

<table>
<thead>
<tr>
<th>Product</th>
<th>Aralast NP</th>
<th>Glassia</th>
<th>Prolastin-C</th>
<th>Zemaira</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dosage form</td>
<td>powder for solution</td>
<td>premixed solution</td>
<td>powder for solution</td>
<td>powder for solution</td>
</tr>
<tr>
<td>Concentration</td>
<td>1 gm/50 mL</td>
<td>1 gm/50 mL</td>
<td>1 gm/20 mL</td>
<td>1 gm/20 mL</td>
</tr>
<tr>
<td>Rate of infusion (mL/kg/minute)</td>
<td>0.08</td>
<td>0.04</td>
<td>0.08</td>
<td>0.08</td>
</tr>
<tr>
<td>Usual infusion time</td>
<td>30-40 minutes</td>
<td>60-80 minutes</td>
<td>15 minutes</td>
<td>15 minutes</td>
</tr>
<tr>
<td>Stability after mixing</td>
<td>3 hours</td>
<td>Premixed</td>
<td>3 hours</td>
<td>3 hours</td>
</tr>
<tr>
<td>Refrigeration required</td>
<td>No</td>
<td>Yes; stable for 1 month at room temperature</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Vial size (gm)</td>
<td>0.5 and 1 gm</td>
<td>1 gm/50 mL</td>
<td>1 gm</td>
<td>1 gm</td>
</tr>
</tbody>
</table>
References


Revision History

<table>
<thead>
<tr>
<th>Revision Date</th>
<th>Revision Summary</th>
</tr>
</thead>
<tbody>
<tr>
<td>12/16/2016</td>
<td>No criteria changes with this annual update</td>
</tr>
<tr>
<td>12/11/2015</td>
<td>No criteria changes</td>
</tr>
</tbody>
</table>