PreferredOne®

PRIOR AUTHORIZATION POLICY

POLICY: Alpha$_1$-Proteinase Inhibitor Products Prior Authorization Policy
- Aralast NP® (alpha$_1$-proteinase inhibitor [human] intravenous infusion – Shire)
- Glassia® (alpha$_1$-proteinase inhibitor [human] intravenous infusion – Shire)
- Prolastin®-C and Prolastin®-C Liquid (alpha$_1$-proteinase inhibitor [human] intravenous infusion – Grifols Therapeutics)
- Zemaira® (alpha$_1$-proteinase inhibitor [human] intravenous infusion – CSL Behring)

REVIEW DATE: 11/17/2021

OVERVIEW

Alpha$_1$-proteinase inhibitor (also known as alpha$_1$-antitrypsin [AAT]), is indicated for use as a chronic augmentation and maintenance therapy in adults with **alpha$_1$-proteinase deficiency and clinical evidence of emphysema**.[1-5] The following products are available commercially in the US: Prolastin-C (also available as Prolastin-C Liquid), Aralast NP, Zemaira, and Glassia. The products vary in their availability and in some of their purification and viral inactivation processes.

Disease Overview

AAT deficiency is a rare, chronic, hereditary, autosomal co-dominant disorder marked by low concentrations of AAT which leads to progressive, severe emphysema that often does not manifest until the third to fourth decades of life.[1] Treatment is aimed at raising serum levels of AAT above a theoretical protective threshold of 11 mcM (mcmol/L); epidemiological data suggest lower probability of chronic obstructive pulmonary disease (COPD) above this level.[6] Of note, older laboratory techniques (e.g., radial immunodiffusion) measured non-purified levels of AAT, which tend to overestimate the concentration by 35% to 40%. To distinguish between non-purified and purified standards, the former are expressed in mg/dL and the latter are expressed in mcM. An AAT level of 80 mg/dL measured by radial immunodiffusion corresponds to a plasma AAT level of 11 mcM. Alpha$_1$-proteinase inhibitor is the only treatment approved to correct AAT deficiency.

Guidelines

A European Respiratory Society (ERS) statement addresses diagnosis and treatment of pulmonary disease in AAT deficiency (2017).[8] It is noted that augmentation therapy has been shown to reduce progression of emphysema in severe AAT deficiency. There is no evidence to support efficacy of AAT augmentation therapy for current smokers of any phenotype. These guidelines support earlier American Thoracic Society (ATS)/ERS guidelines (2003) which state that intravenous augmentation therapy is recommended for individuals with established airflow obstruction from AAT deficiency.[7]

The Canadian Thoracic Society updated its guidelines (2012) regarding AAT deficiency testing and augmentation therapy.[9] The guidelines state that evidence supports the consideration of AAT augmentation therapy in non-smoking or ex-smoking patients with COPD due to emphysema and a documented AAT deficiency (level ≤ 11 mcmol/L). Patients should also be receiving other pharmacological and non-pharmacologic therapies, including comprehensive case management and pulmonary rehabilitation.

The Medical and Scientific Advisory Committee of the Alpha-1 Foundation guidelines (2016) provide similar recommendations.[10] Intravenous AAT augmentation is strongly recommended in non-smoking or ex-smoking patients with forced expiratory volume (FEV_1) 30 to 65% of predicted due to well-documented benefit in this group. Weaker recommendations also support treatment of patients with FEV_1 below 30%

of predicted or above 65% of predicted. Usual management of COPD should also be provided, with strong emphasis on facilitating tobacco cessation. Of note, AAT replacement therapy is not recommended for patients who continue to smoke.

Other Uses with Supportive Evidence

In the ATS/ERS 2003 guidelines, it is stated that AAT replacement therapy is a reasonable option for AAT deficiency-associated panniculitis.[7] Although no controlled trials provide a clear treatment recommendation, augmentation therapy with purified human alpha$_1$-proteinase inhibitor or fresh frozen plasma to restore plasma and local tissue levels of AAT appears to be rational, safe, and effective. In a review of treatment options for panniculitis in AAT deficiency, augmentation therapy with alpha$_1$-proteinase inhibitor was noted to be the most successful medical treatment.[11]

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of alpha$_1$-proteinase inhibitor. All approvals are provided for the duration noted below.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of alpha$_1$-proteinase inhibitor (e.g., Aralast NP, Glassia, Prolastin-C, Prolastin-C Liquid, Zemaira) is recommended in those who meet one of the following criteria:

FDA-Approved Indication

1. **Alpha$_1$-Antitrypsin Deficiency with Emphysema (or Chronic Obstructive Pulmonary Disease).** Approve for 1 year if the patient meets the following criteria (A, B, and C):
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** Patient has a baseline (pretreatment) alpha$_1$-antitrypsin serum concentration of < 80 mg/dL or 11 mcM (11 mcmol/L); AND
   - **C)** According to the prescriber, the patient is a current non-smoker.

Other Uses with Supportive Evidence

2. **Alpha$_1$-Antitrypsin Deficiency-Associated Panniculitis.** Approve for 1 year if the patient is ≥ 18 years of age.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

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

1. **Alpha$_1$-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 (2003) state that the pathophysiology of liver disease in AAT deficiency is different from that of lung disease, and the use of alpha$_1$-proteinase inhibitor is not discussed for these patients.[7] There is an absence of information that suggests alpha$_1$-proteinase inhibitor is useful in patients with AAT deficiency-related liver disease.
2. **Bronchiectasis (without alpha$_1$-antitrypsin deficiency).** Studies have not demonstrated alpha$_1$ proteinase inhibitor to be effective for this condition. The ATS/ERS standards for the diagnosis and

management of individuals with AAT deficiency (2003) state 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.[7] Studies suggest that bronchiectasis is more a result of emphysematous changes in the parenchyma than of AAT deficiency.

3. **Chronic Obstructive Pulmonary Disease (COPD) without Alpha$_1$-Antitrypsin Deficiency.** The Global Initiative for Chronic Obstructive Lung Disease guidelines for the diagnosis, management, and prevention of COPD (updated 2021) state that never or ex-smokers with an FEV_1 of 35 to 60% of predicted may be most suitable for AAT deficiency augmentation therapy; newer evidence suggests that individuals with higher FEV_1 values may also be candidates.[12] However, this therapy is not recommended for COPD that is unrelated to AAT deficiency.

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

REFERENCES

1. Aralast NP® intravenous infusion [prescribing information]. Lexington, MA: Shire; December 2018.
2. Zemaira® intravenous infusion [prescribing information]. Kankakee, IL: CSL Behring; April 2019.
3. Prolastin®-C intravenous infusion [prescribing information]. Research Triangle Park, NC: Grifols Therapeutics; June 2018.
4. Prolastin®-C Liquid intravenous infusion [prescribing information]. Research Triangle Park, NC: Grifols Therapeutics; August 2018.
5. Glassia® intravenous infusion [prescribing information]. Lexington, MA: Shire; June 2017.
6. Brantly ML, Lascano JE, Shahmohammadi A. Intravenous alpha-1 antitrypsin therapy for alpha-1 antitrypsin deficiency: the current state of the evidence. *Chronc Obstr Pulm Dis.* 2018;6(1):100-114.
7. American Thoracic Society and the European Respiratory Society. Standards for the diagnosis and management of individuals with alpha-1 antitrypsin deficiency. *Am J Respir Crit Care Med.* 2003;168:818-900.
8. Miravitlles M, Dirksen A, Ferrarotti I, et al. European Respiratory Society statement: diagnosis and treatment of pulmonary disease in alpha1-antitrypsin deficiency. *Eur Respir J.* 2017;50(5).
9. Marciniuk DD, Hernandez P, Balter M, et al. Alpha-1 antitrypsin deficiency targeted testing and augmentation therapy: A Canadian Thoracic Society clinical practice guideline. *Can Respir J.* 2012;19:109-116.
10. Sandhaus RA, Turino G, Brantly ML, et al. The diagnosis and management of alpha-1 antitrypsin deficiency in the adult. *Chronic Obstr Pulm Dis.* 2016;3(3):668-682.
11. Sabbagh DK, Barmayehvar B, Nguyen T, Edgar RG, Turner AM. Managing panniculitis in alpha-1 antitrypsin deficiency: systematic review of evidence behind treatment. *World J Dermatol.* 2018;7(1):1-8
12. Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. Updated 2021. Available at: https://goldcopd.org/2021-gold-reports/. Accessed on November 10, 2021.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	**Alpha$_1$-Antitrypsin Deficiency with Emphysema (or Chronic Obstructive Pulmonary Disease):** A criterion was added to specify that the patient must be ≥ 18 years of age, in alignment with product labeling. **Alpha$_1$-Antitrypsin Deficiency-Associated Panniculitis:** A criterion was added requiring that the patient be ≥ 18 years of age.	10/21/2020
Annual Revision	**Conditions Not Recommended for Approval:** "Cystic Fibrosis" was removed from Conditions Not Recommended for Approval.	11/17/2021

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Minneapolis, MN 55459-0052
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Fax: 763.847.4010
customerservice@preferredone.com

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You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights, electronically through the Office for Civil Rights Complaint Portal, available at https://ocrportal.hhs.gov/ocr/portal/lobby.jsf, or by mail or phone at:

U.S. Department of Health and Human Services
200 Independence Avenue, SW
Room 509F, HHH Building
Washington, D.C. 20201
1-800-368-1019, 800-537-7697 (TDD)

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U.S. Department of Health and Human Services
200 Independence Avenue, SW
Room 509F, HHH Building
Washington, D.C. 20201
1-800-368-1019, 800-537-7697 (TDD)

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