

## Medical Policy Bulletin

Title:

Alpha 1-Antitrypsin Therapy (e.g., Prolastin-C, Aralast NP, Glassia, Zemaira)

Policy #:

MA08.050c

The Company makes decisions on coverage based on the Centers for Medicare and Medicaid Services (CMS) regulations and guidance, benefit plan documents and contracts, and the member's medical history and condition. If CMS does not have a position addressing a service, the Company makes decisions based on Company Policy Bulletins. Benefits may vary based on contract, and individual member benefits must be verified. The Company determines medical necessity only if the benefit exists and no contract exclusions are applicable. Although the Medicare Advantage Policy Bulletin is consistent with Medicare's regulations and guidance, the Company's payment methodology may differ from Medicare.

When services can be administered in various settings, the Company reserves the right to reimburse only those services that are furnished in the most appropriate and cost-effective setting that is appropriate to the member's medical needs and condition. This decision is based on the member's current medical condition and any required monitoring or additional services that may coincide with the delivery of this service.

This Policy Bulletin document describes the status of CMS coverage, medical terminology, and/or benefit plan documents and contracts at the time the document was developed. This Policy Bulletin will be reviewed regularly and be updated as Medicare changes their regulations and guidance, scientific and medical literature becomes available, and/or the benefit plan documents and/or contracts are changed.

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### Policy

**Coverage is subject to the terms, conditions, and limitations of the member's Evidence of Coverage.**

**The Company reserves the right to reimburse only those services that are furnished in the most appropriate and cost-effective setting that is appropriate to the member's medical needs and condition.**

In the absence of coverage criteria from applicable Medicare statutes, regulations, NCDs, LCDs, CMS manuals, or other Medicare coverage documents, this policy uses internal coverage criteria developed by the Company in consideration of peer-reviewed medical literature, clinical practice guidelines, and/or regulatory status.

#### **MEDICALLY NECESSARY**

##### **EMPHYSEMA WITH ALPHA-1 ANTITRYPSIN DEFICIENCY**

Alpha-1 antitrypsin (AAT) therapy (e.g., Prolastin-C, Aralast NP, Glassia, Zemaira) is considered medically necessary and, therefore, covered for individuals 18 years of age and older who have AAT deficiency and clinical evidence of chronic emphysema without evidence of AAT-associated liver disease, when all of the following criteria are met:

- The individual has a low serum concentration of AAT less than 80 mg/dL (radial immunodiffusion) or 50 mg/dL (nephelometry) or less than 11  $\mu\text{mol/L}$  (nephelometry) or less than 0.8 g/L (35% of normal), which is considered the threshold thought to protect against emphysema.
- The individual has a documented diagnosis of congenital AAT deficiency confirmed by one of the following:
  - Pi\*ZZ, Pi\*Z(null) or Pi(null)(null) protein phenotypes (homozygous)
  - Other rare AAT disease-causing alleles associated with serum AAT level  $<11 \mu\text{mol/L}$
- The individual has progressive emphysema with a documented rate of decline in forced expiratory volume in 1 second (FEV<sub>1</sub>).
- The individual is a nonsmoker.

**ACUTE GRAFT-VERSUS-HOST DISEASE (GVHD) AFTER HEMATOPOIETIC CELL TRANSPLANTATION**  
AAT therapy (e.g., Prolastin-C, Aralast NP, Glassia, Zemaira) administered intravenously is considered medically necessary and, therefore, covered for individuals 18 years of age and older who have acute graft-versus-host disease

(GVHD) following hematopoietic cell transplantation in conjunction with systemic corticosteroids following no response (steroid-refractory disease) to first-line therapy options.

## **EXPERIMENTAL/INVESTIGATIONAL**

All other uses of AAT therapy (e.g., Prolastin-C, Aralast NP, Glassia, Zemaira) are considered experimental/investigational and, therefore, not covered unless the indication is supported as an accepted off-label use, as defined in the Company medical policy on off-label coverage for prescription drugs and biologics.

## **REQUIRED DOCUMENTATION**

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include, but are not limited to: records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the drug.

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## [Guidelines](#)

There is no Medicare coverage determination addressing this drug; therefore, the Company policy is applicable.

## **BENEFIT APPLICATION**

Subject to the terms and conditions of the applicable Evidence of Coverage, alpha-1 antitrypsin (AAT) therapy (e.g., Prolastin-C, Aralast NP, Glassia, Zemaira) is covered under the medical benefits of the Company's Medicare Advantage products when the medical necessity criteria listed in this medical policy are met.

For Medicare Advantage members, certain drugs are available through either the member's medical benefit (Part B benefit) or pharmacy benefit (Part D benefit), depending on how the drug is prescribed, dispensed, or administered. This medical policy only addresses instances when AAT therapy (e.g., Prolastin-C, Aralast NP, Glassia, Zemaira) is covered under a member's medical benefit (Part B benefit). It does not address instances when AAT therapy (e.g., Prolastin-C, Aralast NP, Glassia, Zemaira) is covered under a member's pharmacy benefit (Part D benefit).

## **US FOOD AND DRUG ADMINISTRATION (FDA) STATUS**

Alpha-1 proteinase inhibitor/Alpha-1 antitrypsin therapy (Prolastin-C) was approved by the FDA on October 16, 2009, for the treatment of individuals with AAT deficiency and evidence of emphysema.

Alpha-1 proteinase inhibitor/Alpha-1 antitrypsin therapy (Aralast NP) was approved by the FDA on May 4, 2007, for chronic augmentation therapy in patients having AAT deficiency with clinically evident emphysema.

Alpha-1 proteinase inhibitor/Alpha-1 antitrypsin therapy (Glassia) was approved by the FDA on July 1, 2010, and is indicated for chronic augmentation and maintenance therapy in adults with emphysema.

Alpha-1 proteinase inhibitor/Alpha-1 antitrypsin therapy (Zemaira) was approved by the FDA on July 8, 2003, for treatment of individuals with deficiency and evidence of emphysema.

## **PEDIATRIC USE**

AAT therapy is not indicated for use in pediatric individuals less than 18 years of age.

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## [Description](#)

Alpha-1 antitrypsin (AAT; also known as congenital alpha-1 proteinase inhibitor) deficiency is an autosomal, codominant genetic disorder, differentiated by deficient serum and lung concentrations of AAT. The most common form of AAT deficiency is associated with allele Z, or homozygous proteinase inhibitor (Pi)\*Z (ZZ). A deficiency in

AAT leaves the neutrophil elastase uninhibited. Uncontrolled neutrophil elastase leads to progressive destruction of the pulmonary connective tissue and loss of the alveoli.

Some individuals with certain phenotypic variants have an increased risk of developing progressive emphysema. Individuals with the Pi\*ZZ variant typically have serum AAT levels less than 35% of the average normal. Ninety-five percent of clinically symptomatic AAT-deficient individuals are Pi\*ZZ phenotype. Individuals with Pi(null)(null) are associated with undetectable serum AAT levels or levels less than 1% of the normal amount. Individuals with these low serum AAT levels have a markedly increased risk of developing emphysema over their lifetime. In addition, Pi\*SZ individuals, whose serum AAT levels range from approximately 9 to 23  $\mu$ M, are considered to have moderately increased risk of developing emphysema.

AAT (alpha-1 proteinase inhibitor) is used as a replacement therapy for individuals with severe AAT deficiency and clinical evidence of emphysema. Several biological drugs have been approved by the US Food and Drug Administration (FDA) for AAT therapy, with orphan drug status. Prolastin, Aralast NP, Glassia, and Zemaira were approved by the FDA for the treatment of individuals with AAT deficiency and evidence of emphysema. Prolastin was replaced by Prolastin-C in spring 2010.

AAT therapy (e.g., Prolastin-C, Aralast NP, Glassia, Zemaira) uses highly purified human AAT derived from human plasma. Studies comparing AAT preparations involved a limited number of participants with AAT deficiency and emphysema. All preparations produced similar increases in the serum AAT concentration and antigenic AAT activity in lung epithelial lining fluid. Data from cohort studies, although limited, indicate that such replacement therapy is associated with a lower rate of decline of forced expiratory volume, thus protecting the lung tissue from further destruction. Safety and effectiveness have not been established in pediatric individuals.

American Thoracic Society guidelines recommend using AAT therapy for individuals with moderate airflow obstruction with a forced expiratory volume in 1 second (FEV<sub>1</sub>) that is 30% to 65% predicted. The guidelines also recommend continuing optimal management of stable individuals with AAT deficiency, which should include many of the interventions recommended for AAT-replete individuals with emphysema.

There may be additional indications contained in the Policy section of this document due to evaluation of criteria highlighted in the Company's off-label policy, and/or review of clinical guidelines issued by leading professional organizations and government entities.

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## Coding

**Inclusion of a code in this table does not imply reimbursement. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.**

**The codes listed below are updated on a regular basis, in accordance with nationally accepted coding guidelines. Therefore, this policy applies to any and all future applicable coding changes, revisions, or updates.**

**In order to ensure optimal reimbursement, all health care services, devices, and pharmaceuticals should be reported using the billing codes and modifiers that most accurately represent the services rendered, unless**

otherwise directed by the Company.

The Coding Table lists any CPT, ICD-10, and HCPCS billing codes related only to the specific policy in which they appear.

CPT Procedure Code Number(s)

N/A

ICD - 10 Procedure Code Number(s)

N/A

ICD - 10 Diagnosis Code Number(s)

Report the most appropriate diagnosis code in support of medically necessary criteria as listed in the policy.

HCPCS Level II Code Number(s)

J0256 Injection, alpha 1 proteinase inhibitor (human), not otherwise specified, 10 mg

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

Revenue Code Number(s)

N/A

#### Policy History

##### Revisions From MA08.050c:

09/16/2025	<p>This version of the policy will become effective 09/16/2025.</p> <p>This policy has been updated to communicate the coverage criteria, in alignment with US Food and Drug Administration (FDA) and National Comprehensive Cancer Network (NCCN).</p> <p>The coverage criteria for the following indications were revised to include clinically evident emphysema as per FDA labeling.</p> <p>All of the ICD-10 CM codes have been removed from this policy, since they are informational. Report the most appropriate diagnosis code in support of medically necessary criteria as listed in the policy.</p>
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##### Revisions From MA08.050b:

03/28/2025	The policy has been reviewed and reissued to communicate the Company's continuing position on alpha 1-antitrypsin therapy (e.g., Prolastin-C®, Aralast NP®, Glassia®, Zemaira®).
05/07/2024	The policy has been reviewed and reissued to communicate the Company's continuing position on alpha 1-antitrypsin therapy (e.g., Prolastin-C®, Aralast NP®, Glassia®, Zemaira®).
09/05/2023	The policy has been reviewed and reissued to communicate the Company's continuing position on alpha 1-antitrypsin therapy (e.g., Prolastin-C®, Aralast NP®, Glassia®, Zemaira®).
06/01/2022	The policy has been reviewed and reissued to communicate the Company's continuing position on alpha 1-antitrypsin therapy (e.g., Prolastin-C®, Aralast NP®, Glassia®, Zemaira®).
11/17/2021	The policy has been reviewed and reissued to communicate the Company's continuing position on alpha 1-antitrypsin therapy (e.g., Prolastin-C®, Aralast NP®, Glassia®, Zemaira®).
01/04/2021	This version of the policy will become effective 01/04/2021. The following criteria have been <b>added</b> to this policy in accordance with the National Comprehensive Cancer Network 03/23/2020: criteria for acute steroid-resistant graft versus host disease in individuals who have undergone a hematopoietic cell transplantation.

##### Revisions From MA08.050a:

03/02/2020	<p>This version of the policy will become effective 03/02/2020.</p> <p>The following criteria have been <b>added</b> to this policy:</p> <ul style="list-style-type: none"> <li>• The individual has a documented diagnosis of congenital alpha1-antitrypsin deficiency confirmed by one of the following: <ul style="list-style-type: none"> <li>○ PiZZ, PiZ(null) or Pi(null)(null) protein phenotypes (homozygous)</li> <li>○ Other rare AAT disease-causing alleles associated with serum alpha1-antitrypsin (AAT) level &lt;11µmol/L</li> </ul> </li> <li>• The Individual must be 18 years or older for Alpha 1-antitrypsin therapy</li> </ul> <p>The following ICD-10 CM code has been <b>deleted</b> from this policy:</p> <p>J43.8 Other emphysema The following HCPCS code has been <b>deleted</b> from this policy:</p> <p>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</p> <p>The following ICD-10 CM code has been <b>added</b> to this policy:</p> <p>J43.9 Emphysema, unspecified</p> <hr/> <p><b>Note:</b> on 01/14/2020 the following revisions were made to this policy in Notification:</p> <p>ICD-10 code will NOT be added to this policy: J43.9 Emphysema, unspecified. This unspecified code will NOT be added and the more specific ICD-10 codes per policy criteria remain.</p> <p>A billing requirement statement has been added to clarify, that for alpha 1-antitrypsin therapy (e.g., Prolastin-C®, Aralast NP™, Glassia™, Zemaira™), both of the following diagnoses are required:</p> <p>E88.01 Alpha-1-antitrypsin deficiency AND J43.1 panlobular emphysema</p>
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**Revisions From MA08.050:**

09/26/2018	This policy has been reissued in accordance with the Company's annual review process.
06/07/2017	This policy has been reissued in accordance with the Company's annual review process.
11/09/2016	This policy has been reviewed and reissued to communicate the Company's continuing coverage of Alpha 1-antitrypsin therapy (eg, Prolastin-C®, Aralast NP™, Glassia™, Zemaira™).
10/14/2015	This policy has been reviewed and reissued to communicate the Company's continuing coverage of Alpha 1-antitrypsin therapy (eg, Prolastin-C®, Aralast NP™, Glassia™, Zemaira™).
01/01/2015	<p>This is a new policy. This policy was posted for notification on 10/01/2014. On 10/02/2014, the policy was updated and contains the following modifications:</p> <p>The title of the policy was changed from Alpha 1-Proteinase Inhibitor Therapy (eg, Prolastin-C®, Aralast™, Aralast NP™, Glassia™, Zemaira™) to Alpha 1-Antitrypsin Therapy (eg, Prolastin-C®, Aralast NP™, Glassia™, Zemaira™).</p> <p>Aralast™ was removed from the policy as the drug is no longer available on the market.</p>

Version Effective Date:

01/04/2021

Version Issued Date:

01/04/2021

Version Reissued Date:

09/16/2025