Pharmacy Management Drug Policy

SUBJECT: Alpha-1 Antitrypsin Therapy (AAT); Alpha-1 Proteinase Inhibitors (Human): Prolastin-C®, Zemaira®, Aralast NP® and Glassia®
POLICY NUMBER: PHARMACY-02
EFFECTIVE DATE: 06/2005
LAST REVIEW DATE: 11/19/2025

If the member's subscriber contract excludes coverage for a specific service or prescription drug, it is not covered under that contract. In such cases, medical or drug policy criteria are not applied. This drug policy applies to the following line/s of business:

Policy Application

Category:	☒ Commercial Group (e.g., EPO, HMO, POS, PPO)	☒ Medicare Advantage
	☒ On Exchange Qualified Health Plans (QHP)	☐ Medicare Part D
	☒ Off Exchange Direct Pay	☒ Essential Plan (EP)
	☒ Medicaid & Health and Recovery Plans (MMC/HARP)	☒ Child Health Plus (CHP)
	☐ Federal Employee Program (FEP)	☐ Ancillary Services
	☒ Dual Eligible Special Needs Plan (D-SNP)	

DESCRIPTION:

Prolastin-C®, Aralast NP®, Zemaira®, and Glassia® are all FDA approved agents for use as replacement therapy in congenital alpha-1 antitrypsin (AAT) deficiency with clinical emphysema**.** AAT deficiency is a hereditary **recessive genetic disorder** that increases the risk of chronic obstructive pulmonary disease (COPD), especially emphysema and chronic bronchitis. People with alpha-1 antitrypsin deficiency are at risk of degeneration of lung function, which may significantly affect quality of life and life expectancy.

AAT protects the delicate tissues of the lung by inhibiting the destructive action of an enzyme called neutrophil elastase. Neutrophil elastase is released by white blood cells, and its primary function is to digest bacteria and other foreign particles in the lungs. When circulating levels of AAT drop below a minimal protective level the alveolar walls are damaged from excess neutrophil elastase.
When a person with AAT deficiency inhales irritants or contracts a lung infection, the neutrophil elastase released in the lungs continues to act uncontrolled, leading to destruction of healthy lung tissue. Patients with this disorder develop early onset panacinar emphysema (i.e., affecting all parts of the lobules). They are also at risk for developing chronic liver disease (hepatitis, cirrhosis), panniculitis (an inflammation of the layer of fat beneath the skin) and vasculitis. AAT deficiency represents about 3% of all emphysema cases reported in the United States.

POLICY:

Based upon our criteria and review of the peer-reviewed literature, treatment with **Prolastin-C®, Aralast NP®**, **Zemaira®, and Glassia®** administered in accordance with FDA guidelines, has been medically proven to be effective and therefore, appropriate if **all** the following criteria are met:

1. Patient must be followed by and have a prescription written by a pulmonologist **AND**
2. Patient must currently be a non-smoker documented by a negative cotinine urine test.
   - If using nicotine replacement products but no longer smoking, then urine anabasine measurements should also be ordered and must be negative **AND**
3. Patient must have one of the high-risk genotypes (such as PiZZ, PiSZ, PiZ(null), Pi(null,null), Pi(malton,malton), Pi(Siiyama,Siiyama)) or a dysfunctional AAT protein (such as PiF or Pi

Pittsburg genotypes) as they are at the greatest risk for developing panacinar emphysema [please see exclusive criteria are if patient has a PiMZ genotype] **AND**

4. Treatment should only be initiated when patient's alpha 1-antitrypsin (AAT) levels are less than 11 micromol/L **OR** <57 mg/dl by nephelometry **AND** have documented evidence of emphysema as FEV1≤ 65% of predicted value.
   - Augmentation therapy is **NOT** recommended for patients without symptomatic emphysema
   - For those who meet the AAT level but have FEV1 > 65%, discussion with pulmonologist regarding potential benefits of therapy with consideration of cost (there is currently lack of evidence for benefit in this group. Factors such as age, rapid decline in FEV1, decreasing diffusing capacity, or progression of emphysema on imaging should be considered) **AND**
5. Patients should demonstrate 1 or more of the following: signs of significant lung disease such as chronic productive cough or unusual frequency of lower respiratory infection, airflow obstruction, accelerated decline of FEV1 or chest radiograph or CT scan evidence of emphysema, especially in the absence of a recognized risk factor (smoking, occupational dust exposure, etc.) **AND**
6. **Prolastin-C is the preferred product.** Patient must have documentation of serious side effects or drug failure with Prolastin-C or have a contraindication to this therapy before treatment with Aralast NP, Zemaira or Glassia will be approved. **This applies to both New Starts (all LOBs, including Medicare) and Recertification requests for non-preferred products (See exception below for Medicare recert requests).**
   - Recertification requests for Medicare Advantage members established on Aralast NP, Zemaira or Glassia will NOT be required to have a trial Prolastin-C
7. Approval dates are based on the patient's contract. Please see chart in the policy guideline
8. Approved dosage for all the drugs listed above is 60mg/kg IV infusion once weekly (Prolastin-C, Glassia, Aralast NP and Zemaira.). Doses higher than this are not recommended by clinical guidelines and therefore will not be covered.

POLICY GUIDELINES:

1. Unless otherwise stated above within the individual drug criteria, approval time periods are listed in the table below.
   - Continued approval at time of recertification will require documentation that the drug is providing ongoing benefit to the patient in terms of improvement or stability in disease state or condition.
2. Clinical documentation must be submitted for each request (initial and recertification) unless otherwise specified (e.g., provider attestation required). Supporting documentation includes, but is not limited to, progress notes documenting previous treatments/treatment history, diagnostic testing, laboratory test results, genetic testing/biomarker results, imaging and other objective or subjective measures of benefit which support continued use of the requested product is medically necessary. Also, ongoing use of the requested product must continue to reflect the current policy's preferred formulary. Recertification reviews may result in the requirement to try more cost-effective treatment alternatives as they become available (i.e., generics, biosimilars, or other guideline supported treatment options). Requested dosing must continue to be consistent with FDA-approved or off-label/guideline-supported dosing recommendations.

GUIDELINES FOR APPROVAL TIME PERIODS

Line of Business	Medical Initial approval	Medical Recertification
Commercial, Exchange, and SafetyNet (Medicaid, HARP, CHP, Essential Plan)	All sites of service – 2 years	All sites of service – 2 years
Medicare	All sites of service – 2 years	All sites of service - 2 years

3. This policy is applicable to drugs that are included on a specific drug formulary. If a drug referenced in this policy is non-formulary, please reference the Coverage Exception Evaluation Policy for All Lines of Business Formularies policy for review guidelines.
4. For contracts where Insurance Law § 4903(c-1), and Public Health Law § 4903(3-a) are applicable, if trial of preferred drug(s) is the only criterion that is not met for a given condition, and one of the following circumstances can be substantiated by the requesting provider, then trial of the preferred drug(s) will not be required.
   - The required prescription drug(s) is (are) contraindicated or will likely cause an adverse reaction or physical or mental harm to the member;
   - The required prescription drug is expected to be ineffective based on the known clinical history and conditions and concurrent drug regimen;
   - The required prescription drug(s) was (were) previously tried while under the current or a previous health plan, or another prescription drug or drugs in the same pharmacologic class or with the same mechanism of action was (were) previously tried and such prescription drug(s) was (were) discontinued due to lack of efficacy or effectiveness, diminished effect, or an adverse event;
   - The required prescription drug(s) is (are) not in the patient's best interest because it will likely cause a significant barrier to adherence to or compliance with the plan of care, will likely worsen a comorbid condition, or will likely decrease the ability to achieve or maintain reasonable functional ability in performing daily activities;
   - The individual is stable on the requested prescription drug. The medical profile of the individual (age, disease state, comorbidities), along with the rational for deeming stability as it relates to standard medical practice and evidence-based practice protocols for the disease state will be taken into consideration.
   - The above criteria are not applicable to requests for brand name medications that have an AB rated generic. We can require a trial of an AB-rated generic equivalent prior to providing coverage for the equivalent brand name prescription drug.
5. Patients **MUST** have clinically demonstrable panacinar emphysema
6. Patients with emphysema due to AAT deficiency should be maintained on regimens similar to those patients with emphysema not associated with AAT deficiency, including: maximum doses of beta-adrenergic bronchodilators, inhaled corticosteroids, anticholinergics and antibiotics, when appropriate. Patients should also have vaccinations against influenza and pneumococcus and supplemental oxygen therapy when indicated.
7. Treatment will only be covered when administered as an IV infusion.
8. Safety and effectiveness in children have not been established
9. This policy does not apply to Medicare Part D and D-SNP pharmacy benefits. The drugs in this policy may apply to all other lines of business including Medicare Advantage.
10. For members with Medicare Advantage, medications with a National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) will be covered pursuant to the criteria outlined by the NCD and/or LCD. NCDs/LCDs for applicable medications can be found on the CMS website at https://www.cms.gov/medicare-coverage-database/search.aspx. Indications that have not been addressed by the applicable medication's LCD/NCD will be covered in accordance with criteria determined by the Health Plan (which may include review per the Health Plan's Off-Label Use of FDA Approved Drugs policy). Step therapy requirements may be imposed in addition to LCD/NCD requirements.
11. All requests will be reviewed to ensure they are being used for an appropriate indication and may be subject to an off-label review in accordance with our Off-Label Use of FDA Approved Drugs Policy (Pharmacy-32).

12. All utilization management requirements outlined in this policy are compliant with applicable New York State insurance laws and regulations. Policies will be reviewed and updated as necessary to ensure ongoing compliance with all state and federally mandated coverage requirements.
13. Manufacturers may either discontinue participation in, or may not participate in, the Medicaid Drug Rebate Program (MDRP). Under New York State Medicaid requirements, physician-administered drugs must be produced by manufacturers that participate in the MDRP. Products made by manufacturers that do not participate in the MDRP will not be covered under Medicaid Managed Care/HARP lines of business. Drug coverage will not be available for any product from a non-participating manufacturer. For a complete list of New/Reinstated & Terminated Labelers please visit: https://www.medicaid.gov/medicaid/prescriptiondrugs/medicaid-drug-rebate-program/newreinstated-terminated-labeler-information/index.html

EXCLUSIVE CRITERIA:

The use of alpha-1 Antitrypsin therapy will not be covered in any of the following situations:
1. Active smokers
2. Current non-smokers who start smoking after initial approval can be denied further treatment
3. Treatment of cystic fibrosis
4. Liver transplant recipients
5. Treatment of liver disease due to alpha-1 Antitrypsin deficiency
6. Augmentation therapy in general will not be granted for PiMZ heterozygotes or homozygous normal genotype (i.e., PiMM). Please note, commercial genotyping may identify a PiZ(null) heterozygote as PiMZ, because in the absence of an S or Z allele, most laboratories will assume the second allele is M. If a patient with a documented PiMZ genotype and has an unusually low AAT level, this possibility should be considered.

CODES:

Eligibility for reimbursement is based upon the benefits set forth in the member's subscriber contract. CODES MAY NOT BE COVERED UNDER ALL CIRCUMSTANCES. PLEASE READ THE POLICY AND GUIDELINES STATEMENTS CAREFULLY.

Codes may not be all inclusive as the AMA and CMS code updates may occur more frequently than policy updates.

Code Key:
Experimental/Investigational = (E/I),
Not medically necessary/ appropriate = (NMN).

HCPCS:
J0256: Aralast NP, Prolastin-C, Zemaira 10mg per unit
J0257: Glassia 10mg per unit

Unit Threshold = 700

UPDATES:

Date:	Revision:
11/19/2025	Revised
05/08/2025	Reviewed / P&T Committee Approval

03/06/2025	Revised
11/21/2024	Revised
08/21/2024	Revised
06/20/2024	Revised
05/09/2024	Reviewed / P&T Committee Approval
05/11/2023	Reviewed / P&T Committee Approval
3/23	Revised
5/22	Reviewed / P&T Committee Approval
9/21	Revised
5/21	P&T Committee Approval
8/20	Revised
5/20	P&T Committee Approval
3/20	Revised
5/19	P&T Committee Approval
9/18	Revised
9/17	P&T Committee Approval
9/16	Revised
12/15	Revised
1/15	Revised
8/13	Revised
5/13	Revised
3/13	Revised
11/11	Revised
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7/09	Revised
5/08	Revised
9/07	Revised
10/06	Revised
9/05	Revised
8/06	Revised
6/05	Created

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