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# CONCERT GENETICS GENETIC TESTING: LUNG DISORDERS

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See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

## OVERVIEW

One of the most common forms of inherited lung disorders is alpha-1 antitrypsin deficiency (AATD). AATD is an autosomal recessive genetic disorder that results in decreased production of the alpha-1 antitrypsin (AAT) protein, or production of abnormal types of the protein that are functionally deficient. Individuals with AATD have an increased risk to develop lung and liver disease. Genetic testing to diagnose AATD aids in directing proper treatment and identifying at-risk family members.

## POLICY REFERENCE TABLE

### Coding Implications

This clinical policy references Current Procedural Terminology (CPT®). CPT® is a registered trademark of the American Medical Association. All CPT codes and descriptions are copyrighted 2022, American Medical Association. All rights reserved. CPT codes and CPT descriptions are from the current manuals and those included herein are not intended to be all-inclusive and are included for informational purposes only. Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

Please see the [Concert Genetics Platform](#) for a comprehensive list of registered tests.

<a href="#">Criteria Sections</a>	Example Tests (Labs)	Common CPT Codes	Common ICD Codes	<a href="#">Ref</a>
<a href="#">Alpha-1 Antitrypsin Deficiency</a>				
<a href="#">SERPINA1 Known Familial Variant Analysis</a>	SERPINA1 Targeted Variant Analysis (PreventionGenetics, part of Exact Sciences)	81403	E88.01	5
<a href="#">SERPINA1 Common Variant Analysis or Sequencing and/or Deletion/Duplication Analysis</a>	Alpha-1 Antitrypsin (AAT) Mutation Analysis (Quest Diagnostics)	81332	E88.01	1
	SERPINA1 Full Gene Sequencing and Deletion/Duplication (Invitae)	81479		
<a href="#">Other Covered Lung Disorders</a>				
<a href="#">Other Covered Lung Disorders</a>	See list below	81400-81408		2, 3, 4

## OTHER RELATED POLICIES

This policy document provides criteria for Genetic Testing for Lung Disorders. Please refer to:

- **Genetic Testing: Multisystem Inherited Disorders, Intellectual Disability, and Developmental Delay** for criteria related to diagnostic testing for cystic fibrosis and other multisystem inherited disorders.
- **Genetic Testing: General Approach to Genetic and Molecular Testing** for criteria related to genetic testing for lung disorders and disease that are not specifically discussed in this or another non-general policy.

## CRITERIA

It is the policy of health plans affiliated with Centene Corporation® that the specific genetic testing noted below is **medically necessary** when meeting the related criteria:

### ALPHA-1 ANTITRYPSIN DEFICIENCY

#### *SERPINA1* Known Familial Variant Analysis

- I. *SERPINA1* targeted variant analysis for a known familial variant (81332, 81403) is considered **medically necessary** when:
  - A. The member/enrollee has a [close relative](#) with a known pathogenic or likely pathogenic variant in *SERPINA1*.
- II. *SERPINA1* targeted variant analysis for a known familial variant (81332, 81403) is considered **investigational** for all other indications.

#### *SERPINA1* Common Variant Analysis or Sequencing and/or Deletion/Duplication Analysis

- I. *SERPINA1* common variant analysis (81332) or sequencing and/or deletion/duplication analysis (81479) to establish a diagnosis of alpha-1 antitrypsin (AAT) deficiency is considered **medically necessary** when:
  - A. The member/enrollee has abnormally low (less than 120 mg/dL) or borderline (90-140 mg/dL) alpha-1 antitrypsin levels (as measured by nephelometry), **AND**
  - B. Any of the following:
    1. Early-onset emphysema (45 years of age or younger), **OR**
    2. Emphysema in the absence of additional risk factor (e.g., smoking, occupational dust exposure), **OR**
    3. Emphysema with prominent basilar hyperlucency, **OR**
    4. Otherwise unexplained liver disease, **OR**
    5. Necrotizing panniculitis, **OR**
    6. C-ANCA positive vasculitis (i.e., granulomatosis with polyangiitis), **OR**
    7. Bronchiectasis without evident etiology, **OR**
    8. A sibling with known AAT deficiency.

- II. *SERPINA1* common variant analysis (81332) or sequencing and/or deletion/duplication analysis (81479) to establish a diagnosis of alpha-1 antitrypsin deficiency is considered **investigational** for all other indications.

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## OTHER COVERED LUNG DISORDERS

The following is a list of conditions that have a known genetic association. Due to their relative rareness, it may be appropriate to cover these genetic tests to establish or confirm a diagnosis.

- I. Genetic testing to establish or confirm one of the following genetic lung disorders to guide management is considered **medically necessary** when the member/enrollee demonstrates clinical features\* consistent with the disorder (the list is not meant to be comprehensive, see II below):
  - A. [Familial Pulmonary Fibrosis](#)
  - B. [Primary Ciliary Dyskinesia](#)
  - C. Pulmonary lymphangiomyomatosis (LAM)
  - D. Pulmonary alveolar proteinosis (PAP)
- II. Genetic testing to establish or confirm the diagnosis of all other lung disorders not specifically discussed within this or another medical policy will be evaluated by the criteria outlined in *General Approach to Genetic and Molecular Testing* (see policy for criteria).

\*Clinical features for a specific disorder may be outlined in resources such as [GeneReviews](#), [OMIM](#), [National Library of Medicine](#), [Genetics Home Reference](#), or other scholarly source.

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## NOTES AND DEFINITIONS

1. **Close relatives** include first, second, and third degree blood relatives:
  - a. **First-degree relatives** are parents, siblings, and children
  - b. **Second-degree relatives** are grandparents, aunts, uncles, nieces, nephews, grandchildren, and half siblings

- c. **Third-degree relatives** are great grandparents, great aunts, great uncles, great grandchildren, and first cousins

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## BACKGROUND AND RATIONALE

### ALPHA-1 ANTITRYPSIN DEFICIENCY

#### ***SERPINA1* Known Familial Variant Analysis**

##### *Genetic Support Foundation*

The Genetic Support Foundation's Genetics 101 information on genetic testing says the following about testing for familial pathogenic variants:

Genetic testing for someone who may be at risk for an inherited disease is always easier if we know the specific genetic cause. Oftentimes, the best way to find the genetic cause is to start by testing someone in the family who is known or strongly suspected to have the disease. If their testing is positive, then we can say that we have found the familial pathogenic (harmful) variant. We can use this as a marker to test other members of the family to see who is also at risk.

#### ***SERPINA1* Common Variant Analysis or Sequencing and/or Deletion/Duplication Analysis**

##### *American Thoracic Society and European Respiratory Society*

The American Thoracic Society and European Respiratory Society published a joint statement on the diagnosis and management of individuals with alpha-1 antitrypsin deficiency (2003) which provided recommendations for diagnostic testing.

A normal range of plasma alpha-1 antitrypsin (measured via nephelometry) is 83/120 - 200/220 mg/dL. Individuals with borderline normal levels of plasma alpha-1 antitrypsin (90-140 mg/dL) or with abnormally low levels (below 120 mg/dL) should be evaluated for alpha-1 antitrypsin deficiency. (p. 826)

“The following features should prompt suspicion by physicians that their patient may be more likely to have AAT deficiency:

- Early-onset emphysema (age of 45 years or less)

- Emphysema in the absence of a recognized risk factor (smoking, occupational dust exposure, etc.)
- Emphysema with prominent basilar hyperlucency
- Otherwise unexplained liver disease
- Necrotizing panniculitis
- Anti-proteinase 3-positive vasculitis (C-ANCA [anti-neutrophil cytoplasmic antibody]-positive vasculitis)
- Family history of any of the following: emphysema, bronchiectasis, liver disease, or panniculitis
- Bronchiectasis without evident etiology...” (p. 820)

The statement also recommended that individuals with a sibling with AAT deficiency should also be offered genetic testing. (p. 827)

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Reviews, Revisions, and Approvals	Revision Date	Approval Date
Policy developed.	03/23	03/23
Semi-annual review. Updated title to reflect V1.2024 version. Overview, coding, reference-table, background and references updated. Throughout policy: replaced “coverage criteria” with “criteria. For Policy Reference Table: under “SERPINA1 Common Variant...” added “E88.01”. For Background and Rationale; under “SERPINA1 Known Familial Variant Analysis: replaced “inheritance patterns” with “genetic testing”.	10/23	10/23

## REFERENCES

1. American Thoracic Society; European Respiratory Society. American Thoracic Society/European Respiratory Society statement: standards for the diagnosis and management of individuals with alpha-1 antitrypsin deficiency. *Am J Respir Crit Care Med.* 2003;168(7):818-900. doi:10.1164/rccm.168.7.818
2. Adam MP, Ardinger HH, Pagon RA, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2023. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK1116/>
3. Online Mendelian Inheritance in Man, OMIM®. McKusick-Nathans Institute of Genetic Medicine, Johns Hopkins University (Baltimore, MD). World Wide Web URL: <https://omim.org/>

4. MedlinePlus [Internet]. Bethesda (MD): National Library of Medicine (US). Available from: <https://medlineplus.gov/genetics/>.
5. Genetic Support Foundation. Genetics 101 Genetic Testing: Familial Pathogenic Variant. Accessed 10/4/2022. <https://geneticsupportfoundation.org/genetics-101/#>

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### **Important Reminder**

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members/enrollees. This clinical policy is not intended to

recommend treatment for members/enrollees. Members/enrollees should consult with their treating physician in connection with diagnosis and treatment decisions.

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**Note: For Medicaid members/enrollees**, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

**Note: For Medicare members/enrollees**, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs, and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Refer to the CMS website at <http://www.cms.gov> for additional information.

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