CONCERT GENETIC TESTING: LUNG DISORDERS

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

Below is a list of higher volume tests and the associated laboratories for each coverage criteria section. This list is not all inclusive.

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.
## Coverage Criteria

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## OTHER RELATED POLICIES

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

- **Genetic Testing: Multisystem Inherited Disorders, Intellectual Disability, and Developmental Delay** for coverage criteria related to diagnostic testing for cystic fibrosis and other multisystem inherited disorders.

- **Genetic Testing: General Approach to Genetic Testing** for coverage 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:
CONCERT GENETIC TESTING: LUNG DISORDERS

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 to 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.
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 lymphangioleiomyomatosis (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 Testing (see policy for coverage 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.

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
BACKGROUND AND RATIONALE

Alpha-1 Antitrypsin Deficiency - *SERPINA1* Known Familial Variant Analysis

**Genetic Support Foundation**

The Genetic Support Foundation’s Genetics 101 information on inheritance patterns 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/enrollees of the family to see who is also at risk.

Alpha-1 Antitrypsin Deficiency - *SERPINA1* Common Variant Analysis or Sequencing and/or Deletion/Duplication Analysis

**American Thoracic Society and European Respiratory Society**


A normal range of plasma alpha-1 antitrypsin (measured via nephelometry) is 83/120 to 200/220 mg/dL. Individuals with borderline normal levels of plasma alpha-1 antitrypsin (90 to 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)

### REFERENCES


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/](https://omim.org/)


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](http://www.cms.gov) for additional information.

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