GENETIC TESTING: LUNG DISORDERS (REQUIRES PREAUTHORIZATION)

V.70

V.70 GENETIC TESTING: LUNG DISORDERS (REQUIRES PREAUTHORIZATION)

DESCRIPTION

One of the most common forms of inherited lung disorders is alpha-1 antitrypsin deficiency (AATD), which 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 for lung and liver disease to develop. Genetic testing to diagnose AATD aids in directing proper treatment and identifying at-risk family members.

With the use of donor-derived cell-free DNA (dd-cfDNA), biomarker tests have been developed as an alternative to more invasive procedures for post-lung transplant care to optimize graft longevity while avoiding side effects and toxicity of immunosuppressive therapies.

Dates

Original Effective
04-20-2021
Last Review
08-07-2024
Next Review
08-11-2025

REFERENCE TABLE

The tests, associated laboratories, CPT codes, and ICD codes contained within this document serve only as examples to help users

registered tests.

Coverage Criteria Sections	Example Tests (Labs)	Common CPT Codes	Common ICD Codes	
Alpha-1 Antitrypsin Deficiency				
SERPINA1 Common Variant Analysis or Sequencing and/or Deletion/Duplication Analysis	Alpha-1 Antitrypsin (AAT) Mutation Analysis (Quest Diagnostics)	81332	E88.01	
	SERPINA1 Full Gene Sequencing and Deletion/Duplication (Invitae)	81479		
Donor-Derived Cell-free DNA for Lung Transplant Rejection				
Evidence-Based Donor-Derived Cell-free DNA for Lung Transplant Rejection	Prospera Lung (Natera)	81479	T86.810, Z48.24, Z94.2	
	AlloSure Lung (CareDx)	0540U		
Emerging Evidence Donor-Derived Cell-free DNA for Lung Transplant Rejection	Eurofins TRAC dd-cfDNA (Transplant Genomics Inc)	0118U		
Other Covered Lung Disorders				
Other Covered Lung Disorders	See list below	81400-81408		

RELATED POLICIES

V.62 Genetic Testing: Multsystem Inherited Disorders, Intellectual Disability, and Developemental Delay for coverage criteria related to diagnostic testing for cystic fibrosis and other multisystem inherited disorders.

V.74 Genetic Testing: General Approach to Genetic and Molecular 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, including known familial variant testing.

BlueCross BlueShield Nebraska

ALPHA-1 ANTITRYPSIN DEFICIENCY

SERPINA1 Known Familial Variant Analysis

I. *SERPINA1* targeted variant analysis for a known familial variant (81332, 81403) may be considered **scientifically validated** when:
   A. The member 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** when the above criteria is not met and 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 may be considered **scientifically validated** when:

A. The member 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.

above criteria are not met and for all other indications.

DONOR-DERIVED CELL-FREE DNA FOR LUNG TRANSPLANT REJECTION

Evidence-Based Donor-Derived Cell-free DNA for Lung Transplant Rejection

I. The use of peripheral blood measurement of donor-derived cell-free DNA tests (81479 0540U) with sufficient evidence of clinical utility and validity in the management of patients after lung transplantation is considered **medically necessary** when:

A.The member has undergone lung transplantation, **AND**

B.The test has not been performed in the last 12 months, **AND**

C.The member meets at least one of the following:

1.The member has clinical signs of acute rejection, **OR**

2.A biopsy was done and is inconclusive for rejection, **OR**

3.The member is being monitored for adequate immunosuppression.

II.The use of peripheral blood measurement of donor-derived cell-free DNA tests (81479) in the management of patients after lung transplantation is considered **investigational** for all other indications.

Emerging Evidence Donor-Derived Cell-free DNA for Lung Transplant Rejection

I. Donor-derived cell-free DNA tests with insufficient evidence of clinical validity (0118U) in the management of patients after lung transplantation are considered**investigational.**

OTHER COVERED LUNG DISORDERS

I. Genetic testing to establish or confirm one of the following genetic lung disorders to guide management may be considered **scientifically validated** when the member 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.

BACKGROUND

ALPHA-1 ANTITRYPSIN DEFICIENCY

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 and 827)

“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)

-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)

DONOR-DERIVED CELL-FREE DNA FOR LUNG TRANSPLANT REJECTION

Evidence-Based Donor-Derived Cell-free DNA for Lung Transplant Rejection

Centers for Medicare and Medicaid Services

The CMS local coverage determination (LCD) entitled "MolDX: Molecular Testing for Solid Organ Allograft Rejection" states the following regarding donor-derived cell-free DNA tests in individuals who have had solid organ transplantation:

"This Medicare contractor will provide limited coverage for molecular diagnostic tests used in the evaluation and management of patients who have undergone solid organ transplantation. These tests can inform decision making along with standard clinical assessments in their evaluation of organ injury for active rejection (AR).

These tests may be ordered by qualified physicians considering the diagnosis of AR affiliated with a transplant center, helping to rule in or out this condition when assessing the need for or results of a diagnostic biopsy. They should be considered along with other clinical evaluations and results and may be particularly useful in patients with significant contraindications to invasive procedures.

The intended use of the test must be:

-To assist in the evaluation of adequacy of immunosuppression, wherein a non-invasive or minimally invasive test can be used in lieu of a tissue biopsy in a patient for whom information from a tissue biopsy would be used to make a management decision regarding immunosuppression, OR
-As a rule-out test for AR in validated populations of patients with clinical suspicion of rejection with a non-invasive or minimally

rejection after a physician-assessed pretest, OR
-To assess rejection status in patients that have received a biopsy, but the biopsy results are inconclusive or limited by insufficient material."

Concert Note

For monitoring patients post lung transplantation, absent clear, specific and evidence-based guideline recommendations for a particular regimen of screening, a default frequency of once every 12 months will be adopted.

Quick Code Search

Use this feature to find out if a procedure and diagnosis code pair will be approved, denied or held for review. Simply put in the procedure code, then the diagnosis code, then click "Add Code Pair". If the codes are listed in this policy, we will help you by showing a dropdown to help you.

Procedure

Please type a procedure code

Enter at least the first 3 characters of the code

Diagnosis

Please type a diagnosis code

Enter at least the first 3 characters of the code

Add

CODES

+ **CPT-PLA**

+ **CPT4**

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REVISIONS

01-01-2025
Added criteria for donor derived cell-free DNA tests. Updated background and references.

01-01-2024
Updated Background and References.

09-29-2023
Removed "medically necessary" and replaced with "scientifically validated" and also added "investigational when the above criteria are not met and for all other indications"

06-01-2023
Minor changes (formatting) made to policy for 07/01/2023

01-01-2023
Minor changes to policy and updated references

06-14-2022
No changes made to content.

05-10-2022
Added 81222 & 81223

01-01-2022
Separated out targeted mutation analysis, common variant analysis and sequencing.

Cross® and Blue Shield® brand names within the state of Nebraska.