Dean Health Plan Coverage Policy

Policy Name:	**GENETIC TESTING: LUNG DISORDERS MP9599**
Effective Date:	**January 01, 2025**

Important Information – Please Read Before Using This Policy

These services may or may not be covered by Dean Health Plan. Coverage is subject to requirements in applicable federal or state laws. Please refer to the member's plan document for other specific coverage information. If there is a difference between this general information and the member's plan document, the member's plan document will be used to determine coverage. With respect to Medicare, Medicaid, and other government programs, this policy will apply unless these programs require different coverage.

Members may contact Dean Health Plan Customer Service at the phone number listed on their member identification card to discuss their benefits more specifically. Providers with questions about this medical policy see Provider Communications for additional information. https://deancare.com/Providers/Provider-communications

Dean Health Plan medical policies are not medical advice. Members should consult with appropriate health care providers to obtain needed medical advice, care and treatment.

OVERVIEW

One of the most common 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.
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.

POLICY REFERENCE TABLE

The tests, associated laboratories, CPT codes, and ICD codes contained within this document serve only as examples to help users navigate claims and corresponding coverage criteria; as such, they are not comprehensive and are not a guarantee of coverage or non-coverage. Please see the Concert Platform for a comprehensive list of registered tests.

Use the current applicable CPT/HCPCS code(s). The following codes are included below for informational purposes only and are subject to change without notice. Inclusion or exclusion of a code does not constitute or imply member coverage or provider reimbursement.

Dean Health Plan Coverage Policy

Coverage Criteria Sections	Example Tests (Labs)	Common CPT Codes	Common ICD Codes	Ref
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	1
	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	5
	AlloSure Lung (CareDx)			
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		2, 3, 4

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 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.

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COVERAGE CRITERIA

ALPHA-1 ANTITRYPSIN DEFICIENCY

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 has any of the following:

1. Abnormally low (less than 120 mg/dL) or borderline (90-140 mg/dL) alpha-1 antitrypsin levels (as measured by nephelometry), **OR**
2. Early-onset emphysema (45 years of age or younger), **OR**
3. Emphysema in the absence of additional risk factor (e.g., smoking, occupational dust exposure), **OR**
4. Emphysema with prominent basilar hyperlucency, **OR**
5. Otherwise unexplained liver disease, **OR**
6. Necrotizing panniculitis, **OR**
7. C-ANCA positive vasculitis (i.e., granulomatosis with polyangiitis), **OR**
8. Bronchiectasis without evident etiology, **OR**
9. 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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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) 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

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 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 and Molecular 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.

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PRIOR AUTHORIZATION

Prior authorization is not required. However, services with specific coverage criteria may be reviewed retrospectively to determine if criteria are being met. Retrospective denial may result if criteria are not met.

BACKGROUND AND RATIONALE

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)
- 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)

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 invasive test to make a clinical decision regarding obtaining a biopsy, OR
- For further evaluation of allograft status for the probability of allograft 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.

Emerging Evidence Donor-Derived Cell-free DNA for Lung Transplant Rejection
Tests that have limited established clinical utility or validity as defined in the Concert policy for General Approach to Genetic and Molecular testing do not meet the threshold for coverage. Evidence for validity may include a Technology Assessment conducted by an independent third party (e.g.MolDx Tech, ECRI, Optum Genomic) and/or evidence-based guidelines published by professional societies. Such evidence was not identified for the tests referenced by this policy.

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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; 1993-2024. 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. Centers for Medicare & Medicaid Services. Medicare Coverage Database: Local Coverage Determination. MolDX: Molecular Testing for Solid Organ Allograft Rejection (L38582). Available at: https://www.cms.gov/medicare-coverage-database/view/lcd.aspx?lcdid=38582

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Note: The Health Plan uses the genetic testing clinical criteria developed by Concert Genetics, an industry-leader in genetic testing technology assessment and policy development.

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