

# Genetic Testing for Cystic Fibrosis

Policy Number: PG0387  
Last Review: 06/26/2019



**IMPORTANT | Paramount medical policies only apply to Paramount Advantage Medicaid claims with dates of service before Feb. 1, 2023.** Please contact Anthem, for Medicaid claims with dates of service on or after Feb. 1, 2023.

## GUIDELINES

- This policy does not certify benefits or authorization of benefits, which is designated by each individual policyholder terms, conditions, exclusions and limitations contract. It does not constitute a contract or guarantee regarding coverage or reimbursement/payment. Self-Insured group specific policy will supersede this general policy when group supplementary plan document or individual plan decision directs otherwise.
- Paramount applies coding edits to all medical claims through coding logic software to evaluate the accuracy and adherence to accepted national standards.
- This medical policy is solely for guiding medical necessity and explaining correct procedure reporting used to assist in making coverage decisions and administering benefits.

## SCOPE

- ☒ Professional  
☒ Facility

## DESCRIPTION

Cystic fibrosis (CF) is an autosomal recessive genetic disorder (i.e., an individual needs to inherit a copy of a pathogenic CFTR variant from both parents in order to have the disease). It is characterized by impairment in the transport of chloride and sodium across cell membranes, which can result in an imbalance of water absorption, thereby causing dehydration. The liquid depletion results in the presence of thick and sticky mucus that causes blockage of ducts and tubes in various organs, including the lungs, pancreas, liver, and intestines.

Some individuals may be diagnosed with *CFTR*-Related Disorder (CRD) when they have a clinical feature suggestive of CF such as pancreatitis, chronic sinusitis, or absence of the vas deferens but do not meet diagnostic criteria for CF. Individuals with *CFTR*-Related Disorder may have an intermediate or normal sweat chloride test and fewer than 2 *CFTR* mutations. Additionally, some individuals may be diagnosed with *CFTR*-Related Metabolic Syndrome (CRMS) when they have a positive newborn screening test but are asymptomatic and have inconclusive diagnostic workup.

CF affects approximately 30,000 individuals in the United States, and 70,000 worldwide. While the overall birth prevalence in the United States is approximately 1 in 3500, prevalence rates vary by ethnicity, with whites having the highest rates at 1 in every 3000 births. Lower prevalence is observed in Asian Americans (1 in 35,000), African Americans (1 in 15,000), Hispanic Americans (ranging from 1 in 9200 to 1 in 13,500), and Native Americans (1 in 10,900). With improved treatments, the life expectancy in individuals with CF continues to increase. In 2017 the predicted median survival was estimated to be 43.6 years. While CF affects males and females equally, males have a greater median survival.

A majority of CF treatments target CF symptoms and include pancreatic enzyme supplements for pancreatic-insufficient patients, antibiotics to reduce infections, and medications that alter mucus consistency. CF is caused by presence of a pathogenic variant on both copies (i.e. two mutations) of the cystic fibrosis transmembrane conductance regulator (ATP-binding cassette sub-family C, member 7) (*CFTR*) gene. Pathogenic variants in this gene result in impairment of the *CFTR* protein, which serves as a chloride channel allowing transport of chloride

and sodium through the cell membrane. More than 1900 variants have been described in the *CFTR* gene. However, most of these pathogenic variants are rare and their functional role has not been elucidated.

Genetic testing for *CFTR* has a number of different applications, which include carrier testing and screening, prenatal diagnosis, preimplantation genetic diagnosis (PGD), newborn screening, and identification of individuals who will benefit from specific drug therapies. A number of clinical laboratories in the United States offer genetic testing for *CFTR*. Laboratories typically offer a panel of 23-25 common *CFTR* mutations that is recommended by the American College of Medical Genetics (ACMG), as well as testing for additional variants depending upon the laboratory. Full gene sequencing, deletion/duplication analysis, and targeted testing for known familial variants are also available.

## **POLICY**

### **Paramount Commercial Insurance Plans, Medicare Advantage Plans, and Paramount Advantage Medicaid**

**Effective 10/1/2019, Genetic testing (CFTR gene) for cystic fibrosis (CF) (81220-81224) requires prior authorization for all product lines.**

## **COVERAGE CRITERIA**

### **Paramount Commercial Insurance Plans, Medicare Advantage Plans, and Paramount Advantage Medicaid**

Pre-test genetic counseling (as well as post-test genetic counseling) is recommended when considering genetic testing related to carrier status. Documentation of pre-test genetic counseling is required for coverage of carrier screening.

Pre-test genetic counseling should address the following topics (ACMG, 2008):

- A general description of the disorder(s) offered in the carrier screen
- Discussion of variable expressivity and incomplete penetrance if applicable
- Discussion of residual risk in light of a negative screening result
- A description of what it means to be a “carrier”
- Carrier screening is voluntary; Informed consent must be obtained.
- Informed consent includes discussion of confidentiality, discrimination (i.e. discussion of the Genetic Information Non-Discrimination Act, and applicable state laws), potential psychosocial issues, and economic considerations.

Post-test genetic counseling should address the following topics with a positive carrier screening result:

- Discussion of findings- what the individual is a carrier of, description of the condition, and discussion of risk to fetus or future pregnancies
- Possible reproductive options
- Implications for family members; encouragement to share information with family members

Post-test genetic counseling should address residual risk after a negative carrier screening test.

If obstetric care providers are uncomfortable providing genetic counseling related to carrier screening, referral to a certified genetics professional (such as a genetic counselor) is warranted.

Preconception or prenatal carrier testing for Cystic Fibrosis (CF) with a targeted mutation analysis (23-25 mutations) as recommended by the American College of Medical Genetics (ACMG) is considered medically necessary for a parent or prospective parent.

For individuals seeking carrier testing, and who have a family history of CF, genetic testing for the known familial mutation is considered medically necessary. If the familial mutation is unknown, the targeted mutations panel (ACMG) is medically necessary.

- If both partners have the targeted mutations panel (ACMG) and one partner (who is related to an individual with CF) is negative, but the other reproductive partner tests positive for a *CFTR* mutation, expanded screening (*CFTR* sequencing followed by deletion/duplication studies [if sequencing is negative]) is medically necessary for the partner who previously tested negative.
- If both partners have the targeted mutations panel (ACMG) and the partner (who is not related to an

individual with CF) is negative, but the partner who is related to an individual is positive, further expanded screening (CFTR sequencing followed by deletion/duplication studies [if sequencing is negative]) may be considered for the partner who previously screened negative if they are of an ethnic/geographic background associated with a lower detection rate on the targeted mutations panel (e.g. African American, Asian, Hispanic populations, etc).

- If the partner with a known familial mutation tests negative for the familial mutation, a targeted mutations panel (ACMG) is medically necessary.
- If the partner with a known familial mutation test positive (for either the known familial mutation or a mutation from the targeted panel), the targeted mutation panel (ACMG) is warranted for the other reproductive partner, however if they are of an ethnic/geographic background associated with a lower detection rate on the ACMG panel, sequencing followed by deletion/duplication studies [if sequencing is negative] for CFTR is medically necessary.

Expanded CFTR genetic testing (sequencing followed by deletion/duplication studies [if sequencing is negative]) is considered medically necessary for:

- The reproductive partner of an individual with CF
- The reproductive partner of an individual whom is a known CF carrier
- The reproductive partner of an individual with congenital bilateral absence of vas deferens (CBAVD)
- A man with CBAVD

For individuals being considered for diagnostic cystic fibrosis genetic testing due to:

- Signs/symptoms of Cystic Fibrosis and sweat chloride test is positive, intermediate, or inconclusive

The targeted mutation panel (ACMG) is medically necessary, and if negative (or if 1 mutation is only found), sequencing followed by duplication/deletion studies (if sequencing is negative) are considered medically necessary.

CFTR sequence analysis followed by deletion/duplication analysis is medically necessary as the initial diagnostic test for:

- Individuals of an ethnic/geographic background where the detection rate on the targeted mutations panel (ACMG) is low
- Prenatal testing for a high-risk fetus
- Prenatal testing in a low-risk fetus with an echogenic bowel identified on prenatal ultrasound examination
- An infant with an elevated IRT assay on newborn screening and an intermediate result on sweat chloride testing
- A symptomatic infant (e.g. with meconium ileus) who is too young to provide adequate volumes of sweat

CFTR sequence analysis is medically necessary for the determination of genotype for treatment with Kalydeco (ivacaftor) or Orkambi (lumacaftor/ivacaftor) in an individual with CF

CFTR intron 8 poly-T analysis when the following criteria are met:

- Individual diagnosed with CFTR-related metabolic syndrome or CFTR-related disorders (not classic CF); OR
- Male diagnosed with CBAVD; OR
- R117H mutation detected on CF standard or expanded genetic testing

Genetic testing for cystic fibrosis (CF) is non-covered for any indication or test other than those listed above including, but may not limited to, the following:

- An at-risk (unaffected) individual or affected individual when a family member has been tested for mutations and received a result of VUS (also known as unclassified variant or variant of uncertain significance)
- Direct-to-consumer (DTC) genetic testing
- Parental carrier screening when affected child has a positive CF newborn screening result

## CODING/BILLING INFORMATION

The inclusion or exclusion of a code in this section does not necessarily indicate coverage. Codes referenced in this clinical policy are for informational purposes only.

Codes that are covered may have selection criteria that must be met.

Payment for supplies may be included in payment for other services rendered.

CPT CODES	
81220	CFTR (cystic fibrosis transmembrane conductance regulator) (e.g., cystic fibrosis) gene analysis; common variants (e.g., ACMG/ACOG guidelines)
81221	CFTR (cystic fibrosis transmembrane conductance regulator) (e.g., cystic fibrosis) gene analysis; known familial variants
81222	CFTR (cystic fibrosis transmembrane conductance regulator) (e.g., cystic fibrosis) gene analysis; duplication/deletion variants
81223	CFTR (cystic fibrosis transmembrane conductance regulator) (e.g., cystic fibrosis) gene analysis; full gene sequence
81224	CFTR (cystic fibrosis transmembrane conductance regulator) (e.g., cystic fibrosis) gene analysis; intron 8 poly-T analysis (e.g., male infertility)

## REVISION HISTORY EXPLANATION

### ORIGINAL EFFECTIVE DATE: 07/26/2018

Date	Explanation & Changes
07/26/2018	<ul style="list-style-type: none"><li>Genetic testing (CFTR gene) for cystic fibrosis (CF) (81220-81224) does not require prior authorization when determined to be medically necessary as the medical criteria and guidelines in the policy are met</li><li>Policy created to reflect most current clinical evidence per The Technology Assessment Working Group (TAWG)</li></ul>
06/26/2019	<ul style="list-style-type: none"><li>Genetic testing (CFTR gene) for cystic fibrosis (CF) (81220-81224) does require prior authorization when determined to be medically necessary as the medical criteria and guidelines in the policy are met</li><li>Testing criteria were updated. Policy updated to reflect most current clinical evidence</li></ul>
07/25/2019	<ul style="list-style-type: none"><li>Verbiage clarification within the Green Box of the policy</li><li>Deleted the information about meeting criteria and medical necessity and indicated "Genetic testing for cystic fibrosis requires prior authorization for all product lines" thus following standard documentation</li></ul>
12/28/2020	<ul style="list-style-type: none"><li>Medical policy placed on the new Paramount Medical policy format</li></ul>
03/01/2023	<ul style="list-style-type: none"><li>Medical Policy updated to reflect Medicaid coverage to Anthem as of 02/01/2023</li></ul>

**Paramount reserves the right to review and revise our policies periodically when necessary. When there is an update, we will publish the most current policy to**

**<https://www.paramounthealthcare.com/services/providers/medical-policies/> .**

## REFERENCES/RESOURCES

Centers for Medicare and Medicaid Services, CMS Manual System and other CMS publications and services

Ohio Department of Medicaid

American Medical Association, *Current Procedural Terminology (CPT®)* and associated publications and services

Centers for Medicare and Medicaid Services, Healthcare Common Procedure Coding System, HCPCS Release and Code Sets

U.S. Preventive Services Task Force, <http://www.uspreventiveservicestaskforce.org/>  
Industry Standard Review

Hayes, Inc.

Industry Standard Review

Ong, T, et al, GeneReviews®, Cystic Fibrosis and Congenital Absence of the Vas Deferens,  
<https://www.ncbi.nlm.nih.gov/books/NBK1250/>

Cystic Fibrosis Foundation, Diagnosis of Cystic Fibrosis: Consensus Guidelines from the Cystic Fibrosis Foundation, 2017

The American College of Medical Genetics (ACMG), Cystic Fibrosis Population Carrier Screening: 2004 Revision of ACMG Mutation Panel, 2004

Best Practice Guidelines for Molecular Genetic Diagnosis of Cystic Fibrosis and CFTR-Related Disorders- Updated European Recommendations, 2009

The American College of Obstetricians and Gynecologists (ACOG), Committee Opinion 691, Carrier Screening for Genetic Conditions, March 2017

The National Society of Genetic Counselors (NSGC), Molecular Testing for Cystic Fibrosis Carrier Status Practice Guidelines, Recommendations from NSGC, 2013