



**GENETIC TESTING
FOR CYSTIC FIBROSIS
HS-026**



Harmony Behavioral Health, Inc.

Harmony Behavioral Health of Florida, Inc.

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**Genetic Testing
For Cystic Fibrosis**

Policy Number: HS-026

Original Effective Date: 6/19/2008

**Revised Date(s): 7/17/2009; 7/28/2010;
8/2/2011**

DISCLAIMER

The Clinical Coverage Guideline is intended to supplement certain standard WellCare benefit plans. The terms of a member's particular Benefit Plan, Evidence of Coverage, Certificate of Coverage, etc., may differ significantly from this Coverage Position. For example, a member's benefit plan may contain specific exclusions related to the topic addressed in this Clinical Coverage Guideline. When a conflict exists between the two documents, the Member's Benefit Plan always supersedes the information contained in the Clinical Coverage Guideline. Additionally, Clinical Coverage Guidelines relate exclusively to the administration of health benefit plans and are NOT recommendations for treatment, nor should they be used as treatment guidelines. The application of the Clinical Coverage Guideline is subject to the benefit determinations set forth by the Centers for Medicare and Medicaid Services (CMS) National and Local Coverage Determinations and state-specific Medicaid mandates, if any.

APPLICATION STATEMENT

The application of the Clinical Coverage Guideline is subject to the benefit determinations set forth by the Centers for Medicare and Medicaid Services (CMS) National and Local Coverage Determinations and state-specific Medicaid mandates, if any.

BACKGROUND

Mutations of the *CFTR* gene are detected as abnormalities in the DNA sequence of the gene. DNA samples can be obtained from either peripheral blood or a tissue sample, such as cells from the inside of the cheek. DNA sequencing of all coding regions on the gene is the most accurate way to detect mutations but is time consuming and expensive. For this reason, genetic carrier testing for CF will often begin with testing for five most common *CFTR* gene mutations.

It is recommended that CF carrier screening is offered to non-Jewish Caucasians and Ashkenazi Jews and made available to other ethnic and racial groups. All couples should be informed of their chances of disease through educational brochures, informed consent process, or informational Web site. Asian Americans and Native Americans without Caucasian admixture must be informed about the rarity of the disease and the very low yield of the test in their respective populations. African American couples should be made aware that only 50% of at-risk couples will be detected. It is recommended that preconception screening be performed whenever possible, although it is recognized that testing will often occur in the prenatal setting.

Ideally, genetic carrier testing includes three components: informed consent, laboratory analysis, and counseling by a genetics professional. At present, three prenatal screening models for CF are being used: the one-step model, the modified one-step model, and the two-step model. Genetic carrier testing for CF is often performed in the prenatal setting using a one-step or two-step (sequential) approach. The one-step protocol requires both the woman and her partner to submit samples simultaneously for genetic analysis. Testing is performed on one of the samples; the partner is screened only if the first carries the mutation. The test result is positive only if both partners are carriers. Testing using a modified one-step model, which is recommended by the ACMG, is performed on samples collected at the outset from both partners (as in the one-step model). DNA testing is then performed on all of the samples from both partners. Notification is made when a mutation is found in either partner, and counseling is provided. In prenatal screening for CF, confirmatory testing of any type should be considered when test results indicate any of the following: (1) a cystic fibrosis mutation is identified in an individual; (2) a cystic fibrosis mutation is identified in both members of a couple; or (3) a fetus with two CF mutations is identified (Hayes, 2004).

In 2001, recommendations for CF screening were made jointly by the ACOG, the ACMG, and the National Institutes of Health Genome Center. It was recommended that a panethnic mutation panel be used that includes all mutant CF alleles having a frequency of 0.1 percent in the general U.S. population. This was modified in 2004 to encompass 23 mutations (see Table below). Screening for other alleles is optional. Vendors offer expanded panels of up to nearly 100 mutations, but this is still only a fraction of the 1,300 reported CF mutations. Even if the entire gene is sequenced, not all CF mutations will be identified. Those not yet identified presumably act in promoter regions or perturb post-translational modification.

ΔF508	ΔI507	G542X	G551D	W1282Z	N1303K
R533X	621 + 1G > T	R117H	1717 - 1G > A	A455E	R560T
R1162X	G85E	R334W	R347P	711 + 1G > T	1898 + 1G > A
2184delA	3120 + 1G > A	3849 + 10kbC > T	2789 + 5G > A	3659delC	

POSITION STATEMENT

Genetic testing for cystic fibrosis using the American College of Medical Genetics (ACMG) mutation core panel **is considered medically necessary** for the following indications:

- Adults with a documented family history of cystic fibrosis; **OR**

- Reproductive partners of individuals with cystic fibrosis; **OR**
- Couples of child bearing age and who are planning a pregnancy; **OR**
- Couples seeking prenatal testing; **OR**
- Patients who have had a negative sweat test but exhibit well-documented symptoms and signs of cystic fibrosis; **OR**
- Infants with well documented meconium ileus or other symptoms and signs indicative of cystic fibrosis who are too young to produce adequate volumes of sweat for a sweat chloride test; **OR**
- Infants with an elevated immunoreactive trypsinogen (IRT) value on newborn screening; **OR**
- Males with congenital bilateral absence of vas deferens (CBAVD).

WellCare considers genetic testing for cystic fibrosis **NOT medically necessary** for the following indications:

- General newborn screening; **OR**
- Well newborn infants; **OR**
- Persons who have undergone previous genetic testing for cystic fibrosis; **OR**
- Couples who have a child with cystic fibrosis; **OR**
- Patients diagnosed with cystic fibrosis with a positive sweat chloride test.

Genetic counseling services must be provided that are accurate and provide balanced information to afford individuals the opportunity to make autonomous decisions. Every attempt should be made to protect individual rights and genetic and medical privacy rights and to prevent discrimination and stigmatization.

CODING

CPT®* Codes

- 83891** Molecular diagnostics; isolation or extraction of highly purified nucleic acid, each nucleic acid type (i.e., DNA, RNA)
83896 Molecular diagnostics; nucleic acid probe, each
83898 Molecular diagnostics; amplification, target, each nucleic acid sequence
83900 Molecular diagnostics; amplification, target, multiplex, first two nucleic acid sequences
83901+ Molecular diagnostics; amplification, target, multiplex, each additional nucleic acid sequence beyond 2
+List separately in addition to code for primary procedure
83904 Molecular diagnostics; mutation identification by sequencing, single segment, each segment
83908 Molecular diagnostics; amplification, signal, each nucleic acid sequence
83909 Molecular diagnostics; separation and identification by high resolution technique (e.g., capillary electrophoresis), each nucleic acid preparation
83912 Molecular diagnostics; interpretation and report
83914 Mutation identification by enzymatic ligation or primer extension, single segment, each segment (e.g., oligonucleotide ligation assay (OLA), single base chain extension (SBCE), or allele-specific primer extension (ASPE))

ICD-9-CM Procedure Codes - No specific codes

HCPCS Codes

- S3835*** Complete gene sequence analysis for cystic fibrosis
***S - Codes are NON COVERED FOR MEDICARE – Refer to HCPCS Level II Temporary National Codes**

ICD-9-CM Diagnosis Codes

- 277.00** Cystic fibrosis without mention of meconium ileus
- 277.01** Cystic fibrosis with mention of meconium ileus
- 277.02** Cystic fibrosis with pulmonary manifestations
- 277.03** Cystic fibrosis with gastrointestinal manifestations
- 277.09** Cystic fibrosis with other manifestations
- 752.89** Males with congenital bilateral absence of vas deferens (CBAVD)
- 796.6** Elevated Immunoreactive Trypsinogen (IRT) value on newborn screening
- V18.19** Family History of Cystic Fibrosis
- V77.6** Special Screening for Cystic Fibrosis, excludes newborn screening for this Coverage Guidelines.
- V82.71** Screening for Genetic Disease Carrier Status, excludes newborn screening for this Coverage Guidelines.

*Current Procedural Terminology (CPT®) ©2010 American Medical Association: Chicago, IL.

REFERENCES

Peer Reviewed

1. Gabbe: Obstetrics: Normal and Problem Pregnancies, 5th Ed. 2007.
2. Hayes Directory. Genetic Carrier Testing for Cystic Fibrosis. June 7, 2004.
3. Hayes Brief, Nasal Potential Difference (NPD) Test For Cystic Fibrosis (CF), August 24, 2006.

Government Agencies, Professional and Medical Organizations

1. American College of Medical Genetics (ACMG). Laboratory standards and guidelines for population-based cystic fibrosis carrier screening. 2001.
2. American College of Obstetricians and Gynecologists (ACOG). Ob-Gyns offering large-scale cystic fibrosis screening. December 12, 2001.
3. Centers for Medicare and Medicaid Services (CMS), National Coverage Determination (NCD). Sweat Test (190.5).
4. Food and Drug Administration (FDA). CLIA—Clinical Laboratory Improvement Amendments. April 30, 2003.
5. NIH Consensus Development Program. Genetic Testing for Cystic Fibrosis. 1997.

HISTORY AND REVISIONS

Date	Action
12/1/2011	<ul style="list-style-type: none">• New template design approved by MPC.
8/2/2011	<ul style="list-style-type: none">• Approved by MPC. No changes.