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.

DISCLAIMER

The Clinical Coverage Guideline (CCG) is intended to supplement certain standard WellCare benefit plans and aid in administering benefits. Federal and state law, contract language, etc. take precedence over the CCG (e.g., Centers for Medicare and Medicaid Services [CMS] National Coverage Determinations [NCDs], Local Coverage Determinations [LCDs] or other published documents). 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 CCG. Additionally, CCGs relate exclusively to the administration of health benefit plans and are NOT recommendations for treatment, nor should they be used as treatment guidelines. Providers are responsible for the treatment and recommendations provided to the member. The application of the CCG 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. All links are current at time of approval by the Medical Policy Committee (MPC) and are subject to change prior to the annual review date. Lines of business (LOB) are subject to change without notice; current LOBs can be found at www.wellcare.com. All guidelines can be found at this site as well but selecting the Provider tab, then “Tools” and “Clinical Guidelines”.

BACKGROUND

The American College of Obstetricians and Gynecologists (ACOG) note that it is more cost effective and practical to perform initial carrier screening for the patient only. If the patient is a cystic fibrosis (CF) carrier, then her partner should be tested. It is important that CF screening continues to be offered to women of reproductive age. It is becoming increasingly difficult to assign a single ethnicity to individuals however screening is most efficacious in the non-Hispanic white and Ashkenazi Jewish populations.1

During pregnancy, concurrent screening of the patient and her partner is suggested if there are time constraints for

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decisions regarding prenatal diagnostic evaluation. Given that CF screening has been a routine part of reproductive care for women since 2001, it is prudent to determine if the patient has been previously screened before ordering CF screening that may be redundant. If a patient has been screened previously, CF screening results should be documented but the test should not be repeated.¹

The following are various carrier screening scenarios with associated management guidelines: ¹

- A woman is a carrier of a CF mutation and her partner is unavailable for testing or paternity is unknown. Consider genetic counseling to review the risk of having an affected child and prenatal testing options.

- Prenatal diagnosis is being performed for other indications and CF carrier status is unknown. CF screening can be performed concurrently on the patient and partner. Chorionic villi or amniocytes may be maintained in culture by the diagnostic laboratory until CF screening results are available for the patient or couple. If both partners are carriers, the sample can then be tested for CF.

- Both partners are CF carriers. Genetic counseling is recommended to review prenatal testing and reproductive options. Prenatal diagnosis should be offered for the couple’s known specific mutations.

- Both partners are unaffected but one or both has a family history of CF. Genetic counseling and medical record review should be performed to identify if Cystic Fibrosis Transmembrane Regulator (CFTR) mutation analysis in the affected family member is available.

- A woman’s reproductive partner has CF or apparently isolated congenital bilateral absence of the vas deferens. The couple should be referred to a genetics professional for mutation analysis and consultation.

- An individual has two CF mutations but has not previously received a diagnosis of CF. These individuals usually have a mild form of the disease and should be referred to a specialist for further evaluation. Genetic counseling is recommended.

NOTE: Complete analysis of the CFTR gene by DNA sequencing is not appropriate for routine carrier screening.

NOTE: Newborn screening panels that include CF screening do not replace maternal carrier screening.

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.²³

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.²³

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 pan-ethnic 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.¹²³
Hayes cited strong support for the following indications:  
- Confirmation of diagnosis in member’s with clinical symptoms of cystic fibrosis and/or having a high sweat chloride level;  
- Identifying newborns with cystic fibrosis;  
- Determining prenatal diagnosis to identify a fetus or embryo with cystic fibrosis;  
- Pre-conception screening among the general population;  
- Carrier testing in member’s with a family history of cystic fibrosis;  
- Identifying individuals with the p.Gly551Asp variant who may respond to treatment with ivacaftor.

**POSITION STATEMENT**

**Applicable To:**
- ✔ Medicaid – All Markets  
- ✔ Medicare – California (Easy Choice Health Plan), Hawaii

*NOTE: For all other Medicare markets, please refer to the approved vendor for requests.*

**Exclusions**

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.

**Coverage**

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.

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  
- Members with a negative sweat test* but exhibit 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).

* The sweat test is an important diagnostic tool in cystic fibrosis and may be covered when used for that purpose (CMS, n.d.).

**CODING**

**CPT® Codes**

81220 CFTR (cystic fibrosis transmembrane conductance regulator) (eg, cystic fibrosis) gene analysis; common variants (eg, ACMG/ACOG guidelines)

81221 CFTR (cystic fibrosis transmembrane conductance regulator) (eg, cystic fibrosis) gene analysis; common variants (eg, ACMG/ACOG guidelines), known familial variants

81222 CFTR (cystic fibrosis transmembrane conductance regulator) (eg, cystic fibrosis) gene analysis;
common variants (eg, ACMG/ACOG guidelines), duplication/deletion variants

81223  CFTR (cystic fibrosis transmembrane conductance regulator) (eg, cystic fibrosis) gene analysis; full gene sequence

81224  CFTR (cystic fibrosis transmembrane conductance regulator) (eg, cystic fibrosis) gene analysis; common variants (eg, ACMG/ACOG guidelines), intron 8 poly-T analysis (eg, male infertility)

81403  Molecular pathology procedure, Level 4

88230  Tissue culture for non-neoplastic disorders; lymphocyte

88262  Chromosome analysis; count 15-20 cells, 2 karyotypes, with banding

HCPCS Codes – No specific codes.

ICD-10-PCS Codes – No specific codes.

ICD-10-CM Diagnosis Codes
E84.0 – E84.8  Cystic fibrosis with pulmonary manifestations (E84.0)
E84.9  Cystic Fibrosis Unspecified
P09  Abnormal findings on neonatal screening
Q55.0,Q55.1,Q55.20-,Q55.29,Q55.4-Q55.8  Absence and aplasia of testis (Q55.0)
Q55.9  Congenital malformation of male genital organ, unspecified
Q55.3  Atresia of Vas Deferens
Z13.228  Encounter for screening for other metabolic disorders
Z13.71  Encounter for nonprocreative screening for genetic disease carrier status
Z14.1  Cystic fibrosis carrier
Z36  Encounter for antenatal screening of mother
Z83.49  Family history of other endocrine, nutritional and metabolic diseases

Coding information is provided for informational purposes only. The inclusion or omission of a CPT, HCPCS, or ICD-10 code does not imply member coverage or provider reimbursement. Consult the member's benefits that are in place at time of service to determine coverage (or non-coverage) as well as applicable federal / state laws.

REFERENCES

MEDICAL POLICY COMMITTEE HISTORY AND REVISIONS

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<tr>
<td>8/7/2014</td>
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