illumina®

Reimbursement for Cystic Fibrosis Genetic Testing in the United States

A review of coverage, coding, and payment for cystic fibrosis (CF) carrier screening and diagnostic testing.

Introduction

In recent years, innovative technologies have fueled the development of new molecular pathology tests that improve our capacity to screen and diagnose diseases. One example of this is the Illumina MiSeqDx™ Cystic Fibrosis System, which uses next-generation sequencing to provide more accurate and comprehensive carrier screening and diagnosis assays for CF. To keep pace with these new technologies, the American Medical Association (AMA) Current Procedural Terminology (CPT®)[1] established a new set of molecular pathology (MoPath) codes for clinical laboratories to use when billing for their tests.

This data sheet reviews the current coverage, coding, and payment landscape for CF carrier screening and diagnostics testing using the MiSeqDx Cystic Fibrosis System. For these MoPath codes, carrier screening is defined as an assay used to assess individuals without any apparent signs or symptoms for a genetic abnormality that is not expressed but can be passed onto offspring. Diagnostic testing is defined as an assay used to diagnose patients who display signs and symptoms of an illness.

Coverage

In general, CF genetic testing is widely covered for both carrier screening and confirmatory diagnostic testing (Figures 1 and 2). Private payers generally separate coverage guidelines for CF carrier screening versus confirmatory diagnostic testing. For both indications, the majority of payers have either issued positive coverage policies or no policies at all. The absence of a coverage policy does not necessarily indicate non-coverage, but implies that the procedure may be covered if medical necessity can be justified.

Based on private payer coverage guidelines, CF carrier screening is generally covered for individuals who meet any of the following criteria:

- Couples seeking prenatal care
- Couples who are planning a pregnancy
- Persons with a family history of CF
- Persons with a 1st degree relative identified as a CF carrier
- Reproductive partners of persons with CF

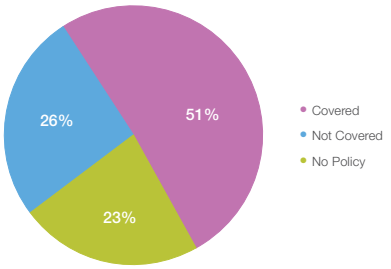
Additionally, CF diagnostic testing is typically covered for individuals who meet any of the following criteria:

- Individual who exhibits symptoms of CF but has a negative sweat test
- Infant with meconium ileus or other symptoms indicative of CF who is too young to produce inadequate volumes of sweat for a sweat chloride test
- Male infertility from either of the following:
  - Congenital bilateral absence of vas deferens (CBAVD)
  - Azoospermia or severe oligospermia (i.e., < 5 million sperm/milliliter) with palpable vas deferens

The majority of state Medicaid agencies do not have policies specifically addressing coverage for CF genetic testing (carrier screening or diagnostic testing), but instead have general coverage policies for laboratory services performed by CLIA-approved labs.

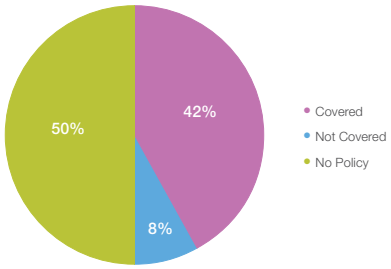
Local Medicare Administrative Contractors (MACs) have generally issued negative coverage determinations for all CF genetic testing services, citing their determination that such testing is statutorily excluded as a Medicare benefit.

Figure 1: Private Payer Coverage by Number of Covered Lives: Carrier Screening



Based on an analysis of n = 170,665,015 payers performed by Quorum Consulting in December 2012.

Figure 2: Private Payer Coverage by Number of Covered Lives: Diagnostic Testing



Based on an analysis of n = 170,665,015 payers performed by Quorum Consulting in December 2012.

Coding

There are five Current Procedural Terminology (CPT®) codes for *CFTR* analysis, which are segmented by the types of genetic variants interrogated (Table 1). In general, each code corresponds to specific analyses that may be performed for carrier screening and/or diagnostic testing indications.

The CPT codes in Table 1 are available for laboratories to use if they accurately describe the services performed for CF genetic testing. It is the responsibility of each laboratory to determine the most appropriate CPT codes that should be used to bill for their services.

Table 1: CPT Codes for *CFTR* Analysis

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

AMA Clinical Vignettes

The following clinical vignettes provided by the AMA describe common clinical scenarios in which each code for *CFTR* analysis may be billed[2,3]:

- **CPT 81220:** A 26-year–old Caucasian female, approximately eight weeks pregnant and otherwise in good health, visits her obstetrician for a first prenatal visit. After discussing advantages and limitations of prenatal CF carrier screening with her obstetrician an anticoagulated peripheral blood sample is sent to the laboratory to be tested for common mutations and variants associated with CF.
- **CPT 81221:** A 1-year–old Caucasian male, whose 6-year–old brother was previously diagnosed with CF is brought by his mother to the pediatrician for genetic testing. The brother was previously demonstrated to be a compound heterozygote carrying one copy each of the common *CFTR* DeltaF508 mutation as well as a rare variant not included in assays which test for common variants of *CFTR* but known to cause CF. An anticoagulated peripheral blood sample is sent to the laboratory for testing of these known mutations.
- **CPT 81222:** A 17-year–old Caucasian female, previously diagnosed with CF based on convincing clinical criteria and two elevated sweat chloride results, visits her pediatrician with her father to discuss potential additional genetic testing. Previous tests with a screening assay for common mutations and variants followed by *CFTR* full gene sequence analysis revealed only heterozygosity for the DeltaF508 mutation. An anticoagulated peripheral blood sample is forwarded to a reference laboratory for deletion/duplication analysis for an uncommon *CFTR* mutation.
- **CPT 81223:** A 17-year–old Caucasian female with chronic rhinosinusitis, idiopathic bronchiectasis, and two sweat chloride measurements in the intermediate range (40–60 meq/L) is suspected by her pediatrician of having an atypical form of CF. A tube of anticoagulated peripheral blood is submitted to the laboratory for full *CFTR* gene sequence analysis.
- **CPT 81224:** Following recent consultation with his family physician regarding his wife's difficulty in conceiving a child, a 34-year–old Caucasian male is referred to an urologist for infertility workup. Physical further examination and testing reveals bilateral absence of the vas deferens. The urologist recommends genetic analysis of the *CFTR* gene to look for common *CFTR* mutations and assess the intron 8 polyT region frequently associated with male infertility. An anticoagulated peripheral blood sample is forwarded to the laboratory for testing.

Payment

For 2013, the Centers for Medicare & Medicaid Services (CMS) assigned the local Medicare Administrative Contractors (MACs) the responsibility of setting regional fee schedule amounts for the new MoPath code set (including payment rates for CF testing) via gapfilling.

Gapfilling is used when a comparable test does not exist. CMS instructs local MACs to establish payment rates in the first year based on charges and routine discounts to charges, resources required, and other payers' payment rates. For reimbursement in the second year and beyond, CMS calculates a national payment rate by using the median of the local MAC fee schedules.

On September 30, 2013, CMS released the 2014 national Medicare fee schedule amounts for the MoPath codes, which were based on the final gapfill rates determined by each MAC[4]. However, the national fee schedule did not include any payment rates for the cystic fibrosis testing codes. Since payment rates will vary by payer (both private and public), laboratories are encouraged to contact individual payers directly to clarify the fee schedule amounts for these codes in 2014.

References

1. CPT is a registered trademark of the American Medical Association. ©2012 American Medical Association. All rights reserved.
2. American Medical Association. 2012 Current Procedural Terminology: Changes, An Insider's View.
3. © American Medical Association 2011. All rights reserved.
4. Centers for Medicare & Medicaid Services. Gapfill Pricing Inquiries. Accessed on October 1, 2013 (www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/ClinicalLabFeeSched/Gapfill-Pricing-Inquiries.html)

Illumina is providing this review of the molecular pathology reimbursement landscape in collaboration with Quorum Consulting for educational purposes only. The content should not be considered legal advice. For official ruling on the MoPath codes readers should consult CMS, the AMA and other sources as appropriate.

Illumina • 1.800.809.4566 toll-free (U.S.) • +1.858.202.4566 tel • techsupport@illumina.com • www.illumina.com

© 2013 Illumina, Inc. All rights reserved.

Illumina, illumina*Dx*, BaseSpace, BeadArray, BeadXpress, cBot, CSPro, DASL, DesignStudio, Eco, GAIIx, Genetic Energy, Genome Analyzer, GenomeStudio, GoldenGate, HiScan, HiSeq, Infinium, iSelect, MiSeq, Nextera, NuPCR, SeqMonitor, Solexa, TruSeq, TruSight, VeraCode, the pumpkin orange color, and the Genetic Energy streaming bases design are trademarks or registered trademarks of Illumina, Inc. All other brands and names contained herein are the property of their respective owners.
Pub. No. 0676-2013-034 Current as of 22 October 2013

illumina®

AGAATGATAACAGTAACACACTTCTGTTAACCTTAAGATTACTTGATCCACTGATTCAACGTACCGTAACGAACGTATCAATTGAGACTAAATATTAACGTACCATTAAGAGCTACCGTCTTCTGTTAACCTTAAGATTACTTGATCCACTGATTCAAC
TCAACGTACCGTAACGAACGTATCATTAAGATTACTTGATCCACTGATTCAACGTACCGTAACGAACGTATCAATTGAGACTAAATATTAACGTACCATTAAGAGCTACCGTGCAACGACGAAAAGAATGATAACAGTAACACACTTCTGTTAACCTT
CGACGAAAAGAATGATAACAGTAACACACTTCTGTTAACCTTAAGATTACTTGATCCACTGATTCAACGTACCGTAAAGATTACTTGATCCACTGATTCAACGTACCGTAACGAACGTATCAATTGAGACTAAATATTAACGTACCATTAAGAGCTACC
AACGTACCATTAAGAGCTACCGTGCAACAGTAACACACTTCTGTTAACCTTAAGATTACTTGATCCACTGATTCAACGTACCGTAACGAACGTATCAATTGAGACTAAATATTAACGTACCATTAAGAGCTACCGTGCAACGACGAAAAGAATGATAA
AGAATGATAACAGTAACACACTTCTGTTAACCTTAAGATTACTTGATCCACTGATTCAACGTACCGTAACGAACGTATCAATTGAGACTAAATATTAACGTACCATTAAGAGCTACCGTCTTCTGTTAACCTTAAGATTACTTGATCCACTGATTCAAC
GATTACTTGATCCACTGATTCAACGTTAAGATTACTTGATCCACTGATTCAACGTACCGTAACGAACGTATCAATTGAGCTTCTGTTAACCTTAAGATTACTTGATCCACTGATTCAACGTACCGTAACGAACGTATCAATTGAGACTAGCAACGACG
CGTATCAATTGAGACTAAATATTAACGTACCATTAAGAGTCTGTTAACCTTAAGATTACTTGATCCACTGATTCAACGTACCGTAACGAACGTATCAATTGAGACTAAATATTAACGTACCATTAAGAGCTACCGTGCAACGAAAAGAATGATAACAGTA