FEP 2.04.10 Identification of Microorganisms Using Nucleic Acid Probes

Effective Date: April 15, 2018

Description
Nucleic acid probes are available for the identification of a wide variety of microorganisms. Nucleic acid probes can also be used to quantitate the number of microorganisms present. This technology offers advantages over standard techniques when rapid identification is clinically important when microbial identification using standard culture is difficult or impossible, and/or when treatment decisions are based on quantitative results.

FDA REGULATORY STATUS

A list of current U.S. Food and Drug Administration–approved or cleared nucleic acid–based microbial tests is available online.³ Table 1 lists tests approved or cleared by the Food and Drug Administration that do not have specific CPT codes.

Table 1. FDA-Approved/Cleared Tests Without CPT Codes

<table>
<thead>
<tr>
<th>FDA-Approved/Cleared Diagnostic Test</th>
<th>Test Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacillus anthracis</td>
<td>Real-time PCR</td>
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<tr>
<td>Central Nervous System Panel (FilmArray Meningitis/Encephalitis- FDA 510k)</td>
<td>PCR of cerebrospinal fluid</td>
</tr>
<tr>
<td>Coxiella burnetii (Q fever)</td>
<td>Real-time PCR</td>
</tr>
<tr>
<td>Enterococcus faecalis</td>
<td>PNA FISH</td>
</tr>
<tr>
<td>Escherichia coli and Pseudomonas aeruginosa</td>
<td>PNA FISH</td>
</tr>
<tr>
<td>Escherichia coli and/or Klebsiella pneumoniae and Pseudomonas aeruginosa</td>
<td>PNA FISH</td>
</tr>
<tr>
<td>Escherichia coli, Klebsiella pneumoniae, and Pseudomonas aeruginosa</td>
<td>PNA FISH</td>
</tr>
<tr>
<td>Francisella tularensis</td>
<td>Real-time PCR</td>
</tr>
<tr>
<td>Leishmania</td>
<td>Real-time PCR</td>
</tr>
<tr>
<td>Yersinia pestis</td>
<td>Real-time PCR</td>
</tr>
<tr>
<td>Adenovirus</td>
<td>Multiplex real-time RT-PCR</td>
</tr>
<tr>
<td>Avian flu</td>
<td>Real-time RT-PCR</td>
</tr>
<tr>
<td>Human metapneumovirus</td>
<td>Multiplex real-time RT-PCR</td>
</tr>
<tr>
<td>Influenza virus A/H5</td>
<td>Real-time RT-PCR</td>
</tr>
<tr>
<td>Influenza virus H1N1</td>
<td>Real-time RT-PCR</td>
</tr>
<tr>
<td>Dengue virus</td>
<td>Real-time RT-PCR</td>
</tr>
<tr>
<td>Gram-positive/gram-negative bacteria panel</td>
<td>Multiplex nucleic acid amplification</td>
</tr>
</tbody>
</table>

FDA: U.S. Food and Drug Administration; FISH: fluorescence in situ hybridization; PCR: polymerase chain reaction; PNA: peptide nucleic acid; RT: reverse transcriptase.
A list of current U.S. Food and Drug Administration (FDA)-approved or cleared nucleic acid-based microbial tests is available at:
http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/InVitroDiagnostics/ucm330711.htm

POLICY STATEMENT

The use of nucleic acid testing using a direct or amplified probe technique (without quantification of viral load) may be considered medically necessary for the following microorganisms (see Policy Guidelines):

- Bartonella henselae or quintana
- Candida species
- Chlamydia trachomatis
- Clostridium difficile
- Enterococcus, vancomycin-resistant (eg, enterococcus vanA, vanB)
- Enterovirus
- Gardnerella vaginalis
- Herpes simplex virus
- Human papillomavirus
- Legionella pneumophila
- Mycobacterium species
- Mycobacterium tuberculosis
- Mycobacterium avium-intracellulare
- Mycoplasma pneumoniae
- Neisseria gonorrhoeae
- Respiratory virus panel
- Staphylococcus aureus
- Staphylococcus aureus, methicillin-resistant
- Streptococcus, group A
- Streptococcus, group B
- Trichomonas vaginalis

The use of nucleic acid testing using a direct or amplified probe technique (with or without quantification of viral load) may be considered medically necessary for the following microorganisms:

- Cytomegalovirus
- Hepatitis B virus
- Hepatitis C virus
- HIV-1
- HIV-2
- Human herpesvirus 6
- Influenza virus

The use of nucleic acid testing with quantification of viral load is considered investigational for microorganisms that are not included in the list of microorganisms for which probes with or without quantification are considered medically necessary.

The use of nucleic acid testing using a direct or amplified probe technique with or without quantification of viral load is considered investigational for the following microorganisms:

- Chlamydia pneumoniae
- Hepatitis G virus
- Gastrointestinal pathogen panel

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- Central nervous system pathogen panel

**POLICY GUIDELINES**

It should be noted that the technique for quantification includes both amplification and direct probes; therefore, simultaneous coding for both quantification with either amplification or direct probes is not warranted.

Antibiotic sensitivity of streptococcus A cultures is generally not performed for throat cultures. However, if an antibiotic sensitivity is considered, then the most efficient method of diagnosis would be a combined culture and antibiotic sensitivity.

For uncomplicated infections, testing for only 1 candida species, *Candida albicans*, may be considered medically necessary. For complicated infections, testing for multiple candida subspecies may be considered medically necessary. The Centers for Disease Control and Prevention (2010) classifies uncomplicated vulvovaginal candidiasis as being sporadic or infrequent; or mild to moderate; or likely to be *C. albicans*; or in nonimmunocompromised women. Complicated vulvovaginal candidiasis is classified as being recurrent or severe; or not a *C. albicans* species; or in women with uncontrolled diabetes, debilitation, or immunosuppression.

In the evaluation of group B streptococcus, the primary advantage of a DNA probe technique compared with traditional culture techniques is the rapidity of results. This advantage suggests that the most appropriate use of the DNA probe technique is in the setting of impending labor, for which prompt results could permit the initiation of intrapartum antibiotic therapy.

Many probes have been combined into panels of tests. For the purposes of this policy, other than the gastrointestinal pathogen panel, central nervous system panel, and the respiratory virus panel, only individual probes are reviewed.

**BENEFIT APPLICATION**

Screening (other than the preventive services listed in the brochure) is not covered. Please see Section 6 General exclusions.

Benefits are available for specialized diagnostic genetic testing when it is medically necessary to diagnose and/or manage a patient’s existing medical condition. Benefits are not provided for genetic panels when some or all of the tests included in the panel are not covered, are experimental or investigational, or are not medically necessary.

Experimental or investigational procedures, treatments, drugs, or devices are not covered (See General Exclusion Section of brochure).

**RATIONALE**

**Summary of Evidence**

For individuals who have suspected *C. pneumoniae* who receive a nucleic acid probe for *C. pneumoniae*, the evidence includes prospective and retrospective evaluations of the tests’ sensitivity and specificity. Relevant outcomes are test accuracy and validity, other test performance measures, symptoms, and change in disease status. The body of evidence is limited. One study was identified that reported relatively high sensitivity and specificity for a polymerase chain reaction–based test. However, the total number of patients in this study was small (N=56), and most other studies were conducted in the investigational setting. In addition to the limitations in the evidence base on test characteristics, the clinical implications of these tests are unclear. The evidence is insufficient to determine the effects of the technology on health outcomes.
For individuals who have hepatitis who receive a nucleic acid probe for hepatitis G, the evidence is lacking. Relevant outcomes are test accuracy and validity, other test performance measures, symptoms, and change in disease status. The clinical implications of this test are unclear. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have signs and/or symptoms of gastroenteritis who receive nucleic acid–based gastrointestinal pathogen panel, the evidence includes prospective and retrospective evaluations of the tests’ sensitivity and specificity. Relevant outcomes include test accuracy and validity, other test performance measures, symptoms, and change in disease status. The evidence suggests that gastrointestinal pathogen panels are likely to identify both bacterial and viral pathogens with high sensitivity, compared with standard methods. Access to a rapid method for etiologic diagnosis of gastrointestinal infections may lead to more effective early treatment and infection-control measures. However, in most instances, when a specific pathogen is suspected, individual tests could be ordered. There may be a subset of patients with an unusual presentation who would warrant testing for a panel of pathogens at once, but that subset has not been well defined. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have signs and/or symptoms of meningitis and/or encephalitis who receive a nucleic acid–based central nervous system pathogen panel, the evidence includes retrospective evaluations of the tests’ sensitivity and specificity. Relevant outcomes include test accuracy and validity, other test performance measures, symptoms, and change in disease status. Access to a rapid method that can simultaneously test for multiple pathogens may lead to the faster initiation of more effective treatment and conservation of cerebrospinal fluid. The available central nervous system panel is highly specific for the included organisms, but the sensitivity for each pathogen is not well-characterized. More than 15% of positives in the largest clinical validity study were false-positives. A negative panel result does not exclude infection due to pathogens not included in the panel. The evidence is insufficient to determine the effects of the technology on health outcomes.

SUPPLEMENTAL INFORMATION

Practice Guidelines and Position Statements
No guidelines or statements were identified.

U.S. Preventive Services Task Force Recommendations
Not applicable.

Medicare National Coverage
There is no national coverage determination (NCD). In the absence of an NCD, coverage decisions are left to the discretion of local Medicare carriers.

REFERENCES


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84. Hologic. Group A Streptococcal Direct Test (103887 Rev. 001). 2016;

85. Quidel. LyraDirect Strep Assay. n.d.;

86. Meridien Bioscience. Package Insert: Illumigene Group A Streptococcus DNA Amplification Assay. 2015;


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