Identification of Microorganisms using Nucleic Acid Probes AHS – M2097

File Name: identification_of_microorganisms_using_nucleic_acid_probes
Origination: 01/2019
Last CAP Review: 03/2020
Next CAP Review: 03/2021
Last Review: 04/2020

Description of Procedure or Service

Nucleic acid hybridization technologies utilize complementary properties of the DNA double-helix structures to anneal together DNA fragments from different sources. These techniques are utilized in polymerase chain reaction (PCR) and fluorescent resonance energy transfer (FRET) techniques to identify microorganisms (Khan, 2014).

Related Policies
Lyme Disease AHS – G2143
Pathogen Panel Testing AHS – G2149
Diagnostic Testing of Common Sexually Transmitted Infection AHS – G2157
Testing for Mosquito- or Tick-Related Infections AHS – G2158
Diagnosis of Vaginitis Including Multi-Target PCR Testing AHS – M2057

***Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.

Policy

BCBSNC will provide coverage for identification of microorganisms using nucleic probes when it is determined to be medically necessary because the medical criteria and guidelines shown below are met.

Benefits Application

This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

When Identification of Microorganisms Using Nucleic Acid Probes is covered

1. Reimbursement of nucleic acid identification using direct probe, amplified probe, or quantification is allowed for the microorganism’s procedure codes summarized in Table 1 below.

<table>
<thead>
<tr>
<th>Microorganism</th>
<th>Direct Probe</th>
<th>Amplified Probe</th>
<th>Quantification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bartonella henselae or Quintana</td>
<td></td>
<td>87471</td>
<td></td>
</tr>
<tr>
<td>Candida species</td>
<td>87480</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
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<table>
<thead>
<tr>
<th></th>
<th>Code 1</th>
<th>Code 2</th>
<th>Code 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clostridium difficile</td>
<td>87493</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cytomegalovirus</td>
<td>87495</td>
<td>87496</td>
<td>87497</td>
</tr>
<tr>
<td>Enterococcus, Vancomycin-resistant (e.g., enterococcus vanA, vanB)</td>
<td></td>
<td>87500</td>
<td></td>
</tr>
<tr>
<td>Enterovirus</td>
<td></td>
<td>87498</td>
<td></td>
</tr>
<tr>
<td>Hepatitis B</td>
<td></td>
<td>87516</td>
<td>87517</td>
</tr>
<tr>
<td>Herpes virus-6</td>
<td>87531</td>
<td></td>
<td>87533</td>
</tr>
<tr>
<td>HIV-1</td>
<td>87534</td>
<td>87535</td>
<td>87536</td>
</tr>
<tr>
<td>HIV-2</td>
<td>87537</td>
<td>87538</td>
<td>87539</td>
</tr>
<tr>
<td>Legionella pneumophila</td>
<td>87540</td>
<td></td>
<td>87541</td>
</tr>
<tr>
<td>Mycoplasma pneumoniae</td>
<td>87580</td>
<td></td>
<td>87581</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td></td>
<td>87640</td>
<td></td>
</tr>
<tr>
<td>Staphylococcus aureus, methicillin resistant</td>
<td></td>
<td>87641</td>
<td></td>
</tr>
</tbody>
</table>

2. Reimbursement is allowed for PCR testing for Ebola and will currently be submitted with unspecified codes.

3. Reimbursement is allowed for molecular testing for coronavirus disease 2019 (COVID-19) to aid diagnosis.

4. Reimbursement is allowed for PCR testing for the following microorganisms that do not have specific CPT codes. (not an all-inclusive list):

   a. Actinomyces, for identification of actinomyces species in tissue specimens
   b. Adenovirus, to diagnose adenovirus myocarditis, and to diagnose adenovirus infection in immunocompromised hosts, including transplant recipients
   c. Avian influenza A virus, for diagnosis of avian influenza A (H5N1) in persons with both: (i) symptoms consistent with Avian influenza A virus; and (ii) a history of travel to or contact with persons or birds from a country with documented H5N1 avian influenza infections within 10 days of symptom onset.
   d. Bacillus Anthracis
   e. BK polyomavirus in transplant recipients receiving immunosuppressive therapies and persons with immunosuppressive diseases
   f. Bordetella pertussis and B. parapertussis, for diagnosis of whooping cough in individuals with coughing
   g. Brucella spp., for members with signs and symptoms of Brucellosis, and history of direct contact with infected animals and their carcasses or secretions or by ingesting unpasteurized milk or milk products
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h. Burkholderia infections (including B. cepacia, B. gladioli), diagnosis
i. Chancroid (Haemophilus ducreyi), for diagnosis of persons with genital ulcer disease
j. Coxiella burnetii, for confirmation of acute Q fever
k. Epidemic typhus (Rickettsia prowazekii), diagnosis
l. Epstein Barr Virus (EBV): for detection of EBV in post-transplant lymphoproliferative disorder; or for testing for EBV in persons with lymphoma; or for those who are immunocompromised for other reasons.
m. Francisella tularensis, for presumptive diagnosis of tularemia
n. Hantavirus, diagnosis
o. Hemorrhagic fevers and related syndromes caused by viruses of the family Bunyaviridae (Rift Valley fever, Crimean-Congo hemorrhagic fever, hemorrhagic fever with renal syndromes), for diagnosis in acute phase in persons with clinical presentation suggestive of these conditions
p. Hepatitis D virus, for confirmation of active infection in persons with anti-HDV antibodies
q. Hepatitis E virus, for definitive diagnosis in persons with anti-HEV antibodies
r. Human T Lymphotropic Virus type 1 and type 2 (HTLV-I and HTLV-II), to confirm the presence of HTLV-I and HTLV-II in the cerebrospinal fluid of persons with signs or symptoms of HTLV-I/HTLV-II
s. Human metapneumovirus
t. JC polyomavirus, in transplant recipients receiving immunosuppressive therapies, in persons with immunosuppressive diseases, and for diagnosing progressive multifocal leukoencephalopathy in persons with multiple sclerosis or Crohn's disease receiving natalizumab (Tysabri)
u. Leishmaniasis, diagnosis
v. Measles virus (Morbilliviruses), for diagnosis of measles
w. Mumps
x. Mycoplasma genitalium
y. Neisseria meningitidis, to establish diagnosis where antibiotics have been started before cultures have been obtained
z. Parvovirus, for detecting chronic infection in immunocompromised persons
aa. Psittacosis, for diagnosis of Chlamydophila (Chlamydia) psittaci infection
bb. Respiratory syncytial virus (RSV), for confirming the result of rapid antigen detection assay.
c. Rubella, diagnosis
dd. Severe acute respiratory syndrome (SARS), for detection of SARS coronavirus RNA in persons with signs or symptoms of SARS who have traveled to endemic areas or have been exposed to persons with SARS
ee. Toxoplasma gondii, for detection of T. gondii infection in immunocompromised persons with signs and symptoms of toxoplasmosis, and for detection of congenital Toxoplasma gondii infection (including testing of amniotic fluid for toxoplasma infection)
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ff. Varicella-Zoster infections

gg. Whipple's disease (T. whippeli), biopsy tissue from small bowel, abdominal or peripheral lymph nodes, or other organs of persons with signs and symptoms, to establish the diagnosis

hh. Yersinia Pestis

5. Reimbursement is allowed for quantitative PCR testing for the following indications:

a. Adenovirus viral load, to monitor response to antiviral therapy in infected immunocompromised hosts, including transplant recipients

b. BK polyomavirus viral load, for diagnosis and monitoring response to therapy in infected kidney transplant recipients

c. Cytomegalovirus (CMV) viral load, to monitor response to therapy

d. EBV viral load, to monitor for EBV viral replication in solid organ transplant recipients

e. Hepatitis B

f. Hepatitis C

g. Human herpesvirus type 6, to monitor response to therapy in immunocompromised hosts, including transplant recipients

h. HIV RNA viral load testing, to monitor disease progression and response to therapy

When Identification of Microorganisms Using Nucleic Acid Probes is not covered

The status of nucleic acid identification using direct probe, amplified probe, or quantification for the microorganism’s procedure codes considered investigational, is summarized in Table 1 below.

<table>
<thead>
<tr>
<th>Microorganism</th>
<th>Direct Probe</th>
<th>Amplified Probe</th>
<th>Quantification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bartonella henselae or Quintana</td>
<td></td>
<td>87481</td>
<td>87482</td>
</tr>
<tr>
<td>Candida species (For vaginitis, please review Diagnosis of Vaginitis including Multi-Target PCR Testing AHS – M2057)</td>
<td>87485</td>
<td>87486</td>
<td></td>
</tr>
<tr>
<td>Clamydia pneumoniae</td>
<td>87485</td>
<td>87486</td>
<td>87487</td>
</tr>
<tr>
<td>Hepatitis G</td>
<td>87525</td>
<td>87526</td>
<td>87527</td>
</tr>
<tr>
<td>Herpes virus-6</td>
<td>87532</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Legionella pneumophilia</td>
<td></td>
<td></td>
<td>87542</td>
</tr>
<tr>
<td>Mycoplasma pneumoniae</td>
<td></td>
<td></td>
<td>87582</td>
</tr>
</tbody>
</table>
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The technique for quantification includes both amplification and direct probes; therefore, reimbursement of simultaneous coding for both amplification and direct probes is not allowed.

Policy Guidelines

Policy Guidelines
A discussion of every infectious agent that might be detected with a probe technique is beyond the scope of this policy. Many probes have been combined into panels of tests. For the purposes of this policy, other than the respiratory virus panel, only individual probes are reviewed.

Background
Nucleic acid hybridization technologies, including polymerase chain reaction (PCR), ligase- or helicase-dependent amplification, and transcription-mediated amplification, are beneficial tools for pathogen detection in blood culture and other clinical specimens due to high specificity and sensitivity (Khan, 2014). The use of nucleic acid-based methods to detect bacterial pathogens in a clinical laboratory setting offers “increased sensitivity and specificity over traditional microbiological techniques” due to its specificity, sensitivity, reduction in time, and high-throughput capability; however, “contamination potential, lack of standardization or validation for some assays, complex interpretation of results, and increased cost are possible limitations of these tests (Mothershed & Whitney, 2006)”.

Guidelines and Recommendations
Specific guidelines for testing of many organisms listed within the policy coverage criteria is found in the updated 2018 Infectious Diseases Society of America (IDSA) guidelines and recommendations titled, A Guide to Utilization of the Microbiology Laboratory for Diagnosis of Infectious Diseases: 2018 Update by the Infectious Diseases Society of America and the American Society for Microbiology (Miller et al., 2018). “This document is organized by body system, although many organisms are capable of causing disease in >1 body system. There may be a redundant mention of some organisms because of their propensity to infect multiple sites. One of the unique features of this document is its ability to assist clinicians who have specific suspicions regarding possible etiologic agents causing a specific type of disease. When the term “clinician” is used throughout the document, it also includes other licensed, advanced practice providers. Another unique feature is that in most chapters, there are targeted recommendations and precautions regarding selecting and collecting specimens for analysis for a disease process. It is very easy to access critical information about a specific body site just by consulting the table of contents. Within each chapter, there is a table describing the specimen needs regarding a variety of etiologic agents that one may suspect as causing the illness. The test methods in the tables are listed in priority order according to the recommendations of the authors and reviewers (Miller et al., 2018).”


The Committee on Infectious Diseases released joint guidelines with the American Academy of Pediatrics. In it, they note that “the presumptive diagnosis of mucocutaneous candidiasis or thrush usually can be made clinically”. They also state that FISH probes may rapidly detect Candida species from positive blood culture samples, although PCR assays have also been developed for this purpose (Pediatrics, 2018).

Applicable Federal Regulations

As of 06/12/2019, a list of current U.S. Food and Drug Administration (FDA, 2019) approved or cleared nucleic acid-based microbial tests is available at: https://www.fda.gov/medical-devices/vitro-diagnostics/nucleic-acid-based-tests.
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Billing/Coding/Physician Documentation Information

This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at www.bcbsnc.com. They are listed in the Category Search on the Medical Policy search page.

Applicable service codes: 87471, 87472, 87480, 87481, 87482, 87485, 87486, 87487, 87493, 87495, 87496, 87497, 87500, 87498, 87500, 87516, 87517, 87525, 87526, 87527, 87531, 87532, 87534, 87535, 87536, 87537, 87538, 87539, 87540, 87541, 87542, 87580, 87581, 87582, 87634, 87635, 87640, 87641, 87797 – 87799, U0001, U0002

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

Scientific Background and Reference Sources


Policy Implementation/Update Information

1/1/2019  BCBSNC will provide coverage for identification of microorganisms using nucleic probes when it is determined to be medically necessary because the medical criteria and guidelines are met. Medical Director review 1/1/2019. Policy noticed 1/1/2019 for effective date 4/1/2019. (jd)

4/1/2019  Billing/Coding section updated. (jd)

10/29/19  Wording in the Policy, When Covered, and/or Not Covered section(s) changed from Medical Necessity to Reimbursement language, where needed.

12/10/19  Reviewed by Avalon 3rd Quarter 2019 CAB. Within the table under the When Covered section, removed “Gastrointestinal Pathogen Panel” and corresponding codes 87505-87507 and “Respiratory Virus Panel” including corresponding codes 87631-87633; Item 3,
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removed C. difficile and added Mycoplasma genitalium. Under the When Not Covered section, added “Candida species” along w/corresponding codes. The following codes were removed from the Billing/Coding section: 87505, 87506, 87507, 87632, 87633. Medical Director review 11/2019. (jd)


Medical policy is not an authorization, certification, explanation of benefits or a contract. Benefits and eligibility are determined before medical guidelines and payment guidelines are applied. Benefits are determined by the group contract and subscriber certificate that is in effect at the time services are rendered. This document is solely provided for informational purposes only and is based on research of current medical literature and review of common medical practices in the treatment and diagnosis of disease. Medical practices and knowledge are constantly changing and BCBSNC reserves the right to review and revise its medical policies periodically.