BlueCross BlueShield of North Carolina

An independent licensee of the Blue Cross and Blue Shield Association

Corporate Medical Policy

Identification of Microorganisms using Nucleic Acid Probes AHS – M2097

File Name: identification_of_microorganisms_using_nucleic_acid_probes
Origination: 01/2019
Last CAP Review: 03/2021
Next CAP Review: 03/2022
Last Review: 03/2021

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 the medical criteria and guidelines shown below are met.

NOTE: The coverage criteria outlined in this policy are not applicable to diagnostic COVID-19 testing.

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.

Microorganism	Direct Probe	Amplified Probe	Quantification

Bartonella henselae or Quintana		87471	
Candida species (For vaginitis, please review Diagnosis of Vaginitis including Multi-Target PCR Testing AHS – M2057)	87480		
Chlamydia pneumoniae	87485	87486	
Clostridium difficile	87493		
Cytomegalovirus	87495	87496	87497
Enterococcus, Vancomycin-resistant (e.g., enterococcus vanA, vanB)		87500	
Enterovirus		87498	
Hepatitis B		87516	87517
Herpes virus-6	87531		87533
Legionella pneumophila	87540	87541	
Mycoplasma pneumoniae	87580	87581	
Mycoplasma genitalium		87563	
Respiratory syncytial virus		87634	
Staphylococcus aureus		87640	
Staphylococcus aureus, methicillin resistant		87641	

2. 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. Bacillus Anthracis

    d. BK polyomavirus in transplant recipients receiving immunosuppressive therapies and persons with immunosuppressive diseases

    e. Bordetella pertussis and B. parapertussis, for diagnosis of whooping cough in individuals with coughing

    f. 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

    g. Burkholderia infections (including B. cepacia, B. gladioli), diagnosis

    h. Chancroid (Haemophilus ducreyi), for diagnosis of persons with genital ulcer disease

i. Coxiella burnetii, for confirmation of acute Q fever

j. EBOLA

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. Neisseria meningitidis, to establish diagnosis where antibiotics have been started before cultures have been obtained

y. Parvovirus, for detecting chronic infection in immunocompromised persons

z. Psittacosis, for diagnosis of Chlamydophila (Chlamydia) psittaci infection

aa. Rubella, diagnosis

bb. Toxoplasma gondii, for detection of T. gondii infection in immunocompromised persons with signs and symptoms of toxoplasmosis, and for detection of congenital Toxoplasmagondii infection (including testing of amniotic fluid for toxoplasma infection)

cc. Varicella-Zoster infections

dd. 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

ee. Yersinia Pestis

When Identification of Microorganisms Using Nucleic Acid Probes is not covered

Reimbursement is not allowed for nucleic acid identification using direct probe, amplified probe, or quantification for the microorganism's procedure codes summarized in Table 1 below":

Microorganism	Direct Probe	Amplified Probe	Quantification
Bartonella henselae or Quintana			87472
Candida species (For vaginitis, please review Diagnosis of Vaginitis including Multi-Target PCR Testing AHS – M2057		87481	87482
Clamydia pneumoniae			87487
Hepatitis G	87525	87526	87527
Herpes virus-6		87532	
Legionella pneumophila			87542
Mycoplasma pneumoniae			87582

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)."

Centers of Disease Control and Prevention (CDC)

MRSA

The CDC remarks that nucleic acid amplification tests (NAATs, such as PCR) "can be used for direct detection of mecA, the most common gene mediating oxacillin resistance in staphylococci", but will not detect novel resistance mechanisms or uncommon phenotypes (CDC, 2019d).

Candida Auris (C. auris)

The CDC writes that "Molecular methods based on sequencing the D1-D2 region of the 28s rDNA or the Internal Transcribed Region (ITS) of rDNA also can identify *C. auris*." The CDC further notes that various PCR methods have been developed for identifying *C. auris* (CDC, 2020).

Chlamydia Pneumoniae (C. pneumoniae)

The CDC writes that RT-PCR is the "preferred" method of detecting a *C. pneumoniae* infection, with qPCR preferred for an acute infection. The CDC further notes that a positive culture should be confirmed by a second test, such as PCR (CDC, 2019a).

Ebola

The CDC states that for diagnosis of Ebola, "there must be a combination of symptoms suggestive of EVD AND a possible exposure to EVD within 21 days before the onset of symptoms". The CDC notes that PCR is one of the most common diagnostic methods (CDC, 2019b).

Salmonella

The CDC writes that diagnosis requires detection of the *Salmonella* bacteria, be it through culture or a "culture-independent diagnostic test (CIDT)" (CDC, 2019f).

Giardia

The CDC states that fecal immunoassays may be used for detection of *Giardia,* but that only molecular testing can identify *Giardia* subtypes (CDC, 2015b).

Non-Polio Enterovirus

The CDC remarks that their laboratories "routinely" perform qualitative testing for enteroviruses, parechoviruses, and uncommon picornaviruses (CDC, 2018a).

Respiratory Syncytial Virus (RSV)

The CDC writes that real-time reverse transcriptase-polymerase chain reaction (rRT-PCR) is the most commonly used diagnostic test, both for infants/younger children as well as older children (CDC, 2018b).

Mycoplasma Genitalium

The CDC writes that "NAAT is the preferred method for *M. genitalium* detection" (CDC, 2015a).

Miscellaneous

The CDC does not mention the need to quantify [through PCR] *Bartonella, Legionella pneumophila* or *Mycoplasma pneumoniae* (CDC, 2016, 2019c, 2019e). No guidance was found on Hepatitis G.

Committee on Infectious Diseases, American Academy of Pediatrics, 31st Edition (2018-2021, Red Book)

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 05/11/2020, a list of current U.S. Food and Drug Administration (FDA, 2020) approved or cleared nucleic acid-based microbial tests is available at: https://www.fda.gov/medical-devices/vitro-diagnostics/nucleic-acid-based-tests.

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, 87498, 87500, 87516, 87517, 87525, 87526, 87527, 87531, 87532, 87534, 87540, 87541, 87542, 87563, 87580, 87581, 87582, 87634, 87640, 87641, 87797 – 87799, 0219U.

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

CDC. (2015a). 2015 Sexually Transmitted Diseases Treatment Guidelines, Emerging Issues. Retrieved from https://www.cdc.gov/std/tg2015/emerging.htm#myco

CDC. (2015b). Parasites - Giardia, Diagnosis & Detection. Retrieved from https://www.cdc.gov/parasites/giardia/diagnosis.html
CDC. (2016). Bartonella Infection (Cat Scratch Disease, Trench Fever, and Carrión's Disease). Retrieved from https://www.cdc.gov/bartonella/testing-faq/index.html
CDC. (2018a). Non-Polio Enterovirus, CDC Laboratory Testing & Procedures. Retrieved from https://www.cdc.gov/non-polio-enterovirus/lab-testing/testing-procedures.html
CDC. (2018b). Respiratory Syncytial Virus Infection (RSV), For Healthcare Professionals. Retrieved from https://www.cdc.gov/rsv/clinical/index.html#lab
CDC. (2019a). Chlamydia pneumoniae Infection, Diagnostic Methods. Retrieved from https://www.cdc.gov/pneumonia/atypical/cpneumoniae/hcp/diagnostic.html
CDC. (2019b). Ebola (Ebola Virus Disease), Diagnosis. Retrieved from https://www.cdc.gov/vhf/ebola/diagnosis/index.html
CDC. (2019c). Legionella (Legionnaires' Disease and Pontiac Fever). Retrieved from https://www.cdc.gov/legionella/clinicians/diagnostic-testing.html
CDC. (2019d). Methicillin-resistant Staphylococcus aureus (MRSA), Laboratory Testing. Retrieved from https://www.cdc.gov/mrsa/lab/index.html#anchor_1548439781
CDC. (2019e). Mycoplasma pneumoniae Infections. Retrieved from https://www.cdc.gov/pneumonia/atypical/mycoplasma/hcp/diagnostic-methods.html
CDC. (2019f). Salmonella, Diagnostic and Public Health Testing. Retrieved from https://www.cdc.gov/salmonella/general/diagnosis-treatment.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fsalmonella%2Fgeneral%2Fdiagnosis.html
CDC. (2020). Identification of Candida auris. Retrieved from https://www.cdc.gov/fungal/candida-auris/identification.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Ffungal%2Fcandida-auris%2Frecommendations.html
FDA. (2020). Nucleic Acid Based Tests. Retrieved from https://www.fda.gov/medical-devices/vitro-diagnostics/nucleic-acid-based-tests
Khan, A. (2014). Rapid Advances in Nucleic Acid Technologies for Detection and Diagnostics of Pathogens. *J Microbiol Exp, 1*(2). doi:10.15406/jmen.2014.01.00009
Miller, J. M., Binnicker, M. J., Campbell, S., Carroll, K. C., Chapin, K. C., Gilligan, P. H., . . . Yao, J. D. (2018). 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. *Clinical Infectious Diseases*, ciy381-ciy381. doi:10.1093/cid/ciy381
Mothershed, E. A., & Whitney, A. M. (2006). Nucleic acid-based methods for the detection of bacterial pathogens: present and future considerations for the clinical laboratory. *Clin Chim Acta, 363*(1-2), 206-220. doi:10.1016/j.cccn.2005.05.050
Pediatrics, C. o. I. D. A. A. o. (2018). *Red Book® 2018*.

Specialty Matched Consultant Advisory Panel review 3/2020

Medical Director review 3/2020

Specialty Matched Consultant Advisory Panel review 3/2021

Medical Director review 3/2021

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, removed C. dificile 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)

5/12/20 Updated Related Policies section. Under the When Covered section, added item #3: "Reimbursement is allowed for molecular testing for coronavirus disease 2019 (COVID-19) to aid diagnosis." Updated Policy guidelines and references. Added the following codes to the Billing/Coding section: U0001, U0002, and 87635. Specialty Matched Consultant Advisory Panel review 3/2020. Medical Director review 4/2020. (jd)

7/28/20 Reviewed by Avalon 2nd Quarter 2020 CAB. Added Note to Policy statement as follows: "The coverage criteria outlined in this policy are not applicable to diagnostic COVID-19 testing." To Table 1 When Covered section table 1, added the following: Chlamydia pneumoniae, Mycoplasma genitalium, Respiratory syncytial and associated codes; removed HIV 1 and 2. Removed the following statements: "Reimbursement is allowed for PCR testing for Ebola…" and will currently be submitted with unspecified codes along with statement related to coronavirus disease 2019. Item 2: removed statement related to Avian influenza A virus, mycoplasma genitalium, statements related to RSV and SARS, and added "EBOLA". Policy and references updated. The following codes were removed from the tables and Billing/Coding section: U0001, U0002 and 87635, 87534, 87535, 87536, 87537, 87538 and 87539. Medical Director review 7/2020. (jd)

10/1/20 The following code was added to the Billing/Coding section effective 10/1/20: 0219U. (jd)

3/31/21 Specialty Matched Consultant Advisory Panel review 3/2021. Medical Director review 3/2021. (jd)