MASSACHUSETTS

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Medical Policy

Identification of Microorganisms Using Nucleic Acid Probes

Table of Contents

Policy Number: 555

BCBSA Reference Number: 2.04.10 (For Plan internal use only)
NCD/LCD: N/A

Related Policies

- Intravenous Antibiotic Therapy and Associated Diagnostic Testing for Lyme Disease #171
- Multitarget Polymerase Chain Reaction Testing for Diagnosis of Bacterial Vaginosis #711
- Pathogen Panel Testing #045

Policy

Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity
Medicare HMO Blue℠ and Medicare PPO Blue℠ Members

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:

- Bartonella henselae or quintana
- Bordetella pertussis
- Candida species
- Chlamydia pneumoniae
- Chlamydiatrachomatis
- Clostridium difficile
- Enterococcus, vancomycin-resistant (eg, enterococcus vanA, vanB)
- Enterovirus
- Herpes simplex virus
- Human papillomavirus
- Influenza virus
- Legionella pneumophila
- Mumps
- Mycobacterium species
- Mycobacterium tuberculosis
- Mycobacterium avium intracellulare
- Mycoplasma pneumoniae

- Neisseria gonorrhoeae
- Rubeola (measles)
- Staphylococcus aureus
- Staphylococcus aureus, methicillin resistant
- Streptococcus, group A
- Streptococcus, group B
- Trichomonas vaginalis
- Zika virus.

The use of molecular diagnostics for the diagnosis and management of *Borrelia burgdorferi* infection (Lyme disease) is addressed in policy #171.

The use of multitarget polymerase chain reaction testing for the diagnosis of Bacterial vaginosis is addressed in policy #711.

For Candida species, culture for yeast remains the criterion standard for identifying and differentiating these organisms. Although sensitivity and specificity are higher for nucleic acid amplification tests (NAATs) than for standard testing methods, the CDC and other association guidelines do not recommend NAATs as first-line testing for Candida species. The CDC Centers for Disease Control and Prevention (2015) classifies uncomplicated vulvovaginal candidiasis as being sporadic or infrequent; or mild to moderate; or, in non-immunocompromised women, as likely to be caused by C. albicans. A presumptive diagnosis can be made in the clinical care setting. However, for complicated infections, the CDC states that NAATs may be necessary to test for multiple Candida subspecies. Complicated vulvovaginal candidiasis is classified as being recurrent or severe; or, in women with uncontrolled diabetes, debilitation, or immunosuppression, as less likely to be caused by a C. albicans species.

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.

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.

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.

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.

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.

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 of viral load is considered **INVESTIGATIONAL** for the following microorganisms:

- Gardernella vaginalis
- Hepatitis G.

CPT codes 87797, 87798, and 87799 describe the use of direct probe, amplified probe, and quantification, respectively, for infectious agents not otherwise specified. A discussion of every infectious agent that might be detected with a probe technique is beyond the scope of this policy.

The use of the following nucleic acid testing panels (with or without quantification of viral load for viral panel elements) including but not limited to, is considered **INVESTIGATIONAL**:

- Central nervous system pathogen panel
- Gastrointestinal pathogen panel.

Prior Authorization Information

Inpatient

- For services described in this policy, precertification/preauthorization **IS REQUIRED** for all products if the procedure is performed **inpatient**.

Outpatient

- For services described in this policy, see below for products where prior authorization **might be required** if the procedure is performed **outpatient**.

	Outpatient
Commercial Managed Care (HMO and POS)	Prior authorization is **not required**.
Commercial PPO and Indemnity	Prior authorization is **not required**.
Medicare HMO Blue℠	Prior authorization is **not required**.
Medicare PPO Blue℠	Prior authorization is **not required**.

CPT Codes / HCPCS Codes / ICD Codes

Inclusion or exclusion of a code does not constitute or imply member coverage or provider reimbursement. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage as it applies to an individual member.

Providers should report all services using the most up-to-date industry-standard procedure, revenue, and diagnosis codes, including modifiers where applicable.

The following codes are included below for informational purposes only; this is not an all-inclusive list.

The above medical necessity criteria MUST be met for the following codes to be covered for Commercial Members: Managed Care (HMO and POS), PPO, Indemnity, Medicare HMO Blue and Medicare PPO Blue:

CPT Codes

CPT codes:	Code Description
87471	Infectious agent detection by nucleic acid (DNA or RNA); Bartonella henselae and Bartonella quintana, amplified probe technique
87480	Infectious agent detection by nucleic acid (DNA or RNA); Candida species, direct probe technique
87481	Infectious agent detection by nucleic acid (DNA or RNA); Candida species, amplified probe technique
87485	Infectious agent detection by nucleic acid (DNA or RNA); Chlamydia pneumoniae, direct probe technique

87486	Infectious agent detection by nucleic acid (DNA or RNA); Chlamydia pneumoniae, amplified probe technique
87487	Infectious agent detection by nucleic acid (DNA or RNA); Chlamydia pneumoniae, quantification
87490	Infectious agent detection by nucleic acid (DNA or RNA); Chlamydia trachomatis, direct probe technique
87491	Infectious agent detection by nucleic acid (DNA or RNA); Chlamydia trachomatis, amplified probe technique
87493	Infectious agent detection by nucleic acid (DNA or RNA); Clostridium difficile, toxin gene(s), amplified probe technique
87495	Infectious agent detection by nucleic acid (DNA or RNA); cytomegalovirus, direct probe technique
87496	Infectious agent detection by nucleic acid (DNA or RNA); cytomegalovirus, amplified probe technique
87497	Infectious agent detection by nucleic acid (DNA or RNA); cytomegalovirus, quantification
87498	Infectious agent detection by nucleic acid (DNA or RNA); enterovirus, amplified probe technique, includes reverse transcription when performed
87500	Infectious agent detection by nucleic acid (DNA or RNA); vancomycin resistance (eg, enterococcus species van A, van B), amplified probe technique
87501	Infectious agent detection by nucleic acid (DNA or RNA); influenza virus, includes reverse transcription, when performed, and amplified probe technique, each type or subtype
87502	Infectious agent detection by nucleic acid (DNA or RNA); influenza virus, for multiple types or sub-types, includes multiplex reverse transcription, when performed, and multiplex amplified probe technique, first 2 types or sub-types
87503	Infectious agent detection by nucleic acid (DNA or RNA); influenza virus, for multiple types or sub-types, includes multiplex reverse transcription, when performed, and multiplex amplified probe technique, each additional influenza virus type or sub-type beyond 2 (List separately in addition to code for primary procedure)
87516	Infectious agent detection by nucleic acid (DNA or RNA); hepatitis B virus, amplified probe technique
87517	Infectious agent detection by nucleic acid (DNA or RNA); hepatitis B virus, quantification
87520	Infectious agent detection by nucleic acid (DNA or RNA); hepatitis C, direct probe technique
87521	Infectious agent detection by nucleic acid (DNA or RNA); hepatitis C, amplified probe technique, includes reverse transcription when performed
87522	Infectious agent detection by nucleic acid (DNA or RNA); hepatitis C, quantification, includes reverse transcription when performed
87523	Infectious agent detection by nucleic acid (DNA or RNA); hepatitis D (delta), quantification, including reverse transcription, when performed
87528	Infectious agent detection by nucleic acid (DNA or RNA); Herpes simplex virus, direct probe technique
87529	Infectious agent detection by nucleic acid (DNA or RNA); Herpes simplex virus, amplified probe technique
87531	Infectious agent detection by nucleic acid (DNA or RNA); Herpes virus-6, direct probe technique
87532	Infectious agent detection by nucleic acid (DNA or RNA); Herpes virus-6, amplified probe technique
87534	Infectious agent detection by nucleic acid (DNA or RNA); HIV-1, direct probe technique
87535	Infectious agent detection by nucleic acid (DNA or RNA); HIV-1, amplified probe technique, includes reverse transcription when performed
87536	Infectious agent detection by nucleic acid (DNA or RNA); HIV-1, quantification, includes reverse transcription when performed

87537	Infectious agent detection by nucleic acid (DNA or RNA); HIV-2, direct probe technique
87538	Infectious agent detection by nucleic acid (DNA or RNA); HIV-2, amplified probe technique, includes reverse transcription when performed
87539	Infectious agent detection by nucleic acid (DNA or RNA); HIV-2, quantification, includes reverse transcription when performed
87540	Infectious agent detection by nucleic acid (DNA or RNA); Legionella pneumophila, direct probe technique
87541	Infectious agent detection by nucleic acid (DNA or RNA); Legionella pneumophila, amplified probe technique
87550	Infectious agent detection by nucleic acid (DNA or RNA); Mycobacteria species, direct probe technique
87551	Infectious agent detection by nucleic acid (DNA or RNA); Mycobacteria species, amplified probe technique
87555	Infectious agent detection by nucleic acid (DNA or RNA); Mycobacteria tuberculosis, direct probe technique
87556	Infectious agent detection by nucleic acid (DNA or RNA); Mycobacteria tuberculosis, amplified probe technique
87560	Infectious agent detection by nucleic acid (DNA or RNA); Mycobacteria avium-intracellulare, direct probe technique
87561	Infectious agent detection by nucleic acid (DNA or RNA); Mycobacteria avium-intracellulare, amplified probe technique
87580	Infectious agent detection by nucleic acid (DNA or RNA); Mycoplasma pneumoniae, direct probe technique
87581	Infectious agent detection by nucleic acid (DNA or RNA); Mycoplasma pneumoniae, amplified probe technique
87590	Infectious agent detection by nucleic acid (DNA or RNA); Neisseria gonorrhoeae, direct probe technique
87591	Infectious agent detection by nucleic acid (DNA or RNA); Neisseria gonorrhoeae, amplified probe technique
87623	Infectious agent detection by nucleic acid (DNA or RNA); Human Papillomavirus (HPV), low-risk types (eg, 6, 11, 42, 43, 44)
87624	Infectious agent detection by nucleic acid (DNA or RNA); Human Papillomavirus (HPV), high-risk types (eg, 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68)
87625	Infectious agent detection by nucleic acid (DNA or RNA); Human Papillomavirus (HPV), types 16 and 18 only, includes type 45, if performed
87640	Infectious agent detection by nucleic acid (DNA or RNA); Staphylococcus aureus, amplified probe technique
87641	Infectious agent detection by nucleic acid (DNA or RNA); Staphylococcus aureus, methicillin resistant, amplified probe technique
87650	Infectious agent detection by nucleic acid (DNA or RNA); Streptococcus, group A, direct probe technique
87651	Infectious agent detection by nucleic acid (DNA or RNA); Streptococcus, group A, amplified probe technique
87653	Infectious agent detection by nucleic acid (DNA or RNA); Streptococcus, group B, amplified probe technique
87660	Infectious agent detection by nucleic acid (DNA or RNA); Trichomonas vaginalis, direct probe technique
87661	Infectious agent detection by nucleic acid (DNA or RNA); Trichomonas vaginalis, amplified probe technique
87662	Infectious agent detection by nucleic acid (DNA or RNA); Zika virus, amplified probe technique

The following CPT codes are considered investigational for <u>Commercial Members: Managed Care (HMO and POS), PPO, Indemnity, Medicare HMO Blue and Medicare PPO Blue:</u>

CPT Codes

CPT codes:	Code Description
87472	Infectious agent detection by nucleic acid (DNA or RNA); Bartonella henselae and Bartonella quintana, quantification
87475	Infectious agent detection by nucleic acid (DNA or RNA); Borrelia burgdorferi, direct probe technique
87482	Infectious agent detection by nucleic acid (DNA or RNA); Candida species, quantification
87483	Infectious agent detection by nucleic acid (DNA or RNA); central nervous system pathogen (eg, Neisseria meningitidis, Streptococcus pneumoniae, Listeria, Haemophilus influenzae, E. coli, Streptococcus agalactiae, enterovirus, human parechovirus, herpes simplex virus type 1 and 2, human herpesvirus 6, cytomegalovirus, varicella zoster virus, Cryptococcus), includes multiplex reverse transcription, when performed, and multiplex amplified probe technique, multiple types or subtypes, 12-25 targets
87492	Infectious agent detection by nucleic acid (DNA or RNA); Chlamydia trachomatis, quantification
87510	Infectious agent detection by nucleic acid (DNA or RNA); Gardnerella vaginalis, direct probe technique
87511	Infectious agent detection by nucleic acid (DNA or RNA); Gardnerella vaginalis, amplified probe technique
87512	Infectious agent detection by nucleic acid (DNA or RNA); Gardnerella vaginalis, quantification
87525	Infectious agent detection by nucleic acid (DNA or RNA); hepatitis G, direct probe technique
87526	Infectious agent detection by nucleic acid (DNA or RNA); hepatitis G, amplified probe technique
87527	Infectious agent detection by nucleic acid (DNA or RNA); hepatitis G, quantification
87530	Infectious agent detection by nucleic acid (DNA or RNA); Herpes simplex virus, quantification
87533	Infectious agent detection by nucleic acid (DNA or RNA); Herpes virus-6, quantification
87542	Infectious agent detection by nucleic acid (DNA or RNA); Legionella pneumophila, quantification
87552	Infectious agent detection by nucleic acid (DNA or RNA); Mycobacteria species, quantification
87557	Infectious agent detection by nucleic acid (DNA or RNA); Mycobacteria tuberculosis, quantification
87562	Infectious agent detection by nucleic acid (DNA or RNA); Mycobacteria avium-intracellulare, quantification
87563	Infectious agent detection by nucleic acid (DNA or RNA); Mycoplasma genitalium, amplified probe technique
87582	Infectious agent detection by nucleic acid (DNA or RNA); Mycoplasma pneumoniae, quantification
87592	Infectious agent detection by nucleic acid (DNA or RNA); Neisseria gonorrhoeae, quantification
87652	Infectious agent detection by nucleic acid (DNA or RNA); Streptococcus, group A, quantification
0321U	Infectious agent detection by nucleic acid (DNA or RNA), genitourinary pathogens, identification of 20 bacterial and fungal organisms and identification of 16 associated antibiotic-resistance genes, multiplex amplified probe technique
0323U	Infectious agent detection by nucleic acid (DNA and RNA), central nervous system pathogen, metagenomic next-generation sequencing, cerebrospinal fluid (CSF), identification of pathogenic bacteria, viruses, parasites, or fungi

0369U	Infectious agent detection by nucleic acid (DNA and RNA), gastrointestinal pathogens, 31 bacterial, viral, and parasitic organisms and identification of 21 associated antibiotic-resistance genes, multiplex amplified probe technique
0373U	Infectious agent detection by nucleic acid (DNA and RNA), respiratory tract infection, 17 bacteria, 8 fungus, 13 virus, and 16 antibiotic-resistance genes, multiplex amplified probe technique, upper or lower respiratory specimen
0402U	Infectious agent (sexually transmitted infection), Chlamydia trachomatis, Neisseria gonorrhoeae, Trichomonas vaginalis, Mycoplasma genitalium, multiplex amplified probe technique, vaginal, endocervical, or male urine, each pathogen reported as detected or not detected

The following CPT codes are considered investigational for Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity:

CPT Codes

CPT codes:	Code Description
87505	Infectious agent detection by nucleic acid (DNA or RNA); gastrointestinal pathogen (eg, Clostridium difficile, E. coli, Salmonella, Shigella, norovirus, Giardia), includes multiplex reverse transcription, when performed, and multiplex amplified probe technique, multiple types or subtypes, 3-5 targets
87506	Infectious agent detection by nucleic acid (DNA or RNA); gastrointestinal pathogen (eg, Clostridium difficile, E. coli, Salmonella, Shigella, norovirus, Giardia), includes multiplex reverse transcription, when performed, and multiplex amplified probe technique, multiple types or subtypes, 6-11 targets
87507	Infectious agent detection by nucleic acid (DNA or RNA); gastrointestinal pathogen (eg, Clostridium difficile, E. coli, Salmonella, Shigella, norovirus, Giardia), includes multiplex reverse transcription, when performed, and multiplex amplified probe technique, multiple types or subtypes, 12-25 targets

Description

Nucleic Acid Probes

A nucleic acid probe is used to detect and identify species or subspecies of organisms by identifying nucleic acid sequences in a sample. Nucleic acid probes detect genetic materials, such as RNA or DNA, unlike other tests, which use antigens or antibodies to diagnose organisms.

The availability of nucleic acid probes has permitted the rapid direct identification of microorganism DNA or RNA. Amplification techniques result in exponential increases in copy numbers of a targeted strand of microorganism-specific DNA. The most used amplification technique is polymerase chain reaction (PCR) or reverse transcriptase PCR. In addition to PCR, other nucleic acid amplification techniques have been developed, such as transcription-mediated amplification, loop-mediated isothermal DNA amplification, strand displacement amplification, nucleic acid sequence-based amplification, and branched-chain DNA signal amplification. After amplification, target DNA can be readily detected using a variety of techniques. The amplified product can also be quantified to assess how many microorganisms are present. Quantification of the number of nucleic acids permits serial assessments of response to treatment; the most common clinical application of quantification is the serial measurement of HIV RNA (called viral load).

The direct probe technique, amplified probe technique, and probe with quantification methods vary based on the degree to which the nucleic acid is amplified and the method for measurement of the signal. The direct probe technique refers to detection methods in which nucleic acids are detected without an initial amplification step. The amplified probe technique refers to detection methods in which either target, probe, or signal amplification is used to improve the sensitivity of the assay over direct probe techniques, without quantification of nucleic acid amounts.

- Target amplification methods include PCR (including PCR using specific probes, nested or multiplex PCR), nucleic acid-based sequence amplification, transcription-mediated amplification, and strand displacement amplification. Nucleic acid-based sequence amplification and transcription-mediated amplification involve amplification of an RNA (rather than a DNA) target.
- Probe amplification methods include ligase chain reaction.
- Signal amplification methods include branched DNA (bDNA) probes and hybrid capture methods using an anti-DNA/RNA hybrid antibody.

The probe with quantification techniques refers to quantitative PCR or real-time PCR methods that use a reporter at each stage of the PCR to generate absolute or relative amounts of a known nucleic acid sequence in the original sample. These methods may use DNA-specific dyes (ethidium bromide or SYBR green), hybridization probes (cleavage-based [TaqMan] or displaceable), or primer incorporated probes.

Direct assays will generally have lower sensitivity than amplified probes. In practice, most commercially available probes are amplified, with a few exceptions. For this evidence review, indications for direct and/or amplified probes without quantification are considered together, while indications for a probe with quantification are considered separately.

Classically, identification of microorganisms relies either on the culture of body fluids or tissues or identification of antigens, using a variety of techniques including direct fluorescent antibody technique and qualitative or quantitative immunoassays. These techniques are problematic when the microorganism exists in very small numbers or is technically difficult to culture. Indirect identification of microorganisms by immunoassays for specific antibodies reactive with the microorganism is limited by difficulties in distinguishing between past exposure and current infection.

Potential reasons for a nucleic acid probe to be associated with improved clinical outcomes compared with standard detection techniques include the following (note: in all cases, for there to be clinical utility, making a diagnosis should be associated with changes in clinical management, which could include initiation of effective treatment, discontinuation of other therapies, or avoidance of invasive testing):
- Significantly improved speed and/or efficiency in making a diagnosis.
- Improved likelihood of obtaining any diagnosis in cases where standard culture is difficult. Potential reasons for difficulty in obtaining standard culture include low numbers of the organisms (e.g., HIV), fastidious or lengthy culture requirements (e.g., *Mycobacteria, Chlamydia*, *Neisseria* species), or difficulty in collecting an appropriate sample (e.g., herpes simplex encephalitis).
- There is no way to definitively make a diagnosis without nucleic acid testing.
- The use of nucleic acid probe testing provides qualitatively different information than that available from standard cultures, such as information regarding disease prognosis or response to treatment. These include cases where quantification of viral load provides prognostic information or is used to measure response to therapy.

The risks of nucleic acid testing include false-positive and false-negative results, inaccurate identification of pathogens by the device, inaccurate interpretation of test results, or incorrect operation of the instrument.
- False-positive results can lead to unnecessary treatment, with its associated toxicities and side effects, including allergic reaction. In addition, true diagnosis and treatment could be delayed or missed altogether.
- False-negative results could delay diagnosis and initiation of proper treatment.
- It is possible that these risks can be mitigated by the use of a panel of selected pathogens indicated by the clinical differential diagnosis while definitive culture results are pending.

Summary

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, microbial

identification using standard culture is difficult or impossible, and/or treatment decisions are based on quantitative results.

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 a systematic review and a pivotal prospective study. Relevant outcomes include test accuracy and validity, other test performance measures, medication use, 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 that the technology results in an improvement in the net health outcome.

For individuals who have signs and/or symptoms of gastroenteritis who receive a nucleic acid-based gastrointestinal pathogen panel, the evidence includes prospective and retrospective evaluations of the tests' sensitivity and specificity and prospective studies on utility. Relevant outcomes include test accuracy and validity, other test performance measures, medication use, symptoms, and change in disease status. The evidence suggests that 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 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 that the technology results in an improvement in the net health outcome.

For individuals who have signs and/or symptoms of respiratory infection who receive a nucleic acid-based respiratory pathogen panel, the evidence includes a systematic review and 2 randomized controlled trials (RCTs). Relevant outcomes include test accuracy and validity, other test performance measures, medication use, symptoms, and change in disease status. The systematic review reported that all 3 reviewed multiplex polymerase chain reaction systems were highly accurate. One RCT and 1 quasi-RCT evaluated utility of a respiratory panel and found benefits in time-to-treat and length of hospital stay. In addition, 1 subanalysis found fewer antibiotics being prescribed for patients diagnosed with the panel. The panel did not significantly affect duration of antibiotic use, readmission, or mortality rates. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

Policy History

Date	Action
5/2024	Clarified coding information.
1/2024	Clarified coding information.
12/2023	Policy clarified. Transferred respiratory virus panel testing to MP 045 Pathogen Panel Testing.
8/2023	Annual policy review. References added. Policy statements unchanged.
4/2023	Clarified coding information.
1/2023	Clarified coding information.
9/2022	Policy clarified. • Ongoing investigational urinary tract infection panel transferred to new MP 045 Pathogen Panel. • Ongoing medically necessary nucleic acid testing for the following microorganisms transferred to new MP 0045 Pathogen Panel: ▪ Babesiosis ▪ Ehrlichiosis, unspecified ▪ Tick-borne rickettsiosis, unspecified.

8/2022	Clarified coding information. Annual policy review. Description, summary, and references updated. Policy statements unchanged.
7/2022	Clarified coding information.
1/2022	Clarified coding information.
11/2021	Policy clarified to include that urinary tract infection panel is considered investigational.
4/2021	Clarified coding information.
5/2020	Clarified coding information.
3/2020	New medically necessary and investigational indications described. Policy statements changed accordingly and edited for clarity. Clarified coding information. Effective 3/11/2020. Nucleic acid testing is medically necessary for: ▪ Chlamydia pneumoniae ▪ Bordetella Pertussis ▪ Mumps ▪ Rubeola (measles) ▪ Influenza virus ▪ Zika virus. Nucleic acid testing respiratory virus panel (without quantification of viral load) is considered medically necessary. Nucleic acid testing is investigational for: ▪ Central nervous system pathogen panel ▪ Gastrointestinal pathogen panel Nucleic acid testing using direct or amplified probe technique is investigational for Gardernella vaginalis.
1/2020	Clarified coding information.
2/2019	Annual policy review. Description, summary and references updated. Policy statements unchanged.
5/2018	Annual policy review. Investigational statement added for central nervous system pathogen panel. Prior Authorization Information reformatted. Clarified coding information. Effective 5/1/2018.
1/2018	Clarified coding information.
8/2016	Clarified coding information.
7/2016	Annual policy review. *C. difficile* added to list of medically necessary probes. Effective 7/1/2016.
5/2016	Annual policy review. Direct and amplified assays (without quantification) grouped for medically necessary statements. Medically necessary statement added for non-quantified nucleic acid-based testing for enterovirus, *Legionella pneumophila, Mycoplasma pneumoniae,* and *Bartonella spp,* and for quantified testing for human herpesvirus 6. *Borrelia* testing removed from policy. Effective 5/1/2016.
3/2016	Annual policy review. CPT code 87481 is only medically necessary for severe, treatment resistant Candida infection. Effective 3/1/2016.
7/2015	Local Coverage Determination (LCD): Infectious Disease Molecular Diagnostic Testing (L31747) added.
2/2015	Annual policy review. New investigational indications described. Effective 2/1/2015.
1/2015	Clarified coding information.
3/2014	New medical policy describing ongoing investigational and medically necessary indications. Effective 3/1/2014.

Information Pertaining to All Blue Cross Blue Shield Medical Policies

Click on any of the following terms to access the relevant information:

Medical Policy Terms of Use
Managed Care Guidelines
Indemnity/PPO Guidelines
Clinical Exception Process
Medical Technology Assessment Guidelines

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