

## **Medical Coverage Policy**

Effective Date: 12/14/2023 Revision Date: 12/14/2023 Review Date: 12/14/2023 Policy Number: HUM-0578-018

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Change Summary: Updated Title, Coverage Determination, Coverage Limitations, Provider Claims Codes, References

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#### **Disclaimer**

State and federal law, as well as contract language, including definitions and specific inclusions/exclusions, take precedence over clinical policy and must be considered first in determining eligibility for coverage. Coverage may also differ for our Medicare and/or Medicaid members based on any applicable Centers for Medicare & Medicaid Services (CMS) coverage statements including National Coverage Determinations (NCD), Local Medical Review Policies (LMRP) and/or Local Coverage Determinations. Refer to the CMS website. The member's health plan benefits in effect on the date services are rendered must be used. Clinical policy is not intended to preempt the judgment of the reviewing medical director or dictate to health care providers how to practice medicine. Health care providers are expected to exercise their medical judgment in rendering appropriate care. Identification of selected brand names of devices, tests and procedures in a medical coverage policy is for reference only and is not an endorsement of any one device, test or procedure over another. Clinical technology is constantly evolving, and we reserve the right to review and update this policy periodically. No part of this publication may be reproduced, stored in a retrieval system or transmitted, in any shape or form or by any means, electronic, mechanical, photocopying or otherwise, without permission from Humana.

## **Description**

Microbes (eg, bacteria, fungi, parasites, viruses) cause infections in humans. Testing methods for detecting microbes traditionally include detection by cultures or antibody testing. However, since microbes contain genetic material (DNA and RNA), genetic testing methods can be applied to detect pathogens. The genetic material in microbes differs from the genetic material in human cells. Samples used for genetic testing for infectious disease include aspirated fluid around joints, blood, cerebrospinal fluid, sputum, stool and urine. Genetic testing can be used to diagnose infections, identify and type the microbes causing an infection as well as determine if a microbe will respond to a specific treatment.

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Nucleic acid amplification test (NAAT or NAT) is one type of genetic test used for infectious disease. This technique makes numerous copies (amplification) of any genetic material from the microbes present in a sample so that it can be more easily detected. One type of NAAT is polymerase chain reaction (PCR). These tests provide faster results than traditional methods and are more sensitive and specific.

Some newer genetic tests for infectious disease can analyze for several different microbes simultaneously from a single sample. This is called panel testing, also known as molecular panels or multiplex testing. Panel tests may be used to identify infections that have similar signs and symptoms but can be caused by a variety of microbes. Currently, the most common panel tests are respiratory or gastrointestinal infection multiplex NAAT panels. For example, an individual may present with symptoms such as abdominal pain and diarrhea which can be caused by a virus, bacteria or parasite. Genetic testing panels may lead to a quicker diagnosis which can influence treatment decisions but may also include those with unclear medical management. Another indication for multiplex pathogen identification testing are central nervous system (CNS) infections. BioFire FilmArray Meningitis/Encephalitis (ME) Panel is an example of multiplex pathogen test for CNS infections.

Multiplex pathogen identification panels have been suggested for the evaluation of many types of infections including, but may not be limited to, bloodstream, bone and joint, encephalitis, meningitis, surgical wounds and urinary tract infections. Examples of multiplex pathogen identification panels for these infections include, but may not be limited to: (Refer to Coverage Limitations section)

- Accelerate PhenoTest BC Kit
- BioFire Bone and Joint Infection (BJI) Panel
- BioFire FilmArray Blood Culture Identification (BCID2) Panel
- Lesion Infection (Wound)
- Qlear UTI
- Qlear UTI-Reflex ABR
- Urogenital Pathogen with Rx Panel (UPX)

Next-generation sequencing (NGS), also known as high-throughput sequencing or deep sequencing, has been proposed to identify microbial infections for several indications. There are two approaches to NGS: whole genome sequencing or

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targeted sequencing which includes PCR in the process. An example of NGS for infectious disease includes MicroGenDx qPCR and NGS for Infection. (Refer to Coverage Limitations section).

Antibiotic resistance testing, also known as antimicrobial susceptibility testing, provides information that can be used to guide treatment decisions such as the selection of appropriate antibiotic regimens. There are different methods for testing, including conventional methods (phenotypic testing) and newer molecular (genotypic) techniques such as PCR, NAAT and NGS. Examples of molecular antibiotic resistance tests include, but may not be limited to, ABRx Antibiotic Resistance Panel, RevoGene Carba C and XPERT CARBA-R. (Refer to Coverage Limitations Section).

Some laboratories offer panels that include both pathogen identification and antibiotic resistance or sensitivity. Panels are used for many indications including, but may not be limited to, recurrent urinary tract infections (UTIs). Examples of this type of testing include, but may not be limited to, **GENETWORX UTI with ABR, Guidance UTI and Qlear UTI-Reflex ABR.** (Refer to Coverage Limitations section).

Differentiation between bacterial from viral infections is an emerging indication for multiplex pathogen testing. An example of this type of test is **MeMed BV**. (Refer to Coverage Limitations section).

Metagenomic NGS is an evolving, novel molecular technology proposed to detect pathogens for infectious disease and can potentially provide direct, unbiased analysis of microbial composition of specimens without reliance on traditional culture or targeted molecular tests. An example is Johns Hopkins Metagenomic Next-Generation Sequencing Assay for Infectious Disease. (Refer to Coverage Limitations section).

Genetic testing for infectious disease differs from genetic tests for inherited conditions. Microbes associated with infectious disease contain genetic material but the genetic material contained within microbes differs from genetic material within human cells. Genetic testing for inherited conditions, also known as germline mutation testing, analyzes an individual's DNA and can identify genetic mutations to determine inherited risk of disease. An individual's germline DNA is constant and identical in all body tissue types. The DNA and RNA of microbes are present only in

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the tissue sampled, are not representative of an individual's germline DNA and are not inheritable.

**Related Medical Coverage Policies** 

Melatea Mealear Coverage Folicies			
Test/Indication	Medical Coverage Policy		
Molecular testing for bacterial	Molecular Diagnostic Testing for		
vaginosis, vaginal candidiasis or	Reproductive Health		
vaginitis			
Serologic (antibody) testing for SARS-	Severe Acute Respiratory Syndrome		
CoV-2	Coronavirus 2		
	Serologic (Antibody) Testing		
Viral testing for SARS-CoV-2	Severe Acute Respiratory Syndrome		
	Coronavirus 2		
	Viral Testing		

# Coverage Determination

<u>Central Nervous System Infection Multiplex Pathogen Identification Panel</u>

Humana members may be eligible under the Plan for **central nervous system (CNS)** 

**infection multiplex pathogen identification panel** (87483) when an individual presents with signs and symptoms of CNS infection (eg, encephalitis, meningitis).

# <u>Gastrointestinal Multiplex Pathogen Identification Panel – Targeted (Up to 5 Targets)</u>

Humana members may be eligible under the Plan for **gastrointestinal multiplex pathogen identification panel up to 5 targets** (87505) when the following criteria are met:

- Individual presents with signs and symptoms of gastrointestinal infection including travel-related diarrhea (eg, abdominal pain, bloody stool, dehydration, diarrhea, loss of appetite, nausea, vomiting) for greater than 7 days duration;
   AND
- Traditional stool test (eg, culture, microscopic analysis, antigen analysis) results are negative; **AND**

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 Results of the test will determine therapeutic management (eg, antibiotic treatment)

## <u>Gastrointestinal Infection Multiplex Pathogen Identification Panel – Expanded (6</u> to 25 Targets)

Humana members may be eligible under the Plan for **gastrointestinal infection multiplex pathogen identification panel containing 6 to 25 targets** (87506, 87507) when the following criteria are met:

- Individual meets the above <u>criteria for targeted panel</u>; AND
- Individual is immunocompromised and/or considered high-risk for serious complications and includes any of the following:
  - Currently receiving cancer treatment; OR
  - Currently receiving chronic glucocorticoid therapy; OR
  - Diagnosed with human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS); OR
  - Diagnosed with inherited disease that affects the immune system (eg, agammaglobulinemia, selective IgA deficiency); OR
  - Organ transplant recipient

## <u>Respiratory Infection Multiplex Pathogen Identification Panel – Targeted (Up to 5 Targets)</u>

Humana members may be eligible under the Plan for **respiratory infection multiplex pathogen identification panel up to 5 targets** (87631) when the following criteria are met:

 Individual presents with signs and symptoms of respiratory infection (eg, cough, dyspnea [short of breath], fever, sore throat, tight chest, wheezing); AND

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- Individual is immunocompromised and/or considered high-risk for serious complications and includes any of the following:
  - Currently receiving cancer treatment; OR
  - Currently receiving chronic glucocorticoid therapy; OR
  - Diagnosed with human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS); OR
  - Diagnosed with inherited disease that affects the immune system (eg, agammaglobulinemia, selective IgA deficiency); OR
  - Organ transplant recipient; AND
- Results of the test will determine therapeutic management (eg, antibiotic treatment)

## Coverage Limitations

Humana members may **NOT** be eligible under the Plan for **multiplex pathogen identification panels for infectious disease** for any indications other than those listed above including, but may not be limited to:

- Antibiotic resistance including, but may not be limited to:
  - ABRx Antibiotic Resistance Panel
  - Acuitas AMR Gene Panel
  - o RevoGene Carba C
  - XPERT Carba-R
- Aspergillus species (eg, MycoDART Dual Amplification Real-Time PCR Panel for 4 Aspergillus Species [Aspergillus Diagnostic Panel] [0109U])
- Bacteremia
- Blood culture identification (87154) including, but may not be limited to:
  - o BioFire FilmArray Blood Culture Identification 2 (BCID2) Panel

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- ePlex BCID Gram-Positive Panel (0141U)
- ePlex BCID Gram-Negative Panel (0142U)
- Candidiasis, including nails (eg, Candida Comprehensive Panel, T2Candida Panel) (87481)
- Combination pathogen identification and antibiotic resistance or sensitivity
- Differentiation of bacterial from viral infection (eg, MeMed BV [0351U])
- Ear, nose and throat (ENT) (eg, Bacterial ENT Test Panel, Fungal ENT Test Panel, GENETWORx ENT Pathogen Panel, Viral ENT Test Panel)
- Eye infection (eg, Bacterial Eye Infection Test Panel, Fungal Eye Infection Test, Panel Viral Eye Infection Test Panel)
- Fever of unknown origin/acute febrile illness (eg, BioFire Global Fever Panel, BioFire Global Fever Special Pathogens Panel)
- Fungal pathogen identification (eg, ePlex BCID Fungal Pathogens [FP] Panel [0140U])
- Hematuria
- Interstitial cystitis (bladder pain syndrome)
- Myalgia
- Onychomycosis, including dystrophic nails (eg, Nail Fungal Infection Test, Nail PCR Diagnostics)
- Osteomyelitis (including bone and joint infections) (eg, BioFire Joint Infection [JI]
   Panel)
- Pancreatitis
- Pneumonia (eg, BioFire FilmArray Pneumonia Plus Panel)

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- Prostatitis (eg, Guidance Prostatitis)
- Prosthetic joint infection
- Pyelonephritis
- Sepsis (eg, T2Bacteria Panel)
- Tinea pedis
- Urinary tract infection (UTI) including, but may not be limited to:
  - Bridge Urinary Tract Infection Detection and Resistance Test (0321U)
  - GENETWORx Molecular PCR UTI Test (0416U)
  - Guidance UTI
  - Qlear UTI (0371U)
  - Qlear UTI-Reflex ABR (0372U)
  - Urogenital Pathogen with Rx Panel (UPX) (0374U)
- Venous leg ulcer
- Wound infection (eg, GENETWORx Wound Infection Diagnostics, Lesion Infection [Wound] [0370U], Wound Pathogen Panel)

These are considered experimental/investigational as they are not identified as widely used and generally accepted for any other proposed uses as reported in nationally recognized peer-reviewed medical literature published in the English language.

Humana members may **NOT** be eligible under the Plan for the following tests:

- Metagenomic sequencing including, but may not be limited to:
  - Johns Hopkins Metagenomic Next-Generation Sequencing Assay for Infectious Disease (0323U)
  - Karius Test (0152U)

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- MicroGenDx qPCR & NGS for Infection (0112U)
- RNA fluorescence in situ hybridization (FISH) with phenotypic minimum inhibitory concentration (MIC)-based antimicrobial susceptibility including, but may not be limited to:
  - Accelerate PhenoTest BC Kit (0086U)
  - Accelerate PhenoTest BC Kit AST Configuration (0311U)

These are considered experimental/investigational as they are not identified as widely used and generally accepted for the proposed uses as reported in nationally recognized peer-reviewed medical literature published in the English language.

Humana members may **NOT** be eligible under the plan for **multiplex pathogen identification panels for infectious disease** for any of the following:

- Duplicative testing following treatment for clearance of pathogen
- Duplicative testing within an episode for the same diagnosis
- Gastrointestinal panels of 26 or more targets (eg, GI Assay [Gastrointestinal Pathogen with ABR] [0369U])
- Multiplex pathogen identification panel for respiratory infections performed simultaneously with multiplex pathogen identification panel for pneumonia
- Respiratory panels 6 or more targets (87632, 87633) including, but may not be limited to:
  - BioFire FilmArray Respiratory Panel [RP]
  - BioFire Respiratory Panel 2.1 [0202U]
  - BioFire SpotFire Respiratory (R) Panel
  - ePlex Respiratory Pathogen (RP) Panel [0115U]
  - o ePlex Respiratory Pathogen Panel 2 [RP2] [0225U]
  - NxTAG Respiratory Pathogen Panel
  - NxTAG Respiratory Pathogen Panel + SARS-CoV-2
  - QIAstat-Dx Respiratory SARS-CoV-2 Panel [0223U]

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- Respiratory Pathogen with ABR (RPX) (0373U)
- o T.E.N. Upper Respiratory Infection Panel

These are considered not medically necessary as defined in the member's individual certificate. Please refer to the member's individual certificate for the specific definition.

## **Background**

Additional information about **infectious disease** may be found from the following websites:

- Centers for Disease Control and Prevention
- Infectious Diseases Society of America
- National Library of Medicine

# Medical Alternatives

Alternatives to **multiplex pathogen identification panel for bacteremia** include, but may not be limited to:

Blood culture

Alternatives to **multiplex pathogen identification panel for chronic wounds** include, but may not be limited to:

Cultures/pathology of wound, urine and blood

Alternatives to **multiplex pathogen identification panel for onychomycosis** include, but may not be limited to:

- Fungal culture
- Histopathologic examination of nail clippings

Alternatives to **multiplex pathogen identification panel for prostatitis** include, but may not be limited to:

Urinalysis and culture

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Alternatives to multiplex pathogen identification panel for sinusitis and rhinosinusitis include, but may not be limited to:

- Clinical examination
- Nasal/sinus cultures

Alternatives to **multiplex pathogen identification panel for tinea pedis** include, but may not be limited to:

- Clinical examination
- Microscopy and culture of skin scrapings

Alternatives to **multiplex pathogen identification panel for urinary tract infection** include, but may not be limited to:

Urinalysis and culture

Physician consultation is advised to make an informed decision based on an individual's health needs.

## Provider Claims Codes

Any CPT, HCPCS or ICD codes listed on this medical coverage policy are for informational purposes only. Do not rely on the accuracy and inclusion of specific codes. Inclusion of a code does not guarantee coverage and or reimbursement for a service or procedure.

CPT® Code(s)	Description	Comments
81479	Unlisted molecular pathology procedure	Not Covered if used to report any test outlined in Coverage Limitations section

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87154	Culture, typing; identification of blood pathogen and resistance typing, when performed, by nucleic acid (DNA or RNA) probe, multiplexed amplified probe technique including multiplex reverse transcription, when performed, per culture or isolate, 6 or more targets	Not Covered
87481	Infectious agent detection by nucleic acid (DNA or RNA); Candida species, amplified probe technique	Not Covered
87483	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	
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	

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87631	Infectious agent detection by nucleic acid (DNA or RNA); respiratory virus (eg, adenovirus, influenza virus, coronavirus, metapneumovirus, parainfluenza virus, respiratory syncytial virus, rhinovirus), includes multiplex reverse transcription, when performed, and multiplex amplified probe technique, multiple types or subtypes, 3-5 targets	
87632	Infectious agent detection by nucleic acid (DNA or RNA); respiratory virus (eg, adenovirus, influenza virus, coronavirus, metapneumovirus, parainfluenza virus, respiratory syncytial virus, rhinovirus), includes multiplex reverse transcription, when performed, and multiplex amplified probe technique, multiple types or subtypes, 6-11 targets	Not Covered
87633	Infectious agent detection by nucleic acid (DNA or RNA); respiratory virus (eg, adenovirus, influenza virus, coronavirus, metapneumovirus, parainfluenza virus, respiratory syncytial virus, rhinovirus), includes multiplex reverse transcription, when performed, and multiplex amplified probe technique, multiple types or subtypes, 12-25 targets	Not Covered
87798	Infectious agent detection by nucleic acid (DNA or RNA), not otherwise specified; amplified probe technique, each organism	Not Covered if used to report any test outlined in Coverage Limitations section
0086U	Infectious disease (bacterial and fungal), organism identification, blood culture, using rRNA FISH, 6 or more organism targets, reported as positive or negative with phenotypic minimum inhibitory concentration (MIC)-based antimicrobial susceptibility	Not Covered
0109U	Infectious disease (Aspergillus species), real-time PCR for detection of DNA from 4 species (A. fumigatus, A. terreus, A. niger, and A. flavus), blood, lavage fluid, or tissue, qualitative reporting of presence or absence of each species	Not Covered
0112U	Infectious agent detection and identification, targeted sequence analysis (16S and 18S rRNA genes) with drugresistance gene	Not Covered

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0115U	Respiratory infectious agent detection by nucleic acid (DNA and RNA), 18 viral types and subtypes and 2 bacterial targets, amplified probe technique, including multiplex reverse transcription for RNA targets, each analyte reported as detected or not detected	
0140U	Infectious disease (fungi), fungal pathogen identification, DNA (15 fungal targets), blood culture, amplified probe technique, each target reported as detected or not detected	Not Covered
0141U	Infectious disease (bacteria and fungi), gram-positive organism identification and drug resistance element detection, DNA (20 gram-positive bacterial targets, 4 resistance genes, 1 pan gramnegative bacterial target, 1 pan Candida target), blood culture, amplified probe technique, each target reported as detected or not detected	Not Covered
0142U	Infectious disease (bacteria and fungi), gram-negative bacterial identification and drug resistance element detection, DNA (21 gram-negative bacterial targets, 6 resistance genes, 1 pan grampositive bacterial target, 1 pan Candida target), amplified probe technique, each target reported as detected or not detected	Not Covered
0152U	Infectious disease (bacteria, fungi, parasites, and DNA viruses), microbial cell-free DNA, plasma, untargeted next-generation sequencing, report for significant positive pathogens	Not Covered
0202U	Infectious disease (bacterial or viral respiratory tract infection), pathogen-specific nucleic acid (DNA or RNA), 22 targets including severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), qualitative RT-PCR, nasopharyngeal swab, each pathogen reported as detected or not detected	Not Covered
0223U	Infectious disease (bacterial or viral respiratory tract infection), pathogen-specific nucleic acid (DNA or RNA), 22 targets including severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), qualitative RT-PCR, nasopharyngeal swab, each pathogen reported as detected or not detected	Not Covered

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0225U	Infectious disease (bacterial or viral respiratory tract infection) pathogen-specific DNA and RNA, 21 targets, including severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), amplified probe technique, including multiplex reverse transcription for RNA targets, each analyte reported as detected or not detected	Not Covered
0311U	Infectious disease (bacterial), quantitative antimicrobial susceptibility reported as phenotypic minimum inhibitory concentration (MIC)—based antimicrobial susceptibility for each organisms identified	Not Covered
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	Not Covered
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	Not Covered
0351U	Infectious disease (bacterial or viral), biochemical assays, tumor necrosis factor-related apoptosis-inducing ligand (TRAIL), interferon gamma-induced protein-10 (IP-10), and C-reactive protein, serum, algorithm reported as likelihood of bacterial infection	Not Covered
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	Not Covered  New Code Effective  04/01/2023
0370U	Infectious agent detection by nucleic acid (DNA and RNA), surgical wound pathogens, 34 microorganisms and identification of 21 associated antibiotic-resistance genes, multiplex amplified probe technique, wound swab	Not Covered  New Code Effective  04/01/2023

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	Infectious agent detection by nucleic acid (DNA or RNA), genitourinary pathogen, semiquantitative identification, DNA	Not Covered
0371U	from 16 bacterial organisms and 1 fungal organism, multiplex amplified probe technique viaquantitative polymerase chain reaction (qPCR), urine	New Code Effective 04/01/2023
	Infectious disease (genitourinary pathogens), antibiotic-	Not Covered
0372U	resistance gene detection, multiplex amplified probe technique, urine, reported as an antimicrobial stewardship risk score	New Code Effective 04/01/2023
	Infectious agent detection by nucleic acid (DNA and RNA), respiratory tract infection, 17 bacteria, 8 fungus, 13 virus, and	Not Covered
0373U	16 antibiotic-resistance genes, multiplex amplified probe technique, upper or lower respiratory specimen	New Code Effective 04/01/2023
0374U	Infectious agent detection by nucleic acid (DNA or RNA), genitourinary pathogens, identification of 21 bacterial and fungal organisms and identification of 21 associated antibiotic-resistance genes, multiplex amplified probe technique, urine	Not Covered  New Code Effective  04/01/2023
0416U	Infectious agent detection by nucleic acid (DNA), genitourinary pathogens, identification of 20 bacterial and fungal organisms, including identification of 20 associated antibiotic-resistance genes, if performed, multiplex amplified probe technique, urine	Not Covered  New Code Effective  10/01/2023
CPT®		
Category III Code(s)	Description	Comments
No code(s) identified		
HCPCS Code(s)	Description	Comments
No code(s) io	lentified	

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