

## Reimbursement Policy

### Testing for Vector-borne Infections

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#### I. Policy Description

Arthropod vectors, including mosquitoes, ticks, fleas, and mites, that feed on vertebrate hosts can spread bacteria, protozoa, and viruses during feeding to their susceptible host, resulting in a variety of infections and diseases. Arboviruses (arthropod-borne viruses) include Zika virus, West Nile virus (WNV), chikungunya virus, dengue virus (DENV), yellow fever virus (YFV), and Colorado tick fever virus (CTF) to name a few. Malaria and babesiosis are both conditions caused by arthropod-borne protozoan parasites, Plasmodium and Babesia, respectively. Conditions caused by arthropod-borne bacteria include rickettsial diseases, ehrlichiosis, anaplasmosis, and Lyme disease, as well as other Borrelia-associated disorders (Calisher, 1994; CDC, 2024s). Isolation, identification, and characterization of these various infections depend on the causative agent. Identification methods may include culture testing, microscopy, and staining techniques; moreover, molecular testing, such as nucleic acid amplification testing (NAAT), and serologic testing, including immunofluorescence antibody assays and enzyme-linked immunosorbent assays (ELISA), can be used for laboratory diagnosis (Miller et al., 2024).

For Lyme disease and testing for *Borrelia burgdorferi*, please see AHS-G2143 Lyme Disease Testing.

#### II. Indications and/or Limitations of Coverage

Application of coverage criteria is dependent upon an individual's benefit coverage at the time of the request. Specifications pertaining to Medicare and Medicaid can be found in the "Applicable State and Federal Regulations" section of this policy document.

- 1) For individuals suspected of having babesiosis (see Note 1), the use of a Giemsa- or Wright-stain of a blood smear **or** nucleic acid amplification testing (NAAT) **MEETS COVERAGE CRITERIA**.
- 2) For individuals suspected of having babesiosis (see Note 1), the use of either an IgG or IgM indirect immunofluorescence antibody (IFA) assay for Babesia **DOES NOT MEET COVERAGE CRITERIA**.
- 3) For individuals suspected of having a relapsing fever caused by a *Borrelia* spp., the following testing **MEETS COVERAGE CRITERIA**:
  - a) For individuals suspected of having hard tick relapsing fever (HTRF) (see Note 2): serologic assays to detect *Borrelia* antibodies or PCR testing to detect *Borrelia miyamotoi*.

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- b) For individuals suspected of having louse-borne relapsing fever (LBRF) (see Note 3): peripheral blood smear microscopy or PCR testing to detect *Borrelia recurrentis*.
- c) For individuals suspected of having a soft tick relapsing fever (STRF)/tickborne relapsing fever (TBRF) (see Note 4): dark-field microscopy of a peripheral blood smear, microscopy of a Wright- or Giemsa-stained blood smear, PCR testing to detect *Borrelia* spp., or serologic assays to detect *Borrelia* antibodies.
- 4) For individuals suspected of having a relapsing fever caused by a *Borrelia* spp., culture testing for *Borrelia* **DOES NOT MEET COVERAGE CRITERIA**.
- 5) For individuals suspected of having chikungunya (see Note 5), the use of viral culture for diagnosis, NAAT for the presence of chikungunya in a serum sample, or IFA assay for IgM antibodies during both the acute and convalescent phases **MEETS COVERAGE CRITERIA**.
- 6) For individuals suspected of having Colorado tick fever (CTF) (see Note 6), the use of PCR testing or IFA for CTF-specific IgM antibodies **MEETS COVERAGE CRITERIA**.
- 7) For the detection of dengue virus (DENV), the use of NAAT, IgM antibody capture ELISA (MAC-ELISA), **or** NS1 ELISA, as well as a confirmatory plaque reduction neutralization test for DENV, **MEETS COVERAGE CRITERIA** in the following individuals:
  - a) For individuals suspected of having a DENV infection (see Note 7).
  - b) For individuals who are symptomatic for Zika virus infection (see Note 8).
- 8) For individuals suspected of having DENV (see Note 7), the use of IgG ELISA **or** hemagglutination testing **DOES NOT MEET COVERAGE CRITERIA**.
- 9) For individuals suspected of having ehrlichiosis and/or anaplasmosis (see Note 8), the use of NAAT of whole blood, IFA assay for IgG antibodies, or microscopy for morulae detection **MEETS COVERAGE CRITERIA**.
- 10) For individuals suspected of having ehrlichiosis and/or anaplasmosis (see Note 8), the use of an IFA assay for IgM antibodies **or** standard blood culture **DOES NOT MEET COVERAGE CRITERIA**.
- 11) For individuals suspected of having malaria (see Note 10), the use of a rapid immunochromatographic diagnostic test **or** smear microscopy to diagnose malaria, determine the species of *Plasmodium*, identify the parasitic life-cycle stage, and/or quantify the parasitemia (can be repeated up to three times within three days if initial microscopy is negative in suspected cases of malaria) **MEETS COVERAGE CRITERIA**.
- 12) To confirm the species of *Plasmodium* in an individual diagnosed with malaria, PCR testing **MEETS COVERAGE CRITERIA**.
- 13) For individuals suspected of having malaria (see Note 10), the use of IFA for *Plasmodium* antibodies **DOES NOT MEET COVERAGE CRITERIA**.
- 14) For individuals suspected of having a rickettsial disease (see Note 11), the use of an IFA assay for IgG antibodies (two tests occurring a minimum of two weeks apart) **MEETS COVERAGE CRITERIA**.

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- 15) For individuals suspected of having a rickettsial disease (see Note 11), the use of standard blood culture, NAAT, **or** IFA assay for IgM antibodies **DOES NOT MEET COVERAGE CRITERIA**.
- 16) For individuals suspected of having West Nile virus (WNV) disease (see Note 12), the use of IFA for WNV-specific IgG or IgM antibodies in either serum or CSF and a confirmatory plaque reduction neutralization test for WNV **MEETS COVERAGE CRITERIA**.
- 17) To confirm a WNV infection in individuals who are immunocompromised, nucleic acid detection of WNV **MEETS COVERAGE CRITERIA**.
- 18) For immunocompetent individuals suspected of having WNV disease (see Note 12), the use of NAAT for WNV **DOES NOT MEET COVERAGE CRITERIA**.
- 19) For individuals suspected of having a yellow fever virus (YFV) infection (see Note 13), the use of NAAT for YFV or serologic assays to detect virus-specific IgM and IgG antibodies, as well as a confirmatory plaque reduction neutralization test for YFV, **MEETS COVERAGE CRITERIA**.
- 20) For the detection of Zika virus, the use of NAAT **MEETS COVERAGE CRITERIA** in the following individuals:
  - a) Up to 12 weeks after the onset of symptoms for symptomatic (see Note 8) pregnant individuals who, during pregnancy, have **either** lived in or traveled to areas with current or past Zika transmission **or** who have had sex with someone who either lives in or has recently traveled to areas with current or past Zika virus transmission (see Note 14).
  - b) For symptomatic non-pregnant individuals living in or with recent travel to an area with an active CDC Zika Travel Health Notice or an area with current or past Zika virus transmission (see Note 14) when symptoms presented within the last seven days.
- 21) Zika virus NAAT and Zika virus IgM testing, as well as a confirmatory plaque reduction neutralization test for Zika, **MEETS COVERAGE CRITERIA** in **any** of the following situations:
  - a) Up to 12 weeks after the onset of symptoms for symptomatic (see Note 8) pregnant individuals who, during pregnancy, have **either** lived in or traveled to areas with an active CDC Zika Travel Health Notice **or** who have had sex with someone who either lives in or has recently traveled to areas with an active CDC Zika Travel Health Notice (see Note 14).
  - b) For pregnant individuals who have a fetus with prenatal ultrasound findings consistent with congenital Zika virus infection (see Note 15).
  - c) For infants born from individuals who, during pregnancy, tested positive for Zika virus.
  - d) For infants born with signs and symptoms of congenital Zika syndrome (see Note 15) and who have a birthing parent who had a possible Zika virus exposure during pregnancy.
  - e) For symptomatic non-pregnant individuals living in or with recent travel to an area with an active CDC Zika Travel Health Notice or an area with current or past Zika virus transmission (see Note 14) when symptoms presented more than seven days prior to testing.

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- 22) For non-pregnant individuals who have not traveled outside of the United States and its territories and who are symptomatic for Zika virus infection (see Note 8), NAAT and/or IgM testing for Zika detection **DOES NOT MEET COVERAGE CRITERIA.**
- 23) For asymptomatic individuals, testing for babesiosis, chikungunya virus, CTF, DENV, ehrlichiosis and/or anaplasmosis, malaria, rickettsial disease, TBRF, WNV, YFV, or Zika virus during a general exam without abnormal findings **DOES NOT MEET COVERAGE CRITERIA.**

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### NOTES:

**Note 1:** Typical signs and symptoms of babesiosis can include hemolytic anemia, splenomegaly, hepatomegaly, jaundice, and nonspecific flu-like symptoms such as fever, chills, body aches, weakness, and fatigue (CDC, 2024j).

**Note 2:** Typical signs and symptoms of HTRF (caused by *Borrelia miyamotoi*) can include chills or shakes, fatigue, nausea or vomiting, headache, and muscle and joint aches (CDC, 2024a).

**Note 3:** Typical signs and symptoms of LBRF (caused by *Borrelia recurrentis*) can include fever, headache, chills or shakes, muscle and joint aches, and nausea. Though the clinical symptoms of LBRF are similar to STRF, LBRF is usually associated with fewer relapses (CDC, 2024b)

**Note 4:** Typical signs and symptoms of STRF/TBRF (caused by *Borrelia hermsii*, *B. turicatae*, and other *Borrelia* bacteria) can include fever, headache, muscle aches, chills, dizziness, joint pain, nausea and vomiting, appetite loss, and rarely, facial paralysis eye pain or redness, or vision changes (CDC, 2024c).

**Note 5:** Typical signs and symptoms of chikungunya include high fever (>102°F or 39°C), joint pains (usually multiple joints, bilateral, and symmetric), headache, myalgia, arthritis, conjunctivitis, nausea, vomiting, and maculopapular rash (Staples et al., 2024).

**Note 6:** Typical signs and symptoms of CTF can include fever, chills, headache, myalgia, malaise, sore throat, vomiting, abdominal pain, and maculopapular or petechial rash (CDC, 2024e).

**Note 7:** Typical signs and symptoms of dengue include fever, headache, retro-orbital eye pain, myalgia, arthralgia, macular or maculopapular rash, petechiae, ecchymosis, purpura, epistaxis, gingival bleeding, hematuria, leukopenia, thrombocytopenia, hyponatremia, elevated AST and ALT, and nausea and/or vomiting (CDC, 2024f, 2024r).

**Note 8:** Typical signs and symptoms of Zika virus infection can include fever, rash, headache, joint pain, conjunctivitis (red eyes), and muscle pain (CDC, 2024t).

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**Note 9:** Typical signs and symptoms of ehrlichiosis and/or anaplasmosis usually begin 5-14 days after an infected tick bite, and they include fever, headache, malaise, myalgia, and shaking chills. Ehrlichiosis can also present with gastrointestinal issues, including nausea, vomiting, and diarrhea (Biggs et al., 2016).

**Note 10:** Typical signs and symptoms of malaria can include fever, influenza-like symptoms (e.g., chills, headache, body aches), anemia, jaundice, seizures, mental confusion, kidney failure, and acute respiratory distress syndrome (Tan & Abanyie, 2024).

**Note 11:** Typical signs and symptoms of rickettsial diseases (including Rocky Mountain spotted fever, *Rickettsia parkeri* rickettsiosis, *Rickettsia* species 364D rickettsiosis, *Rickettsia* spp. (mild spotted fever), and *R. akari* (rickettsialpox)) usually begin 3 – 12 days after initial bite and can include fever, headache, chills, malaise, myalgia, nausea, vomiting, abdominal pain, photophobia, anorexia, and skin rash. *Rickettsia* species 364d rickettsiosis can also present with an ulcerative lesion with regional lymphadenopathy (Biggs et al., 2016).

**Note 12:** Typical signs and symptoms of WNV include headache, myalgia, arthralgia, gastrointestinal symptoms, and maculopapular rash. Less than 1% of infected individuals develop neuroinvasive WNV with symptoms of meningitis, encephalitis, or acute flaccid paralysis (Nasci et al., 2013).

**Note 13:** Typical signs and symptoms of yellow fever include symptoms of the toxic form of the disease (jaundice, hemorrhagic symptoms, and multisystem organ failure), as well as nonspecific influenza symptoms (fever, chills, headache, backache, myalgia, prostration, nausea, and vomiting in initial illness) (Gershman & Staples, 2024).

**Note 14:** The CDC provides information on the geographic risk classifications of Zika (<https://www.cdc.gov/zika/geo/index.html>), as well as providing travel health notices for pathogens of concern (<https://wwwnc.cdc.gov/travel/notices>).

**Note 15:** Typical signs and symptoms of congenital Zika syndrome can include microcephaly, problems with brain development, feeding problems (e.g., difficulty swallowing), hearing loss, seizures, vision problems, decreased joint movement (i.e., contractures), and stiff muscles (making it difficult to move) (CDC, 2024n).

### III. Applicable State and Federal Regulations

**DISCLAIMER:** If there is a conflict between this Policy and any relevant, applicable government policy for a particular member [e.g., Local Coverage Determinations (LCDs) or National Coverage Determinations (NCDs) for Medicare and/or state coverage for Medicaid], then the government policy will be used to make the determination. For the most up-to-date Medicare policies and coverage, please visit the Medicare search website: <https://www.cms.gov/medicare->

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[coverage-database/search.aspx](#). For the most up-to-date Medicaid policies and coverage, visit the applicable state Medicaid website.

### Food and Drug Administration (FDA)

On 6/29/2017, the FDA approved the Rickettsia Real-Time PCR Assay (K170940) by the Centers for Disease Control and Prevention (CDC) with the following definition: “An in vitro diagnostic test for the detection of Rickettsia spp. nucleic acids in specimens from individuals with signs or symptoms of rickettsial infection and epidemiological risk factors consistent with potential exposure. Test results are used in conjunction with other diagnostic assays and clinical observations to aid in the diagnosis infection, in accordance with criteria defined by the appropriate public health authorities in the Federal government” (FDA, 2018).

On 9/1/2009, the FDA approved the BinaxNOW Malaria Positive Control Kit (K083744) rapid diagnostic test (RDT), an in vitro qualitative immunochromatographic assay, for use by hospital and commercial laboratories, but it is not approved for individual or physician offices (FDA, 2018; Tan & Abanyie, 2024).

As of 8/7/2018, the FDA has approved the following assays for the detection of West Nile Virus (FDA, 2018): West Nile Virus ELISA IgG model EL0300G and West Nile Virus IgM Capture ELISA model EL0300M by Focus Technologies, Inc., West Nile Virus IgM Capture ELISA model E-WNV02M and West Nile Virus IgG Indirect ELISA by Panbio Limited, West Nile Detect IgM ELISA by Inbios Intl, Inc., Spectral West Nile Virus IgM Status Test by Spectral Diagnostics, Inc., and the EUROIMMUN Anti-West Nile Virus ELISA (Biggs et al.) and EUROIMMUN Anti-West Nile Virus ELISA (IgM) by Euroimmun US, Inc.

Many labs have developed specific tests that they must validate and perform in house. These laboratory-developed tests (LDTs) are regulated by the Centers for Medicare and Medicaid (CMS) as high-complexity tests under the Clinical Laboratory Improvement Amendments of 1988 (CLIA '88). LDTs are not approved or cleared by the U. S. Food and Drug Administration; however, FDA clearance or approval is not currently required for clinical use.

### IV. Applicable CPT/HCPCS Procedure Codes

CPT	Code Description
86280	Hemagglutination inhibition test (HAI)
86382	Neutralization test, viral
86619	Antibody; Borrelia (relapsing fever)
86666	Antibody; Ehrlichia
86750	Antibody; Plasmodium (malaria)
86753	Antibody; protozoa, not elsewhere specified

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CPT	Code Description
86757	Antibody; Rickettsia
86788	Antibody; West Nile virus, IgM
86789	Antibody; West Nile virus
86790	Antibody; virus, not elsewhere specified
86794	Antibody; Zika virus, IgM
87040	Culture, bacterial; blood, aerobic, with isolation and presumptive identification of isolates (includes anaerobic culture, if appropriate)
87207	Smear, primary source with interpretation; special stain for inclusion bodies or parasites (eg, malaria, coccidia, microsporidia, trypanosomes, herpes viruses)
87449	Infectious agent antigen detection by immunoassay technique, (eg, enzyme immunoassay [EIA], enzyme-linked immunosorbent assay [ELISA], fluorescence immunoassay [FIA], immunochemiluminometric assay [IMCA]) qualitative or semiquantitative; not otherwise specified, each organism
87468	Infectious agent detection by nucleic acid (DNA or RNA); Anaplasma phagocytophilum, amplified probe technique
87469	Infectious agent detection by nucleic acid (DNA or RNA); Babesia microti, amplified probe technique
87478	Infectious agent detection by nucleic acid (DNA or RNA); Borrelia miyamotoi, amplified probe technique
87484	Infectious agent detection by nucleic acid (DNA or RNA); Ehrlichia chaffeensis, amplified probe technique
87662	Infectious agent detection by nucleic acid (DNA or RNA); Zika virus, amplified probe technique
87798	Infectious agent detection by nucleic acid (DNA or RNA), not otherwise specified; amplified probe technique, each organism
87899	Infectious agent antigen detection by immunoassay with direct optical (ie, visual) observation; not otherwise specified
0043U	Tick-borne relapsing fever Borrelia group, antibody detection to 4 recombinant protein groups, by immunoblot, IgM Proprietary test: Tick-Borne Relapsing Fever Borrelia (TBRF) ImmunoBlots IgM Test Lab/Manufacturer: IGeneX Inc
0044U	Tick-borne relapsing fever Borrelia group, antibody detection to 4 recombinant protein groups, by immunoblot, IgG Proprietary test: Tick-Borne Relapsing Fever Borrelia (TBRF) ImmunoBlots IgG

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CPT	Code Description
	Test Lab/Manufacturer: IGeneX Inc

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*Procedure codes appearing in Medical Policy documents are included only as a general reference tool for each policy. They may not be all-inclusive.*

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