BlueCross BlueShield of Alabama

Name of Blue Advantage Policy:

Intravenous Antibiotic Therapy and Associated Diagnostic Testing for Lyme Disease

Policy #: 359
Latest Review Date: October 2024
Category: Medical

BACKGROUND:

Blue Advantage medical policy does not conflict with Local Coverage Determinations (LCDs), Local Medical Review Policies (LMRPs) or National Coverage Determinations (NCDs) or with coverage provisions in Medicare manuals, instructions or operational policy letters. In order to be covered by Blue Advantage the service shall be reasonable and necessary under Title XVIII of the Social Security Act, Section 1862(a)(1)(A). The service is considered reasonable and necessary if it is determined that the service is:

1. Safe and effective;
2. Not experimental or investigational*;
3. Appropriate, including duration and frequency that is considered appropriate for the service, in terms of whether it is:
   - Furnished in accordance with accepted standards of medical practice for the diagnosis or treatment of the patient's condition or to improve the function of a malformed body member;
   - Furnished in a setting appropriate to the patient's medical needs and condition;
   - Ordered and furnished by qualified personnel;
   - One that meets, but does not exceed, the patient's medical need; and
   - At least as beneficial as an existing and available medically appropriate alternative.

*Routine costs of qualifying clinical trial services with dates of service on or after September 19, 2000, which meet the requirements of the Clinical Trials NCD are considered reasonable and necessary by Medicare. Providers should bill **Original Medicare** for covered services that are related to **clinical trials** that meet Medicare requirements (Refer to Medicare National Coverage Determinations Manual, Chapter 1, Section 310 and Medicare Claims Processing Manual Chapter 32, Sections 69.0-69.11).

POLICY:

Effective for dates of service on or after February 19, 2021:

Treatment of Lyme disease (LD) consists of oral antibiotics, except for the following indications:

Neuroborreliosis

Blue Advantage will treat **an initial 2- to 4-week course of IV antibiotic therapy** as a **covered benefit** in members with neuroborreliosis with objective neurologic complications of documented Lyme disease (see the following for methods of documentation).

Objective neurologic findings include:

- Lymphocytic meningitis with documented cerebrospinal fluid (CSF) abnormalities
- Encephalitis or encephalomyelitis with documented CSF abnormalities
- Cranial neuropathy, other than uncomplicated cranial nerve palsy, with documented CSF abnormalities
- Radiculopathy
- Polyneuropathy

Lyme disease may be documented by serologic testing or by clinical findings of erythema migrans in early infection. Documentation of CSF abnormalities is required for suspected central nervous system infection, as indicated above.

Serologic documentation of infection requires:

- Positive or indeterminate enzyme-linked immunosorbent assay, AND
- Positive immunoblot blot by Centers for Disease Control and Prevention (CDC) criteria.

Documented CSF abnormalities include ALL of the following:

- Pleocytosis;
- Evidence of intrathecal production of *Borrelia burgdorferi* antibodies in CSF; and
- Increased protein levels.

Blue Advantage will treat **polymerase chain reaction (PCR)-based direct detection of B. burgdorferi (by direct or amplified probe) in CSF samples** as a **covered benefit** and may replace serologic documentation of infection in individuals with a short duration of neurologic symptoms (<14 days) during the window between exposure and production of detectable antibodies.

Lyme Carditis

Blue Advantage will treat **a single 2- to 4-week course of IV antibiotics** as a **covered benefit** in individuals with Lyme carditis, as evidenced by positive serologic findings (defined above) and associated with high degree atrioventricular block or a PR interval more than 0.3 seconds. Documentation of Lyme carditis may include PCR-based direct detection of *B. burgdorferi* in the blood when results of serologic studies are equivocal.

Lyme Arthritis

Blue Advantage will treat **a single 2- to 4-week course of IV antibiotic therapy** as a **covered benefit** in the small subset of individuals with well-documented Lyme arthritis who have such severe arthritis that it requires the rapid response associated with IV antibiotics. Documentation of Lyme arthritis may include PCR-based direct detection of *B. burgdorferi* in the synovial tissue or fluid when results of serologic studies are equivocal.

Blue Advantage will treat **one repeat 2- to 4- week course of IV antibiotic therapy** as a **covered benefit** when all of the following criteria are met:

- Criteria for initial course of IV antibiotic therapy are met
- Laboratory values confirming Lyme disease have been obtained within the past 3 months
- The patient has completed the initial course of IV antibiotic therapy
- One or more of the following are met:
    - The initial infection has relapsed
    - Organ damage as a result of Lyme disease has progressed
    - Finding of a new focus or type of organ damage

Antibiotic Therapy

Blue Advantage will treat **intravenous antibiotic therapy for Lyme disease** as a **non-covered benefit** and as **investigational** in the following situations:

- Individuals with symptoms consistent with chronic fatigue syndrome or fibromyalgia, in the absence of objective clinical or laboratory evidence for Lyme disease;
- Individuals with seronegative LD in the absence of CSF antibodies;
- Initial therapy in individuals with Lyme arthritis without coexisting neurologic symptoms;
- Cranial nerve palsy (e.g. Bell's palsy) without clinical evidence of meningitis;
- Post-antibiotic Lyme arthritis (unresponsive to two courses of oral antibiotics or to one course of oral and one course of intravenous antibiotic therapy);
- Individuals with vague systemic symptoms without supporting serologic or CSF studies;
- Individuals with a positive ELISA test, unconfirmed by an immunoblot or Western blot test (see definition above);
- Individuals with an isolated positive serologic test in the setting of multiple negative serologic studies;
- Individuals with chronic ($\geq$ 6 months) subjective symptoms ("post-Lyme syndrome") after receiving recommended treatment regimens for documented LD.

Diagnostic Testing

Blue Advantage will treat **repeat PCR-based direct detection of *B. burgdorferi*** (by direct or amplified probe) as a **non-covered benefit** and as **investigational** in the following situations:

- As a justification for continuation of IV antibiotics beyond 1 month in patients with persistent symptoms
- As a technique to follow therapeutic response

Blue Advantage will treat **PCR-based direct detection of *B. burgdorferi* in urine samples** as a **non-covered benefit** and as **investigational** in all clinical situations.

Blue Advantage will treat **genotyping or phenotyping of *B. burgdorferi*** as a **non-covered benefit** and as **investigational**.

Blue Advantage will treat **other diagnostic testing** as a **non-covered benefit** and as **investigational** including but not limited to "stand alone" C6 peptide ELISA, determination of levels of the B-lymphocyte chemoattractant CXCL 13, or Outer surface protein A (OspA) antigen testing for diagnosis or monitoring treatment.

Blue Advantage does not approve or deny procedures, services, testing, or equipment for our members. Our decisions concern coverage only. The decision of whether or not to have a certain test, treatment or procedure is one made between the physician and his/her patient. Blue Advantage administers benefits based on the members' contract and medical policies. Physicians should always exercise their best medical judgment in providing the care they feel is most appropriate for their patients. Needed care should not be delayed or refused because of a coverage determination.

DESCRIPTION OF PROCEDURE OR SERVICE:

Lyme disease (LD) is a multisystem inflammatory disease caused by the spirochete Borrelia burgdorferi and transmitted by the bite of an infected Ixodes scapularis (northeastern U.S.) or Ixodes pacificus (Pacific coast, most common in Northern California) tick. The disease is characterized by stages, beginning with localized infection of the skin (erythema migrans), followed by dissemination to many sites. Manifestations of early disseminated disease may include lymphocytic meningitis, facial palsy, painful radiculoneuritis, atrioventricular (AV) block, or migratory musculoskeletal pain. Months to years later, the disease may be manifested by intermittent oligoarthritis, particularly involving the knee joint, chronic encephalopathy, spinal pain, or distal paresthesias. While most manifestations of LD can be adequately treated with oral antibiotics, intravenous (IV) antibiotics are indicated in some patients with disseminated Lyme disease. The following paragraphs describe the various manifestations of Lyme disease, therapies, and the various laboratory tests used to support the diagnosis of LD.

Manifestations

Erythema migrans

Erythema migrans appears at the site of the tick bite and manifests generally between 7 to 14 days after the bite. The lesions typically expand slowly over the course of days or weeks, often with central clearing. If multiple lesions are present, it is considered a sign of early disseminated disease.

Neuroborreliosis
Lymphocytic meningitis, characterized by head and neck pain, may occur during the acute disseminated stage of the disease. Inpatients with meningitis, the cerebrospinal fluid (CSF) will typically show a lymphocytic pleocytosis (lymphocyte count greater than normal) with increased levels of protein and normal glucose levels. Intrathecal production of antibodies directed at spirochetal antigens is also typically present. Other manifestations of early disseminated disease can include cranial neuritis (including unilateralor bilateral facial palsy) and peripheral nervous system manifestations. Cranial neuritis, most frequently Bell palsy, may present early in the course of disseminated Lyme disease, occasionally before the development of antibodies. Peripheral nervous system manifestations of Lyme disease include paresthesias or radicular pain with only minimal sensory signs. Patients typically exhibit electromyographic or nerve conduction velocity abnormalities.

Neurological manifestations of late-stage dissemination can include mononeuropathy multiplex, encephalomyelitis, and subtle encephalopathy. A subacute encephalopathy is characterized by subtle disturbances in memory, mood, sleep, or cognition accompanied by fatigue. The symptoms are nonspecific and overlap with fibromyalgia and chronic fatigue syndrome. Much rarer, but of greater concern, is the development of encephalomyelitis, characterized by spastic paraparesis, ataxias, cognitive impairment, bladder dysfunction, and cranial neuropathy.

Lyme Carditis
Lyme carditis may appear during the early dissemination stage of the disease; symptoms include atrioventricular block, tachyarrhythmias, and myopericarditis. The most common abnormality is fluctuating degrees of AV block.

Lyme Arthritis
Lyme arthritis is a late manifestation of infection and is characterized by an elevated IgG response to B. burgdorferi and intermittent attacks of oligoarticular arthritis, primarily in the large joints such as the knee. However, both large and small joints may be affected.

Diagnostic Testing
Overview
The optimum method of testing for Lyme disease depends on the stage of the disease. Diagnostic testing may not be necessary when a diagnosis can be made clinically in patients with a recent tick bite or exposure and the presence of the characteristic rash of erythema migrans, particularly in patients presenting early before the development of a detectable serum antibody response. While diagnosis of Lyme disease is generally based on the clinical picture and demonstration of specific antibodies (see below), polymerase chain reaction (PCR)-based technology can detect the spirochete in the central nervous system in cases of neuroborreliosis, in the synovial fluid of cases of Lyme arthritis, and rarely in skin biopsy specimens of those with atypical dermatologic manifestations. However, while PCR-based tests can identify organisms in skin biopsy specimens of patients with dermatologic manifestations (i.e., erythema migrans), this diagnosis is typically made clinically, and antibiotic therapy is started empirically.

For Lyme neuroborreliosis, CSF examination may be useful in select patients. In patients with suspected neuroborreliosis, evaluation allows for exclusion of bacterial or viral meningitis and can provide a more definitive diagnosis. However, direct detection of B.burgdorferi in CSF, by PCR or culture, is usually not possible in patients with Lyme neuroborreliosis.

Similarly, diagnosis of Lyme arthritis is based on clinical and serologic studies without the need for synovial tissue or fluid. Finally, intrathecal antibody production is considered a more sensitive test than PCR-based cerebral spinal fluid (CSF) detection in patients with suspected neuroborreliosis. Polymerase chain reaction (PCR) may be clinically useful as a second approach in patients with a short duration of neurologic symptoms (<14 days) during the window between exposure and the emergence of detectable levels of antibodies in the CSF. PCR-based detection is typically not performed in the urine due to the variable presence of endogenous polymerase inhibitors that affect test sensitivity.

Fibromyalgia and chronic fatigue syndrome are the diseases most commonly confused with Lyme disease. Fibromyalgia is characterized by musculoskeletal complaints, multiple trigger points, difficulty in sleeping, generalized fatigue, headache, or neck pain. The joint pain associated with fibromyalgia is typically diffuse, in contrast to Lyme arthritis, which is characterized by marked joint swelling in 1 or more joints at a time, with few systemic symptoms. Chronic fatigue syndrome is characterized by multiple subjective complaints, such as overwhelming fatigue, difficulty in concentration, and diffuse muscle and joint pain. In contrast with Lyme disease, both of these conditions lack joint inflammation, have normal neurologic test results, or have test results suggesting anxiety or depression. Neither fibromyalgia nor chronic fatigue syndrome has been shown to respond to antibiotic therapy.

Serologic Tests

The antibody response to infection with B. burgdorferi follows a typical pattern. During the first few weeks after the initial onset of infection, there is no antibody production. The specific IgM response characteristic of acute infection peaks between the third and sixth week. The specific IgG response develops only after months and includes antibodies to a variety of spirochetal antigens. IgG antibodies produced in response to LD may persist for months or years. Thus, detection of IgG antibodies only indicates exposure, either past or present. In LD endemic areas, underlying asymptomatic seropositivity may range from 5%–10%. Thus, as with any laboratory test, interpretation of serologic tests requires close correlation with the patients' signs and symptoms. For example, patients with vague symptoms of LD, chronic fatigue syndrome, or fibromyalgia may undergo multiple serologic tests over many weeks to months to establish the diagnosis of LD. Inevitably, in this setting of repeat testing, one enzyme-linked immunosorbent assay (ELISA) or test, whether IgG or IgM, may be reported as weakly positive or indeterminate. These results most likely represent false positive test results in the uninfected patient who has had long-standing symptoms from a different condition and previously negative test results.

Currently, the Centers for Disease Control and Prevention recommend a 2-tiered method for the serologic diagnosis of Lyme disease. This can be accomplished using the standard 2-tiered testing process, which uses a sensitive enzyme immunoassay (EIA) or immunofluorescence assay, followed by a western immunoblot assay for specimens yielding positive or equivocal

results. Additionally, a modified 2-test methodology can be used, which uses a second EIA in place of the western immunoblot assay.

Enzyme-Linked Immunosorbent Assay for Borrelia Burgdorferi Antibodies
This ELISA test is a screening serologic test for Lyme disease. ELISA tests are available to detect IgM or IgG antibodies or both antibody types together. More recently developed tests using recombinant or synthetic antigens have improved diagnostic sensitivity. For example, the U.S. Food and Drug Administration–approved C6 ELISA is highly sensitive to infection and is under study as an indicator of antibiotic therapy efficacy. A positive or indeterminate ELISA test result alone is inadequate serologic evidence of Lyme disease. All of these tests must be confirmed with a Western blot or a second EIA. The overall predictive values is increased when correlated with the clinical picture.

Western Immunoblot
This immunoblot test is used to confirm the serologic diagnosis of Lyme disease in patients with positive or indeterminate ELISA tests. In contrast with the standard ELISA test, the immunoblot investigates the specific antibody response to the different antigens of B. burgdorferi. Typically, several clinically significant antigens are tested. According to Centers for Disease Control and Prevention criteria, the test result is considered positive if 2 of the 3 most common IgM antibody bands to spirochetal antigens are present, or 5 of the 10 most frequent IgG antibody bands are present. Because Centers for Disease Control and Prevention criteria were developed for surveillance, they are conservative and may miss true Lyme disease cases. Some support the use of more liberal criteria for a positive result in clinical diagnosis; however, alternative criteria have not been well-validated. U.S. criteria for interpreting immunoblot results differ from those in Europe due to differences in prevalent Borrelia species causing disease.

Nonserologic Tests
Polymerase Chain Reaction (PCR)
In contrast to the previously discussed serologic tests, which indirectly assess prior or present exposure to B. burgdorferi, PCR directly tests for the presence of B. burgdorferi DNA. Because PCR technology involves the amplification of DNA from a portion of B. burgdorferi, there is a high-risk of exogenous contamination, resulting in false-positive results. Positive results in the absence of clear clinical indicators or positive serology are not definitive for diagnosis. Also, the test cannot distinguish between live spirochetes or fragments of dead ones. The PCR technique has been studied using various specimens. PCR has the best detection rates for skin biopsies from patients with erythema migrans (but who may not be indicated with a recent history of tick bite or exposure) and for synovial tissue (and synovial fluid, to a lesser extent) from patients with Lyme arthritis. Cerebrospinal fluid may be positive by PCR during the first 2 weeks of infection but after that the detection rate is low. PCR is not recommended for urine or blood specimens. However, PCR-based direct detection of B. burgdorferi in the blood may be useful for documenting Lyme carditis when results of serologic studies are equivocal.

Borrelia PCR also provides information on which of the three major species pathogenic for humans has been found in the specimen tested (genotyping).

T-Cell Proliferative Assay
T-lymphocyte proliferation assays are not recommended as diagnostic tests because they are difficult to perform and standardize, and their sensitivity is not well characterized.

Chemoattractant CXCL13
CXCL13 is a B-lymphocyte chemoattractant that has been reported to be elevated in acute neuroborreliosis and other inflammatory disorders in the central nervous system. It is being investigated as an adjunct in identifying infection and as a potential marker for successful treatment. The Centers for Disease Contril and Prevention notes that standardized interpretation criteria is required before this test can be recommended.

Borrelia Outer surface protein A
Antigen testing of urinary Borrelia Outer surface protein A (OspA) C-terminus peptide has been investigated using the Nanotrap® Antigen Test. This test employs Nanotrap particles to concentrate urinary OspA and uses a highly specific anti-OspA monoclonal antibody as a detector of the C-terminus peptides. Consistent with recommendations from the Centers for Disease Control and Prevention, the manufacturer of the Nanotrap® Antigen Test recommends using the Nanotrap® Antigen Test in conjunction with 2-tiered testing (ELISA with reflex to Western blot) for confirmation of a Lyme disease.

Treatment of Lyme Disease
Recommended treatment regimens are based on the stage and manifestations of Lyme disease.

Most patients can be treated with oral antibiotics, such as doxycycline, amoxicillin, or cefuroxime. Specific durations of therapy are dependent on the type of manifestations present. Treatment with IV antibiotics may be indicated in patients with central nervous system or peripheral neurologic involvement and in a small subset of patients with heart block or documented Lyme arthritis who have not responded to oral antibiotics. Typical IV therapy consists of a 2- to 4-week course of ceftriaxone, cefotaxime or penicillin. No data have suggested that prolonged or repeated courses of IV antibiotics are effective. Lack of effect should suggest an incorrect diagnosis or slow resolution of symptoms, which is commonly seen in Lyme disease. Also, some symptoms may persist after treatment, such as Lyme arthritis; this phenomenon may be related to various self-sustaining inflammatory mechanisms rather than persistent infection.

KEY POINTS:
The most recent literature review was performed through August 15, 2024.

Summary of Evidence
For individuals who are suspected of having Lyme disease who receive genotyping or phenotyping of B. burgdorferi subspecies, the evidence is limited. Relevant outcomes are change in disease status and morbid events. Polymerase chain reaction-based testing for B. burgdorferi genospecies is feasible. However, no evidence was identified that knowledge of the B. burgdorferi genotype or phenotype could be used to improve patient management and outcomes. Additionally, a prospective cohort study reported that use of PCR-based testing in

Lyme disease evaluation did not improve the diagnosis compared to standard 2-tiered testing. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who are suspected of having Lyme disease who receive CXCL13 chemokine concentration testing, the evidence includes a meta-analysis of 18 studies of European cohorts and a US-based retrospective study. Relevant outcomes are a change in disease status and morbid events. Study results have demonstrated a high specificity and strong correlation with B. burgdorferi-specific antibody responses in patients with acute Lyme neuroborreliosis. However, there is wide variability in studies in defining a threshold for a significantly elevated CXCL13 value, which makes clinical performance characteristics unclear. Additional research is needed to determine the diagnostic utility of CXCL13 levels. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.
For individuals who are suspected of having Lyme disease who receive stand-alone C6 peptide assay testing, the evidence includes cohort studies. Relevant outcomes are a change in disease status and morbid events. Limited data have shown specificity is slightly lower with stand-alone C6 peptide testing compared to 2-tiered approaches. Additional research is needed to determine the diagnostic utility of stand-alone C6 testing. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who are suspected of having Lyme disease who receive Borrelia OspA testing, the evidence includes a single cohort study. Relevant outcomes are a change in disease status and morbid events. Limited data have shown that the presence of Borrelia OspA in the urine is linked to concurrent active symptoms (e.g., erythema migrans rash and arthritis), while resolution of these symptoms after therapy is correlated with urinary conversion to OspA negative. Additional research is needed to determine the diagnostic utility of Borrelia OspA testing. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with confirmed Lyme disease who receive prolonged or repeated courses of antibiotic therapy, the evidence includes randomized controlled trials (RCTs). Relevant outcomes are symptoms, change in disease status, morbid events, and health status measures. Oral antibiotics usually are adequate for treatment of Lyme disease, though in some persistent cases, a 2- to 4-week course of intravenous (IV) antibiotics may be appropriate. Evidence from RCTs has not shown a benefit to prolonged (>4 weeks) or repeat courses of oral or IV antibiotics. The evidence is sufficient to determine that the technology is unlikely to improve the net health outcome.

Practice Guidelines and Position Statements
Centers for Disease Control and Prevention
In 2019, the Centers for Disease Control and Prevention (CDC) updated its recommendations for the serological diagnosis of Lyme disease. In addition to the standard 2-tiered testing process (sensitive enzyme immunoassay [EIA] or immunofluorescence assay, followed by a western immunoblot assay for specimens yielding positive or equivocal results), a modified 2-test methodology can be used, which uses a second EIA in place of the western immunoblot assay. Specifically, the CDC noted that "[w]hen cleared by FDA [Food and Drug

Administration] for this purpose, serologic assays that utilize EIA rather than western immunoblot assay in a two-test format are acceptable alternatives for the laboratory diagnosis of Lyme disease."

Regarding treatment of Lyme disease, appropriate, oral antibiotics in the early stages of Lyme disease typically lead to rapid and complete recovery. In those with disseminated, non-cutaneous manifestations of Lyme disease, longer courses of antibiotics or intravenous treatment with antibiotics such as ceftriaxone may be required.

Infectious Diseases Society of America et al
The Infectious Diseases Society of America, American Academy of Neurology, and American College of Rheumatology published guidelines on the prevention, diagnosis, and treatment of Lyme disease in 2020. Overall, antibody tests are considered first-line for diagnosis due to their performance characteristics and availability of accessible, clinically validated assays. Serum antibody tests are recommended to be used in a standard 2-tiered testing protocol, in which an EIA or indirect fluorescent antibody test is followed by immunoglobulin M (IgM) and IgG immunoblots. A modified 2-tiered testing protocol, in which 2 different EIAs are performed sequentially or concurrently without the use of immunoblots can also be used. The overall predictive value of these tests are increased when correlated with specific signs and symptoms, patient history, and risk factors. Antibody testing is limited by false negatives, especially in patients who present with cutaneous symptoms only within 2 weeks after the development of the skin lesion. The guidance notes that nonserological methods have been developed, such as polymerase chain reaction (PCR) assays, but the clinically validity of these approaches is not clear, in part due to the lack of a FDA-cleared test for Lyme disease diagnosis. Additionally, the guidance states that "[m]easurement of CXCL13 has not been sufficiently studied or standardized to recommend at present."

Association of Public Health Laboratories
In April 2024, the Association of Public Health Laboratories published updated guidance on the suggested reporting language, interpretation, and guidance for serologic test results for Lyme disease. The standard 2-tiered testing and modified 2-tiered testing methods are recommended for diagnosis of Lyme disease. In disseminated Lyme disease, standard 2-tiered testing has a high sensitivity (>87%) and specificity (99%) and can provide strong support for a diagnosis. The guidance also notes that "[s]ome laboratories offer tests that have not been cleared by FDA (e.g., molecular tests, antibody tests on samples other than serum). Use of these tests is generally not recommended, as their accuracy and clinical usefulness have not been adequately established."

National Institute for Health and Care Excellence
Guidance on Lyme disease from the National Institute for Health and Care Excellence (NICE) was published in 2018. NICE recommended that if "there is clinical suspicion of Lyme disease in people without erythema migrans," "an enzyme-linked immunosorbent assay (ELISA) test for Lyme disease" should be offered. If the ELISA test is "positive pr equivocal," an "immunoblot test" for Lyme disease should be performed. The NICE recommended oral antibiotics for the treatment of erythem migrans and/or nonfocal symptoms, and a 21-day

course of IV antibiotics for Lyme disease affecting the central nervous or for Lyme carditis when the patients are hemodynamically unstable.

International Lyme and Associated Diseases Society
The International Lyme and Associated Diseases Society published guidelines in 2014 to address three clinical issues: the usefulness of antibiotic prophylaxis of tick bites, the effectiveness of erythema migrans treatment, and antibiotic retreatment in patients with persistent symptoms. The Society noted that the evidence on treatment of tick bites, erythema migrans rashes, and persistent manifestations is limited. Regarding the treatment of patients with persistent symptoms, the Society panel concluded that the evidence for retreatment is adequate to support retreatment but is not strong enough to mandate treatment. The panel determined that there was no compelling evidence supporting withholding antibiotics from symptomatic patients, especially since there is a lack of alternative treatment options. Due to the number of clinical variables and the heterogeneity of the patient population, clinical judgment and patients' values and goals should be considered when planning a treatment strategy.

U.S. Preventive Services Task Force Recommendations
Not applicable.

KEY WORDS:
Intravenous Antibiotic Therapy for Lyme Disease, Lyme Disease, Intravenous Antibiotic Therapy, B lymphocyte chemoattractant, C6 peptide ELISA, Chemoattractant CXCL13, CXCL 13, genotyping of B. burgdorferi, Lyme Disease, PCR based direct detection of B. burgdorferi in urine samples, phenotyping of B. burgdorferi, Borrelia burgdorferi, Outer surface protein A antigen, (OspA), Nanotrap® Antigen Test.

APPROVED BY GOVERNING BODIES:
The FDA has cleared multiple enzyme immunoassay, immunofluorescent assay and Western Blot IgG and IgM tests through the 510(k) process. There are also commercially available laboratory- developed tests for serologic testing for Lyme disease. Clinical laboratories may develop and validate tests in-house and market them as a laboratory service; laboratory-developed tests must meet the general regulatory standards of the Clinical Laboratory Improvement Amendments.

BENEFIT APPLICATION:
Coverage is subject to member's specific benefits. Group-specific policy will supersede this policy when applicable.

CURRENT CODING:

CPT Codes:

86617	Borrelia burgdorferi (Lyme disease) confirmatory test (e.g., Western blot or immunoblot)
86618	Antibody; borrelia burgdorferi (Lyme disease)
86619	Antibody; Borrelia (relapsing fever)
87475	Infectious agent detection by nucleic acid; Borrelia burgdorferi, direct probe technique
87476	Infectious agent detection by nucleic acid; borrelia burgdorferi, amplified probe technique
0041U	Borrelia burgdorferi, antibody detection of 5 recombinant protein groups, by immunoblot, IgM
0042U	Borrelia burgdorferi, antibody detection of 12 recombinant protein groups, by immunoblot, IgG
0316U	Borrelia burgdorferi (Lyme disease), OspA protein evaluation, urine

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POLICY HISTORY:

Adopted for Blue Advantage, June 2009
Available for comment June 26-August 9, 2009
Medical Policy Group, January 2011
Available for comment January 11, 2011 through February 21, 2011
Medical Policy Group, March 2012
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Medical Policy Group, November 2012
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Medical Policy Group, January 2015
Medical Policy Group, October 2015

Medical Policy Group, November 2016
Medical Policy Group, May 2017
Medical Policy Group, July 2017
Medical Policy Group, November 2017
Medical Policy Group, February 2018
Medical Policy Group, March 2018: Reinstated policy effective March 2, 2018.
Medical Policy Group, February 2021
Medical Policy Group, October 2021
Medical Policy Group, March 2022: Quarterly coding update, effective 4/1/22, added new code 0316U to the current coding section.
Medical Policy Group, October 2022
Medical Policy Group, October 2023
UM Committee, December 2023: Policy approved by UM Committee for use for Blue Advantage business.
Medical Policy Group, October 2024
