LOUISIANA BLUE

Intravenous Antibiotic Therapy for Lyme Disease

Policy # 00173
Original Effective Date: 07/15/2005
Current Effective Date: 04/01/2025

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider a 2 to 4 week course of intravenous (IV) antibiotic therapy for the treatment of Lyme disease (LD) to be **eligible for coverage**** for the following conditions:
(Note: Treatment for Lyme disease (LD) consists of oral antibiotics unless the following diagnoses are confirmed)

- Neuroborreliosis with objective neurologic complications of documented Lyme disease (LD); or
- Lyme carditis; or
- Well-documented Lyme arthritis.

Patient Selection Criteria
Coverage eligibility will be considered for the following diagnoses when confirmed as outlined below:

Neuroborreliosis
Neuroborreliosis requires documentation of the following:

- Documentation of the following objective neurologic complications of confirmed Lyme disease:
  - Lymphocytic meningitis with documented cerebrospinal fluid (CSF) abnormalities
  - Cranial neuropathy, other than uncomplicated cranial nerve palsy, with documented cerebrospinal fluid (CSF) abnormalities
  - Encephalitis or encephalomyelitis with documented cerebrospinal fluid (CSF) abnormalities
  - Radiculopathy
  - Polyneuropathy.

Lyme disease (LD) may be documented either on the basis of serologic testing or by clinical findings of erythema migrans in early infection. Documentation of cerebrospinal fluid (CSF) abnormalities is required for suspected central nervous system (CNS) infection, as indicated above.

Serologic documentation of infection requires:

- Positive or indeterminate enzyme-linked immunosorbent assay (ELISA) test; and
- Positive immunoblot by Centers for Disease Control and Prevention (CDC) criteria.

Documented cerebrospinal fluid (CSF) abnormalities include all of the following:

- Pleocytosis;
- Evidence of intrathecal production of *Borrelia burgdorferi* (B. burgdorferi) antibodies in cerebrospinal fluid (CSF); and
- Increased protein levels.

Lyme Carditis

A single 2 to 4 week course of intravenous (IV) antibiotic therapy may be **eligible for coverage**** in individuals with serologically confirmed Lyme disease and Lyme carditis 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

A single 2 to 4 week course of intravenous (IV) antibiotic therapy may be **eligible for coverage**** in the small subset of individuals with well-documented Lyme arthritis who have the following:

- Severe arthritis requiring the rapid response associated with intravenous (IV) antibiotics.

Documentation of Lyme arthritis may include polymerase chain reaction (PCR)-based direct detection of B. *burgdorferi* in the synovial tissue or fluid when results of serologic studies are equivocal.

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers intravenous (IV) antibiotic therapy in the following situations to be **investigational*:**

- Individuals with symptoms consistent with chronic fatigue syndrome or fibromyalgia, in the absence of objective clinical or laboratory evidence of Lyme disease (LD);
- Individuals with seronegative Lyme disease (LD) in the absence of cerebrospinal fluid (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;
- Antibiotic-refractory Lyme arthritis (unresponsive to 2 courses of oral antibiotics or to 1 course of oral and 1 course of intravenous (IV) antibiotic therapy);
- Individuals with vague systemic symptoms without supporting serologic or (CSF) studies;

- Individuals with a positive enzyme-linked immunosorbent assay (ELISA) test, unconfirmed by an immunoblot or Western blot test;
- Individuals with an isolated positive serologic test in the setting of multiple negative serologic studies;
- Individuals with chronic (less than six months) subjective symptoms ("post-Lyme syndrome") after receiving recommended treatment regimens for documented Lyme disease (LD);
- Repeat or prolonged courses (greater than four weeks) of IV antibiotic therapy;
- When patient selection criteria are not met.

Background/Overview

Lyme Disease

Lyme disease is a multisystem inflammatory disease caused by the spirochete *Borrelia burgdorferi* and transmitted by the bite of an infected *Ixodes scapularis* (northeastern region) or *Ixodes pacificus* (Pacific coast, most often in Northern California) tick. The disease is characterized by stages, beginning with localized infection of the skin (erythema migrans), followed by acute dissemination, and then late dissemination to many sites. Manifestations of the 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 Lyme disease 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 Lyme disease.

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. In patients 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 unilateral or 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 disseminated stage of the disease; symptoms include atrioventricular (AV) 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 immunoglobulin G (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 (ie, 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, the 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 CSF detection in patients with suspected neuroborreliosis. 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 with 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 immunoglobulin M (IgM) response characteristic of acute infection peaks between the third and the sixth week. The specific IgG response develops only after months and includes antibodies to a variety of spirochetal antigens. Immunoglobulin G antibodies produced in response to Lyme disease may persist for months or years. Thus detection of IgG antibodies only indicates exposure, either past or present. In Lyme disease-endemic areas, underlying asymptomatic seropositivity may range up to 5% to 10%. Thus, as with any laboratory test, interpretation of serologic tests requires a close correlation with the patient's signs and symptoms. For example, patients with vague symptoms of Lyme disease, chronic fatigue syndrome, or fibromyalgia may undergo multiple serologic tests over many weeks to months to establish the diagnosis of Lyme disease. Inevitably, in this setting of repeat testing, 1 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.

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. 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.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)
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 (CLIA).

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to regulations, other plan medical policies, and accredited national guidelines.

Lyme disease 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), which may be followed by dissemination to many sites. Diagnostic testing for Lyme disease is challenging, and there is the potential for overdiagnosis and overtreatment.

Summary of Evidence
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.

Section Summary: Prolonged or Repeated Courses of Antibiotic Therapy
Oral antibiotics usually are adequate for treatment of Lyme disease, though, in some persistent cases, a 2- to 4-week course of intravenous antibiotics may be appropriate. Evidence from RCT s has not shown a benefit in prolonged (>4 weeks) or repeat courses of oral or intravenous antibiotics.

Additional Information
It is well established that the optimum method of testing for Lyme disease depends on the stage of the disease. Guidelines from the Centers for Disease Control and Prevention and other sources have supported policy statements related to a tiered diagnostic testing strategy. 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.

Supplemental Information

Practice Guidelines and Position Statements
Guidelines or position statements will be considered for inclusion in ‘Supplemental Information' if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

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. Table 1 lists their recommendations regarding diagnosis and treatment for Lyme disease and its various manifestations. 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."

Table 1. Selected Recommendations for Lyme Diagnosis and Treatment

Recommendation	Strength of Recommendation	Level of Evidence
Erythema migrans		
"In patients with potential tick exposure in a Lyme disease endemic area who have 1 or more skin lesions compatible with erythema migrans, we recommend clinical diagnosis rather than laboratory testing."	strong	moderate quality
"In patients with 1 or more skin lesions suggestive of, but atypical for erythema migrans, we suggest antibody testing performed on an acute-phase serum sample (followed by a convalescent-phase serum sample if the initial result is negative) rather than currently available direct detection methods such as polymerase chain reaction (PCR) or culture performed on blood or skin samples."	weak	low quality
"For patients with erythema migrans, we recommend using oral antibiotic therapy with doxycycline, amoxicillin, or cefuroxime axetil."	strong	moderate quality
"We recommend that patients with erythema migrans be treated with either a 10-day course of doxycycline or a 14-day course of amoxicillin or cefuroxime axetil rather than longer treatment courses."	strong	moderate quality
Lyme neuroborreliosis		
"When assessing patients for possible Lyme neuroborreliosis involving either the peripheral nervous system (PNS) or central nervous system (CNS), we recommend serum antibody testing rather than PCR or culture of either cerebrospinal fluid (CSF) or serum."	strong	moderate quality

"In patients with Lyme disease-associated meningitis, cranial neuropathy, radiculoneuropathy or with other PNS manifestations, we recommend using intravenous (IV) ceftriaxone, cefotaxime, penicillin G, or oral doxycycline over other antimicrobials."	strong	moderate quality
"In patients with Lyme disease-associated parenchymal involvement of the brain or spinal cord, we recommend using IV over oral antibiotics."	strong	moderate quality
Lyme carditis		
"In outpatients with Lyme carditis, we suggest oral antibiotics over IV antibiotics."	weak	very low quality
"In the hospitalized patient with Lyme carditis, we suggest initially using IV ceftriaxone over oral antibiotics until there is evidence of clinical improvement, then switching to oral antibiotics to complete treatment."	weak	very low quality
"For the treatment of Lyme carditis, we suggest 14–21 days of total antibiotic therapy over longer durations of treatment."	weak	very low quality
Lyme arthritis		
"When assessing possible Lyme arthritis, we recommend serum antibody testing over PCR or culture of blood or synovial fluid/tissue."	strong	moderate quality
"In seropositive patients for whom the diagnosis of Lyme arthritis is being considered but treatment decisions require more definitive information, we recommend PCR applied to synovial fluid or tissue rather than *Borrelia* culture of those samples."	strong	moderate quality
"For patients with Lyme arthritis, we recommend using oral antibiotic therapy for 28 days."	strong	moderate quality
"In patients with Lyme arthritis with partial response (mild residual joint swelling) after a first course of oral antibiotic, we make no recommendation for a second course of antibiotic versus observation."	no recommendation	knowledge gap
"In patients with Lyme arthritis with no or minimal response (moderate to severe joint swelling with minimal reduction of the joint effusion) to an initial course of oral antibiotic, we suggest a 2- to 4-week course of IV ceftriaxone over a second course of oral antibiotics."	weak	low quality

"In patients who have failed one course of oral antibiotics and one course of IV antibiotics, we suggest a referral to a rheumatologist or other trained specialist for consideration of the use of disease modifying anti-rheumatic drugs (DMARDs), biologic agents, intraarticular steroids, or arthroscopic synovectomy. **Comment:** Antibiotic therapy for longer than 8 weeks is not expected to provide additional benefit to patients with persistent arthritis if that treatment has included 1 course of IV therapy."	weak	very low quality
Persistent symptoms following standard treatment of Lyme disease		
"For patients who have persistent or recurring nonspecific symptoms such as fatigue, pain, or cognitive impairment following recommended treatment for Lyme disease, but who lack objective evidence of reinfection or treatment failure, we recommend against additional antibiotic therapy. **Comment:** Evidence of persistent infection or treatment failure would include objective signs of disease activity, such as arthritis, meningitis, or neuropathy."	strong	moderate quality

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
The NICE recommended oral antibiotics for the treatment of erythema migrans and/or nonfocal symptoms, and a 21-day course of IV antibiotics for Lyme disease affecting the central nervous system or for Lyme carditis when the patients are hemodynamically unstable.

International Lyme and Associated Diseases Society
In 2014, the International Lyme and Associated Diseases Society published guidelines to address 3 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

concluded that the evidence for retreatment is adequate to support retreatment, but is not strong enough to mandate treatment. The Society 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.

Medicare National Coverage
There is no national coverage determination. In the absence of a national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.

Ongoing and Unpublished Clinical Trials
Some currently ongoing or unpublished trials that might influence this review are listed in Table 2.

Table 2. Summary of Key Trials

NCT No.	Trial Name	Enrollment	Completion Date
Unpublished			
NCT04422314[a]	ImmuneSense Lyme Study	893	Dec 2021
NCT03581279[a]	Detection of Borrelia Bacteria in Early Stage Lyme Borreliosis Using the T2Lyme Panel	18	Oct 2019

NCT: national clinical trial.
[a] Industry sponsored or partially sponsored.

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07/07/2006	Format revision including addition of FDA and or other governmental regulatory approval and rationale/source. Coverage eligibility unchanged.
07/10/2007	Medical Director review
07/18/2007	Medical Policy Committee approval. Policy updated with literature search. Policy statements updated; uncomplicated cranial nerve palsy (e.g. Bell's palsy) not considered a medically necessary indication for intravenous antibiotics.
08/06/2008	Medical Director review
08/20/2008	Medical Policy Committee approval. No change to coverage eligibility.
08/06/2009	Medical Policy Committee approval.
08/26/2009	Medical Policy Implementation Committee approval. No change to coverage eligibility.
08/05/2010	Medical Policy Committee review
08/10/2010	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
08/04/2011	Medical Policy Committee review
08/17/2011	Medical Policy Implementation Committee approval. Added a statement that determination of levels of the B lymphocyte chemoattractant CXCL13 for diagnosis or monitoring treatment is considered investigational.
08/02/2012	Medical Policy Committee review
08/15/2012	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
03/04/2013	Coding revised
09/05/2013	Medical Policy Committee review
09/18/2013	Medical Policy Implementation Committee approval. Additional diagnostic testing added to the investigational section.
09/04/2014	Medical Policy Committee review
09/17/2014	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
08/03/2015	Coding update: ICD10 Diagnosis code section added; ICD9 Procedure code section removed.
09/08/2016	Medical Policy Committee review
09/21/2016	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
01/01/2017	Coding update: Removing ICD-9 Diagnosis Codes
12/07/2017	Medical Policy Committee review
12/20/2017	Medical Policy Implementation Committee approval. "Stand-alone" added to the investigational statement on C6 peptide ELISA. Coverage eligibility unchanged.
04/01/2018	Coding update
12/06/2018	Medical Policy Committee review
12/19/2018	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
12/05/2019	Medical Policy Committee review

12/11/2019	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
12/03/2020	Medical Policy Committee review
12/09/2020	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
10/01/2021	Coding update
12/02/2021	Medical Policy Committee review
12/08/2021	Medical Policy Implementation Committee approval. Minor change to add "IV" in front of antibiotic therapy in antibiotic therapy section in Guidelines.
02/07/2022	Coding update
03/03/2022	Medical Policy Committee review
03/09/2022	Medical Policy Implementation Committee approval. Title changed from "Intravenous Antibiotic Therapy and Associated Diagnostic Testing for Lyme Disease" to "Intravenous Antibiotic Therapy for Lyme Disease ". Revised the entire policy to focus primarily on treatment and therapy, including IV antibiotics. Removed some of the content for diagnostic testing, including serology and PCR testing. Revised the Neuroborreliosis Patient Selection Criteria for clarity.
03/02/2023	Medical Policy Committee review
03/08/2023	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
03/07/2024	Medical Policy Committee review
03/13/2024	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
03/07/2024	Medical Policy Committee review
03/13/2024	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
03/06/2025	Medical Policy Committee review
03/12/2025	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

Next Scheduled Review Date: 03/2026

Coding

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Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code
CPT	96365 Delete code effective 04/01/2025: 99601
HCPCS	A4223, G0299, J0696, S9494, S9497, S9500, S9501, S9502, S9503, S9504 Add codes effective 04/01/2025: J0456, J0698, J2540 Delete codes effective 04/01/2025: A4216, A4305, A6457, J0171, J0712, J1335, J1642, J3370, J7030, J7040, J7050, S5501, S9373, S9374, S9379
ICD-10 Diagnosis	A69.20-A69.29

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into

standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment,

would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, “nationally accepted standards of medical practice” means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient’s health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.