Intravenous Antibiotic Therapy and Associated Diagnostic Testing for Lyme Disease

Policy # 00173
Original Effective Date: 07/15/2005
Current Effective Date: 01/11/2021

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 all of the following objective neurologic complications:
    - Lymphocytic meningitis with documented cerebrospinal fluid (CSF) abnormalities; and

- Cranial neuropathy, other than uncomplicated cranial nerve palsy, with documented cerebrospinal fluid (CSF) abnormalities; and
- Encephalitis or encephalomyelitis with documented cerebrospinal fluid (CSF) abnormalities; and
- Radiculopathy; and
- 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.

Based on review of available data, the Company may consider polymerase chain reaction (PCR)-based direct detection of *B. burgdorferi* in cerebrospinal fluid (CSF) samples to be **eligible for coverage**** and may replace serologic documentation of infection in patients with a short duration of neurologic symptoms (<14 days) during the window between exposure and production of detectable antibodies.

Lyme Carditis
A single 2 to 4 week course of intravenous (IV) antibiotic therapy may be **eligible for coverage**** in patients with Lyme carditis. Documentation of the following is required:
- Positive serologic findings (defined above);
- A high degree of atrioventricular (AV) block or a PR interval of >0.3sec.

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 patients 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.

Diagnostic Testing
Based on review of available data, the Company considers repeat polymerase chain reaction (PCR)-based direct detection of *B. burgdorferi* in the following situations to be **investigational*:**

- As a justification for continuation of intravenous (IV) antibiotics beyond one month in patients with persistent symptoms;
- As a technique to follow therapeutic response.

Based on review of available data, the Company considers polymerase chain reaction (PCR)-based direct detection of B. *burgdorferi* in urine samples in all clinical situations to be **investigational.***

Based on review of available data, the Company considers genotyping or phenotyping of *B. burgdorferi* to be **investigational.***

Based on review of available data, the Company considers other diagnostic testing including but not limited to "stand alone" C6 peptide ELISA or determination of levels of the B lymphocyte chemoattractant CXCL13 for diagnosis or monitoring treatment to be **investigational.***

Antibiotic Therapy

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

- Patients with symptoms consistent with chronic fatigue syndrome or fibromyalgia, in the absence of objective clinical or laboratory evidence of Lyme disease (LD);
- Patients with seronegative Lyme disease (LD) in the absence of cerebrospinal fluid (CSF) antibodies;
- Initial therapy in patients 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);
- Patients with vague systemic symptoms without supporting serologic or (CSF) studies;
- Patients with a positive enzyme-linked immunosorbent assay (ELISA) test, unconfirmed by an immunoblot or Western blot test;
- Patients with an isolated positive serologic test in the setting of multiple negative serologic studies;
- Patients 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 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 neurologic

involvement or AV block. The following paragraphs describe the various manifestations of Lyme disease, therapies, and the various laboratory tests used to support the diagnosis of Lyme disease.

Neuroborreliosis
Lymphocytic meningitis, characterized by head and neck pain, may occur during the acute disseminated stage of the disease. Analysis of the cerebrospinal fluid (CSF) is indispensable for the diagnosis of Lyme meningitis. If the patient has Lyme disease, the CSF will show a lymphocytic pleocytosis (lymphocyte count greater than normal) with increased levels of protein. Intrathecal production of antibodies directed at spirochetal antigens is typically present. A normal CSF analysis is strong evidence against Lyme meningitis. The usual treatment consists of 2 weeks of either oral (ambulatory setting) or IV (hospitalized patients) antibiotics.

Cranial neuritis, most frequently Bell palsy, may present early in the course of disseminated Lyme disease, occasionally before the development of antibodies, such that a Lyme disease etiology may be difficult to rule in or out. While Bell palsy typically resolves spontaneously with or without treatment with oral antibiotics, some physicians have recommended a lumbar puncture and a course of IV antibiotics if pleocytosis in the CSF is identified, primarily as a prophylactic measure to prevent further neurologic symptoms.

A subacute encephalopathy may occur months to years after disease onset, characterized by subtle disturbances in memory, mood, sleep, or cognition accompanied by fatigue. These symptoms may occur in the absence of abnormalities in the electroencephalogram, magnetic resonance imaging, or CSF. Also, the symptoms are nonspecific and overlap with fibromyalgia and chronic fatigue syndrome. Thus the diagnosis of Lyme encephalopathy may be difficult and may best be made with a mental status exam or neuropsychological testing. Treatment with IV antibiotics is not indicated unless CSF abnormalities are identified.

Much rarer, but of greater concern, is the development of encephalomyelitis, characterized by spastic paraparesis, ataxias, cognitive impairment, bladder dysfunction, and cranial neuropathy. CSF examination reveals pleocytosis and elevated protein. Selective synthesis of anti-spirochetal antibodies can also be identified. A course of IV antibiotics with 2 weeks of ceftriaxone is suggested when CSF abnormalities are identified.

A variety of peripheral nervous system manifestations of Lyme disease have also been identified. Symptoms of peripheral neuropathy include paresthesias or radicular pain with only minimal sensory signs. Patients typically exhibit electromyographic or nerve conduction velocity abnormalities. CSF abnormalities are usually seen only in those patients with a coexistent encephalopathy.

Lyme Carditis
Lyme carditis may appear during the early disseminated stage of the disease; symptoms include AV block, tachyarrhythmias, and myopericarditis. Antibiotics are typically given, although no evidence has demonstrated hastened resolution of symptoms. Both oral and IV regimens have been advocated. IV regimens are used in patients with high degree AV block or a PR interval on an electrocardiogram more than 0.3 seconds. Patients with milder forms of carditis may be treated with oral antibiotics.

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. Patients with Lyme arthritis may be successfully treated with a 30-day course of oral doxycycline or amoxicillin, but care must be taken to exclude simultaneous involvement, requiring IV antibiotic treatment. In the small subset of patients who do not respond to oral antibiotics, an additional 30-day course of oral or IV antibiotics may be recommended.

Fibromyalgia and Chronic Fatigue Syndrome
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.

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. 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.

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.

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. IgG 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: (1) ELISA or immunofluorescence assay, followed by (2) a confirmatory Western blot (including both IgM and IgG when signs or symptoms have been present ≤30 days; IgG only if symptoms have been present >30 days). A negative ELISA or immunofluorescence assay may be followed by a later (eg, in 4 to 6 weeks) convalescent serum test when symptoms have been present 30 days or less.

ELISA for B. 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. Also, results must be 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 the 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.

Polymerase Chain Reaction

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 the spirochete. 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. CSF 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 3 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.

Evaluation of Chronic Fatigue Syndrome

Aside from the standard evaluation of CSF for pleocytosis, protein levels, and glucose levels, various tests are available to determine whether anti-*B. burgdorferi* antibodies are being selectively produced within the central nervous system. Techniques include various immunoassays. For example, intrathecal antibody production can be detected by the CSF/serum index of *B. burgdorferi* antibodies. CSF and serum samples diluted to match the total IgG concentration in CSF are run in parallel in an IgG ELISA. Excess Borrelia-specific antibody in CSF indicates a positive result. As noted, PCR can also be used to detect the spirochete in the CSF, most successfully within the first 2 weeks of infection.

Evaluation of the Chemoattractant CXCL13
CXCL13 is a B-lymphocyte chemoattractant and has been reported to be elevated in acute neuroborreliosis and is a potential marker for successful treatment.

Treatment of Lyme Disease
As noted, treatment with IV antibiotics may be indicated only in patients with symptoms and laboratory findings consistent with the 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 or 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.

FDA or Other Governmental Regulatory Approval

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

Rationale/Source

Description
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.

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Summary of Evidence

Suspected Lyme Disease
For individuals who are suspected of having Lyme disease who receive genotyping or phenotyping of *B. burgdorferi* subspecies or who receive CXCL13 chemokine concentration testing or C6 peptide assay testing, the evidence is limited. Relevant outcomes are a 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. Additional research is needed to determine the diagnostic utility of CXCL13 and C6 peptide levels. The evidence is insufficient to determine the effects of the technology on health outcomes.

Confirmed Lyme Disease
For individuals with confirmed Lyme disease who receive prolonged or repeated courses of antibiotic therapy, the evidence includes randomized controlled trials. 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 antibiotics may be appropriate. Evidence from randomized controlled trials has not shown a benefit in prolonged (>4 weeks) or repeat courses of oral or intravenous antibiotics. The evidence is sufficient to determine that the technology is unlikely to improve the net health outcome.

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. When laboratory testing is indicated, 2-tiered serologic testing is recommended. The polymerase chain reaction may be clinically useful as a second approach in patients with a short duration of neurologic symptoms (<14 days).

Supplemental Information

Practice Guidelines and Position Statements

Centers for Disease Control and Prevention

The Centers for Disease Control and Prevention has recommended a 2-tier process when testing blood for evidence of antibodies against the Lyme disease bacteria. Both steps can be done using the same blood sample. The first step uses a testing procedure called enzyme immunoassay or, rarely, an indirect immunofluorescence assay. If this first step is negative, no further testing of the specimen is recommended. If the first step is positive or indeterminate (sometimes called “equivocal”), the second step should be performed. The second step uses an immunoblot test, commonly, a Western blot test. Results are considered positive only if the enzyme immunoassay or immunofluorescence assay and the immunoblot are both positive. The Centers for Disease Control and Prevention does not recommend skipping the first test and just doing the Western blot. Doing so will increase the frequency of false-positive results and may lead to misdiagnosis and improper treatment. New tests may be developed as alternatives to one or both steps of the 2-tier process. Before the Centers for Disease Control and Prevention recommends new tests, test performance must be demonstrated to be equal to or better than the results of the existing procedure, and they must be approved by the U.S. Food and Drug Administration.

Regarding treatment, the Centers for Disease Control and Prevention noted that "People with certain neurological or cardiac forms of illness may require intravenous treatment with antibiotics such as ceftriaxone or penicillin."

Infectious Diseases Society of America

As of August 20 20, updated guidelines from the Infectious Diseases Society of America and 12 other organizations are in development.

American College of Rheumatology et al

In 1993, the American College of Rheumatology and the Infectious Diseases Society of America published a position paper on intravenous (IV) antibiotic treatment for Lyme disease, which concluded that “empiric treatment of patients with nonspecific chronic fatigue or myalgia on the basis of positive serologic results alone will result in many more instances of antibiotic toxicity than cures of atypically symptomatic true Lyme disease.... In patients whose only evidence for Lyme

disease is a positive immunologic test, the risks for empiric IV antibiotic treatment outweigh the benefits....” Other studies have also supported the use of oral, not IV, antibiotics in patients with Lyme disease without neurologic involvement.

The final publication of new guidelines for the Prevention, Diagnosis, and Treatment of Lyme Disease is anticipated in early summer 2020.

National Institute for Health and Care Excellence
Guidance on Lyme disease from the National Institute for Health and Care Excellence was published in 2018. The 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 enzyme-linked immunosorbent assay test is “positive or equivocal,” an “immunoblot test” for Lyme disease should be performed. The National Institute for Health and Care Excellence 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 1.

Table 1. Summary of Key Trials

NCT No.	Trial Name	Enrollment	Completion Date
Ongoing			
NCT04422314	ImmuneSense Lyme Study	990	Dec 2021
Unpublished			
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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06/07/2005	Medical Director review
06/21/2005	Medical Policy Committee review
07/15/2005	Managed Care Advisory Council approval
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.

Next Scheduled Review Date: 12/2021

Coding

The five character codes included in the Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)‡, copyright 2019 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

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attributable or related to any use, nonuse or interpretation of information contained in Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines. Fee schedules, relative value units, conversion factors and/or related components are not assigned by the AMA, are not part of CPT, and the AMA is not recommending their use. The AMA does not directly or indirectly practice medicine or dispense medical services. The AMA assumes no liability for data contained or not contained herein. Any use of CPT outside of Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines should refer to the most current Current Procedural Terminology which contains the complete and most current listing of CPT codes and descriptive terms. Applicable FARS/DFARS apply.

CPT is a registered trademark of the American Medical Association.

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

Code Type	Code
CPT	87475, 87476, 96365, 99601
HCPCS	A4216, A4223, A4305, A6457, G0299, J0171, J0696, J0712, J1335, J1642, J3370, J7030, J7040, J7050, S5501, S9373, S9374, S9379, S9494, S9497, S9500, S9501, S9502, S9503, S9504
ICD-10 Diagnosis	A69.20-A69.29, A87.2, G04.81, G04.90-G04.91, G37.4, G50.9-G51.0, G50.19-G20.29, G53, G60.9, H47.091-H47.099, H49.00-H49.03, H49.10-H49.13, H49.20-H49.23, H93.3X1-H93.3X9, H94.00-H94.03, I44.30, I51.89

*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 the Blue Cross and Blue Shield Association technology assessment program (TEC) or other nonaffiliated 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.

Intravenous Antibiotic Therapy and Associated Diagnostic Testing for Lyme Disease

Policy # 00173
Original Effective Date: 07/15/2005
Current Effective Date: 01/11/2021

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.