

**Policy is terminated because Medicaid does not cover these codes, and the codes are not utilized.**

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## **1.0 Description of the Procedure, Product, or Service**

Lyme disease is a multisystem inflammatory disease caused by the spirochete *Borrelia burgdorferi* and transmitted by the bite of an infected ixodid tick endemic to Northeastern, North Central, and Pacific coastal regions of the U.S. 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 nodal 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 recipients with neurologic involvement or atrioventricular heart block. However, overdiagnosis and overtreatment of Lyme disease are common due to its nonspecific symptoms, a lack of standardization of serologic tests, and difficulties in interpreting serologic test results. In particular, recipients with chronic fatigue syndrome or fibromyalgia are commonly misdiagnosed as possibly having Lyme disease and undergo inappropriate IV antibiotic therapy. The purpose of this policy is to provide diagnostic criteria for the appropriate use of IV antibiotic therapy.

The purpose of this policy is to provide diagnostic criteria for the appropriate use of IV antibiotic therapy for Lyme disease. The following Sections describe the various manifestations of Lyme disease that may prompt therapy with IV antibiotics and the various laboratory tests that are used to support the diagnosis of Lyme disease.

### **1.1 Neurologic Manifestations of Lyme Disease (Neuroborreliosis)**

- a. 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 recipient has LD, the CSF will show a lymphocytic pleocytosis (presence of too many cells) 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. Treatment with a two (2) to four (4) week course of IV antibiotics, typically ceftriaxone or cefotaxime, is recommended.
- b. Cranial neuritis, most frequently Bell's palsy, may present early in the course of disseminated LD, occasionally prior to the development of antibodies, such that an LD etiology may be difficult to rule in or out. While Bell's 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.

- c. 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 (EEG), magnetic resonance imaging (MRI), or CSF. In addition, the symptoms are nonspecific and overlap with fibromyalgia and chronic fatigue syndrome. Thus diagnosis of Lyme encephalopathy may be difficult and may be best diagnosed with a mental status exam or neuropsychological testing. However, treatment with IV antibiotics is generally not indicated unless CSF abnormalities are identified.
- d. 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 a pleocytosis and an elevation in protein. Selective synthesis of anti-spirochetal antigens can also be identified. A course of IV antibiotics with three (3) to four (4) weeks of ceftriaxone is suggested when CSF abnormalities are identified.
- e. A variety of peripheral nervous system manifestations of LD have also been identified. Symptoms of peripheral neuropathy include paresthesias, or radicular pain with only minimal sensory signs. Recipients typically exhibit electromyographic (EMG) or nerve conduction velocity abnormalities. CSF abnormalities are usually seen only in those recipients with a coexistent encephalopathy.

## 1.2 Cardiac Manifestations of Lyme Disease

Lyme carditis may appear during the early dissemination stage of the disease; symptoms include atrioventricular heart block, tachyarrhythmias, and myopericarditis. Antibiotics are typically given, although no evidence proves that this therapy hastens the resolution of symptoms. Both oral and IV regimens have been advocated. Intravenous regimens are typically used in recipients with a high degree atrioventricular block or a PR interval on the electrocardiogram (EKG) of greater than 0.3 second. Recipients with milder forms of carditis may be treated with oral antibiotics.

## 1.3 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. Recipients 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 central nervous system (CNS) involvement, requiring IV antibiotic treatment. In the small subset of recipients that do not respond to oral antibiotics, an additional 30-day course of oral or IV antibiotics may be recommended.

## 1.4 Fibromyalgia and Chronic Fatigue Syndrome

Fibromyalgia and chronic fatigue syndrome are the diseases most commonly confused with LD. 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 one or a few 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 to LD, both of the above conditions lack joint inflammation, have normal neurological test results, or have test results suggesting anxiety or depression.

Neither fibromyalgia nor chronic fatigue syndrome has been shown to respond to antibiotic therapy.

## 1.5 Serologic Tests

### a. Background

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 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 up to 5%–10%. Thus, as with any laboratory test, interpretation of serologic tests requires close correlation with the recipients' signs and symptoms. For example, recipients with vague symptoms of LD, chronic fatigue syndrome, or fibromyalgia may undergo multiple serologic tests over many weeks to months in an effort 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 recipient who has had long-standing symptoms and previously negative test results.

### b. Currently, the Centers for Disease Control and Prevention (CDC) recommend a 2-step method for the serologic diagnosis of LD:

#### 1. Enzyme-Linked Immunosorbent Assay (ELISA)

This test is the initial serologic test for LD. ELISA tests are available to detect IgM or IgG antibodies or to detect both antibody types together. More recently developed tests using recombinant or synthetic antigens have improved diagnostic sensitivity. For example, the FDA-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 an immunoblot test. In addition, results must be correlated with the clinical picture.

#### 2. Immunoblot or Western Blot

This test is used to confirm the serologic diagnosis of Lyme disease in recipients with positive or indeterminate ELISA tests. In contrast to 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 CDC criteria, the test result is considered positive if two (2) of the three (3) most common IgM antibody bands to spirochetal antigens are present, or five (5) of the ten (10) most frequent IgG antibody bands are present. Because the CDC 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. Criteria for interpreting immunoblot results are different in Europe than in the United States due to differences in prevalent *Borrelia* species causing disease.

## 1.6 Other tests include:

### a. Polymerase Chain Reaction (PCR)

In contrast to the above two (2) serologic tests, which only indirectly assess prior or present exposure to *B. burgdorferi*, PCR directly tests for the presence of the spirochete. Because PCR technology involves amplification of DNA from a portion of *B. burgdorferi*, there is a high risk of exogenous contamination, resulting in false positive results. In addition, the test cannot distinguish between live spirochetes or fragments of dead ones. The PCR technique has been studied using a variety of specimens. PCR has the best detection rates for skin biopsies from recipients with erythema migrans and for synovial tissue (and synovial fluid, to a lesser extent) from recipients with Lyme arthritis. CSF may be positive by PCR during the first two weeks of infection, but thereafter the detection rate is low. PCR is not recommended for urine or blood specimens.

*Borrelia* PCR also provides information on which of the three (3) major species pathogenic for humans has been found in the specimen tested (genotyping).

### b. T-Cell Proliferative Assay

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

### c. Evaluation of the Cerebrospinal Fluid (CSF)

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 a variety of 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 two (2) weeks of infection.

### d. Treatment of Lyme Disease

As noted above, treatment with IV antibiotics is generally indicated only in recipients with symptoms and laboratory findings consistent with CNS or peripheral neurologic involvement, and in a small subset of recipients with heart block or documented Lyme arthritis who have not responded to oral antibiotics. Typical IV therapy consists of a two (2) to four (4) week course of ceftriaxone or cefotaxime, both third-generation cephalosporins, or penicillin or chloramphenicol. No data suggest 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 LD. In addition, 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.

## 2.0 Eligible Recipients

### 2.1 General Provisions

To be eligible, NCHC recipients must be enrolled on the date of service.

### 3.0 When the Procedure, Product, or Service Is Covered

#### 3.1 General Criteria

NCHC covers procedures, products, and services related to this policy when they are medically necessary and

- a. the procedure, product, or service is individualized, specific, and consistent with symptoms or confirmed diagnosis of the illness or injury under treatment, and not in excess of the recipient's needs;
- b. the procedure, product, or service can be safely furnished, and no equally effective and more conservative or less costly treatment is available; **AND**
- c. the procedure, product, or service is furnished in a manner not primarily intended for the convenience of the recipient, the recipient's caretaker, or the provider.

#### 3.2 Specific Criteria

Intravenous antibiotic therapy for Lyme disease is covered by the NC Health Choice Program when it is determined to be medically necessary and when the following medical criteria and guidelines are met. Treatment of Lyme disease consists of oral antibiotics, except for the following indications:

- a. A two (2) to four (4) week course of IV antibiotic therapy may be considered medically necessary in recipients with neuroborreliosis with objective neurologic complications of documented LD (Refer to the following for methods of documentation)

1. Objective neurologic findings include:

- (a) Lymphocytic meningitis with documented CSF abnormalities
- (b) Cranial neuropathy, other than uncomplicated cranial nerve palsy, with documented CSF abnormalities
- (c) Encephalitis or encephalomyelitis associated with CSF abnormalities
- (d) Radiculopathy
- (e) Polyneuropathy

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

2. Serologic documentation of infection requires:

- (a) Positive or indeterminate enzyme-linked immunosorbent assay (ELISA), **AND**
- (b) Positive immunoblot blot by CDC criteria.

3. Documented CSF abnormalities include **ALL** of the following:

- (a) Pleocytosis;
- (b) Evidence of intrathecal production of *B. burgdorferi* antibodies in CSF; **AND**
- (c) Increased protein levels.

PCR-based direct detection of *B. burgdorferi* in CSF samples may be considered medically necessary and may replace serologic documentation of infection in recipients with a short duration of neurologic symptoms (<14 days) during the window between exposure and production of detectable antibodies.

- b. A two (2) to four (4) week course of IV antibiotics may be considered medically necessary in recipients with Lyme carditis, as evidenced by positive serologic findings (defined above) and associated with a high degree of atrioventricular block or a PR interval of greater than 0.3 second. Documentation of Lyme carditis may include PCR-based direct detection of *B. burgdorferi* in the blood when results of serologic studies are equivocal.
- c. A two (2) to four (4) week course of IV antibiotic therapy may be considered medically necessary in the small subset of recipients 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.

### 3.3 Policy Guidelines

Three different CPT codes describe direct detection of *B. burgdorferi*: direct probe (87475), amplified probe technique (87476), and quantification (87477). When these codes were introduced in 1998, for the sake of consistency, the same grouping of three (3) codes was used for a wide variety of different organisms. However, only the amplified probe technique (87476) is used clinically for the detection of *B. burgdorferi*. The direct probe technique (87475) is not clinically useful due to the small numbers of organisms present. The quantification technique (87477) has no clinical role at this time since treatment decisions are not based on the quantification of organisms present. Therefore, codes 87475 and 87477 would be considered investigational.

In 1993, the American College of Rheumatology published a position paper on IV antibiotic treatment for Lyme disease, which concluded that “... empiric treatment of recipients 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 recipients with Lyme disease without neurologic involvement.

Practice guidelines regarding the treatment of Lyme disease and including discussion of supportive evidence have been issued by the Infectious Diseases Society of America (IDSA). The IDSA also endorsed the American Academy of Neurology evidence-based practice parameter for the treatment of nervous system Lyme disease. The IDSA guidelines recommend IV antibiotics only in the following situations (note: none of the recommendations suggest longer than a 1-month course of IV antibiotics):

- a. Early neurologic disease
  - 1. Meningitis or radiculopathy: 14–28 days
- b. Cardiac disease
  - 1. Acute onset of varying degrees of intermittent atrioventricular heart block, sometimes in association with clinical evidence of myopericarditis: 14–21 days

- c. Late disease
  - 1. Persistent or recurrent arthritis after initial oral regimen: 14–28 days (a second, four (4)-week oral regimen may also be used)
  - 2. CNS or peripheral nervous system disease: 14–28 days

In the particular case of cranial nerve palsy associated with Lyme disease (most commonly Bell's palsy, also known as 7th nerve palsy) and without clinical evidence of meningitis, the evidence indicates that oral antibiotic therapy is satisfactory. Cranial nerve palsy may, in fact, resolve without treatment, but treatment should be administered to avoid late complications of Lyme disease.

In addition, guidelines recommend symptomatic treatment for symptoms that persist after appropriate antibiotic therapy. For example, in a small number of patients with known prior infection, arthritis may persist despite negative *B. burgdorferi* DNA by PCR in synovial fluid or tissue. Such persistent arthritis is termed "antibiotic-refractory Lyme arthritis," defined as "persistent synovitis for at least two (2) months after completion of a course of intravenous ceftriaxone (or after completion of two four (4)-week courses of an oral antibiotic for recipients unable to tolerate cephalosporins), in conjunction with negative results of PCR." Symptomatic treatment, rather than additional antibiotic treatment, is recommended.

The evidence generally does not support persistent *B. burgdorferi* infection in patients with well-documented infection who have received recommended antibiotic therapy. Blinded, randomized controlled trials of extended antibiotic therapy versus placebo in such patients have shown no consistent differences in outcomes. Therefore, prolonged courses of antibiotic therapy, which may be associated with adverse events, are not recommended.

## 4.0 When the Procedure, Product, or Service Is Not Covered

### 4.1 General Criteria

Procedures, products, and services related to this policy are not covered when

- a. the recipient does not meet the eligibility requirements listed in **Section 2.0**;
- b. the recipient does not meet the medical necessity criteria listed in **Section 3.0**;
- c. the procedure, product, or service unnecessarily duplicates another provider's procedure, product, or service; or
- d. the procedure, product, or service is experimental or investigational.

### 4.2 Specific Criteria

- a. Intravenous antibiotic therapy for LD is considered not medically necessary in the following situations:
  - 1. Recipients with symptoms consistent with chronic fatigue syndrome or fibromyalgia;
  - 2. Recipients with seronegative LD in the absence of CSF antibodies;
  - 3. Initial therapy in recipients with Lyme arthritis without coexisting neurologic symptoms;

4. Cranial nerve palsy (e.g. Bell's palsy) without clinical evidence of meningitis;
  5. Antibiotic-refractory Lyme arthritis (unresponsive to two (2) courses of oral antibiotics or to one (1) course of oral and one (1) course of intravenous antibiotic therapy);
  6. Recipients with vague systemic symptoms without supporting serologic or CSF studies;
  7. Recipients with a positive ELISA test, unconfirmed by an immunoblot or Western blot test (Refer to **Subsection 1.5.b.2**);
  8. Recipients with an isolated positive serologic test in the setting of multiple negative serologic studies.
  9. Recipients with chronic ( $\geq 6$  months) subjective symptoms ("post-Lyme syndrome") after receiving recommended treatment regimens for documented Lyme disease.
- b. Repeat or prolonged courses (e.g., greater than 4 weeks) of IV antibiotic therapy are considered not medically necessary.
  - c. Repeat PCR-based direct detection of *B. burgdorferi* is considered investigational in the following situations:
    1. as a justification for continuation of IV antibiotics beyond one (1) month in recipients with persistent symptoms;
    2. as a technique to follow therapeutic response.
  - d. PCR-based direct detection of *B. burgdorferi* in urine samples is considered investigational in all clinical situations.
  - e. Genotyping or phenotyping of *B. burgdorferi* is considered investigational.

## 5.0 Requirements for and Limitations on Coverage

### 5.1 Prior Approval

Prior approval is not required for home infusion (drugs or administrative fees or outpatient treatment) or for treatment in the office or hospital outpatient settings. If skilled nursing visits in the home are needed, prior approval is required.

## 6.0 Providers Eligible to Bill for the Procedure, Product, or Service

To be eligible to bill for procedures, products, and services related to this policy, providers shall

- a. meet NCHC qualifications for participation;
- b. be currently enrolled with NCHC; **AND**
- c. bill only for procedures, products, and services that are within the scope of their clinical practice, as defined by the appropriate licensing entity.

## 7.0 Additional Requirements

### 7.1 Compliance

Providers must comply with all applicable federal, state, and local laws and regulations, including the Health Insurance Portability and Accountability Act (HIPAA) and record retention requirements.

## 8.0 Policy Implementation/Revision Information

Original Effective Date: July 1, 2010

Revision Information:

Date	Section Revised	Change
July 1, 2010	Throughout	Policy Conversion: Implementation of Session Law 2009-451, Section 10.32 "NC HEALTH CHOICE/PROCEDURES FOR CHANGING MEDICAL POLICY."
February 29, 2012	Throughout	Policy Termination

## Attachment A: Claims-Related Information

Reimbursement requires compliance with all NCHC guidelines.

### A. Claim Type

Professional (CMS-1500/837P transaction)

Institutional (UB-04/837I transaction)

### B. Diagnosis Codes

Providers must bill the ICD-9-CM diagnosis codes(s) to the highest level of specificity that supports medical necessity.

### C. Procedure Code(s)

CPT Codes
86617
87476

### D. Modifiers

Providers are required to follow applicable modifier guidelines.

### E. Billing Units

The appropriate procedure code(s) used determines the billing unit(s).

### F. Place of Service

Outpatient Hospital, Office and Home

### G. Co-payments

Co-payment(s) may apply to covered prescription drugs and services.

### H. Reimbursement

Providers must bill their usual and customary charges.