

## Corporate Medical Policy

### Intravenous Antibiotic Therapy for Lyme Disease

**File Name:** intravenous\_antibiotic\_therapy\_for\_lyme\_disease  
**Origination:** 3/2006  
**Last CAP Review:** 2/2012  
**Next CAP Review:** 2/2013  
**Last Review:** 2/2012

#### Description of Procedure or Service

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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 patients 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, patients 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 following paragraphs 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.

#### Neurologic Manifestations 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. Treatment with a 2- to 4-week course of IV antibiotics, typically ceftriaxone or cefotaxime, is recommended.

Cranial neuritis, most frequently Bell's palsy, may present early in the course of disseminated Lyme disease, occasionally prior to the development of antibodies, such that a Lyme disease 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. 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.

Much rarer, but of greater concern, is the development of encephalomyelitis, characterized by spastic

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paraparesis, ataxias, cognitive impairment, bladder dysfunction, and cranial neuropathy. CSF examination reveals a pleocytosis and an elevation in protein. Selective synthesis of anti-spirochetal antibodies can also be identified. A course of IV antibiotics with 3 to 4 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 (EMG) or nerve conduction velocity abnormalities. CSF abnormalities are usually seen only in those patients with a coexistent encephalopathy.

## **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 patients with a high-degree atrioventricular block or a PR interval on the electrocardiogram of greater than 0.3 second. 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 central nervous system (CNS) 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 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 Lyme disease, both of the above conditions lack joint inflammation, have normal neurologic test results, or have test results suggesting anxiety or depression. Neither fibromyalgia nor chronic fatigue syndrome has been shown to respond to antibiotic therapy.

## **Serologic Tests**

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

Currently, the Centers for Disease Control and Prevention (CDC) recommend a 2-step method for the serologic diagnosis of Lyme disease:

1. Enzyme-Linked Immunosorbent Assay (ELISA) for *Borrelia burgdorferi* Antibodies

This test is a screening serologic test for Lyme disease. ELISA tests are available to detect IgM or IgG

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antibodies or to detect 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 (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. (Western) Immunoblot

This test is used to confirm the serologic diagnosis of Lyme disease in patients 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 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 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.

### **Other tests include:**

#### **Polymerase Chain Reaction (PCR)**

In contrast to the above 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. Positive results in the absence of clear clinical indicators or positive serology are not definitive for diagnosis. 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 patients with erythema migrans (but may not be indicated with 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 thereafter the detection rate is low. PCR is not recommended for urine or blood specimens.

*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; they are difficult to perform and standardize, and their sensitivity is not well characterized.

#### **Evaluation of 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 CNS. 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 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 a potential marker for successful treatment.

#### **Treatment of Lyme Disease**

As noted above, treatment with IV antibiotics is generally indicated only in patients with symptoms and laboratory findings consistent with CNS 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, both third-generation

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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 Lyme disease. 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.

**\*\*\*Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.**

## Policy

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**BCBSNC will provide coverage for intravenous antibiotic therapy for Lyme Disease when it is determined to be medically necessary and when medical criteria and guidelines shown below are met.**

## Benefits Application

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This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

## When Intravenous Antibiotic Therapy for Lyme Disease is covered

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Treatment of Lyme disease consists of oral antibiotics, except for the following indications (I, II or III):

**I.** A 2- to 4-week course of IV antibiotic therapy may be considered medically necessary in patients with neuroborreliosis with objective neurologic complications of documented Lyme disease (see the following for methods of documentation).

**Objective neurologic findings include:**

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

**Serologic documentation of infection requires:**

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

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

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

Polymerase chain reaction (PCR)-based direct detection of *B. burgdorferi* in CSF samples may be considered medically necessary 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.

**II.** A single 2- to 4-week course of IV antibiotics may be considered medically necessary in patients 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

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studies are equivocal.

**III.** A single 2- to 4-week course of IV antibiotic therapy may be considered medically necessary in the small subset of patients 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.

## When Intravenous Antibiotic Therapy and Testing for Lyme Disease is not covered

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Intravenous antibiotic therapy is considered not medically necessary in the following situations:

- Patients with symptoms consistent with chronic fatigue syndrome or fibromyalgia, in the absence of objective clinical or laboratory evidence for Lyme disease;
- Patients with seronegative Lyme disease in the absence of 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 antibiotic therapy);
- Patients with vague systemic symptoms without supporting serologic or CSF studies;
- Patients with a positive ELISA test, unconfirmed by an immunoblot or Western blot test (see definition above);
- Patients with an isolated positive serologic test in the setting of multiple negative serologic studies;
- Patients with chronic (>6 months) subjective symptoms ("post-Lyme syndrome") after receiving recommended treatment regimens for documented Lyme disease.

Repeat or prolonged courses (e.g., greater than 4 weeks) of IV antibiotic therapy are considered not medically necessary.

Repeat PCR-based direct detection of *B. burgdorferi* is considered investigational in the following situations:

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

PCR-based direct detection of *B. burgdorferi* in urine samples is considered investigational in all clinical situations.

Genotyping or phenotyping of *B. burgdorferi* is considered investigational.

Other diagnostic testing is considered investigational, including, but not limited to C6 peptide ELISA or determination of levels of the B lymphocyte chemoattractant CXCL13 for diagnosis or monitoring treatment.

The direct probe technique and the quantification technique for detection of *B. burgdorferi* are considered investigational.

## Policy Guidelines

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Lyme disease is a multisystem inflammatory disease caused by *Borrelia burgdorferi* and transmitted by

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the bite of an infected ixodid tick. Oral antibiotics usually are adequate for treatment of Lyme disease, but in some cases, a 2-4-week course of intravenous (IV) antibiotics may be appropriate such as in cases of Lyme arthritis, carditis or objective neurologic complications. Evidence has not shown a benefit to prolonged (greater than 4 weeks) or repeat courses of IV antibiotics. Therefore, repeat or prolonged courses of antibiotic therapy are considered not medically necessary.

Diagnostic testing for Lyme disease is challenging and can potentially lead to overdiagnosis and overtreatment. 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 studies are needed, serologic testing using the 2-step ELISA followed by Western blot is the recommended first approach. Polymerase chain reaction (PCR), may be considered medically necessary as a second approach in patients with a short duration of neurologic symptoms (<14 days) or uncertainty in serologic testing. For detection of *B. burgdorferi* only the amplified probe technique is used clinically. The direct probe technique is not clinically useful due to the small numbers of organisms present. The quantification technique has no clinical role at this time since treatment decisions are not based on the quantification of organisms present. Other uses for PCR-based testing are considered investigational.

Genotyping or phenotyping of *B burgdorferi* is considered investigational. Additional research is necessary to determine diagnostic and treatment utility of the CXCL13, and its use is considered investigational. Other diagnostic testing approaches, such as C6 peptide, also warrant additional research and therefore, are considered investigational.

## Billing/Coding/Physician Documentation Information

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This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at [www.bcbsnc.com](http://www.bcbsnc.com). They are listed in the Category Search on the Medical Policy search page.

*Applicable codes: 86617, 87475, 87476, 87477*

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

## Scientific Background and Reference Sources

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American College of Rheumatology. Appropriateness of parenteral antibiotic treatment for patients with presumed Lyme disease. A joint statement of the American College of Rheumatology and the Council of the Infectious Diseases Society of America. *Ann Intern Med* 1993; 119(6):518

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BCBSA Medical Policy Reference Manual [Electronic Version]. 5.01.08, 12/09/10

BCBSA Medical Policy Reference Manual [Electronic Version]. 5.01.08, 12/08/11

Specialty Matched Consultant Advisory Panel – 2/29/12

## Policy Implementation/Update Information

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3/2/06 Notification of new policy. Treatment of Lyme Disease consists of oral antibiotics, except for the following indications: A 2-to 4-week course of IV antibiotic therapy may be considered medically necessary (1) in patients with neuroborreliosis with objective neurologic complications of documented Lyme Disease. Objective neurologic findings include lymphocytic meningitis associated with CSF abnormalities, Bell's palsy or other cranial neuropathy associated with CSF abnormalities, encephalitis or encephalomyelitis associated with CSF abnormalities, radiculopathy, polyneuropathy; (2) in patients with Lyme carditis as evidenced by positive serologic findings and associated with a high degree of atrioventricular block or a PR interval of greater than 0.3 second; (3) in the small subset of patients with well-documented Lyme arthritis who have such severe arthritis that it requires the rapid response associated with IV antibiotics.

Lyme Disease may be documented either on the basis of serologic testing or examination of the CSF. Positive serologic diagnosis is defined as both (1) positive or indeterminate ELISA test as characterized by IgG showing a titer >800 (positive) or a titer between 1:200 and 1:400 (indeterminate) or IgM ELISA test showing a titer of >200 (positive) or 1:100 (indeterminate) and (2) positive immunoblot or Western blot as characterized by (1) 2 of the 8 most common IgM antibody bands to spirochetal antigens are present or 5 of the 10 most frequent IgG antibody bands are present. All positive or indeterminate ELISA tests must be confirmed with immunoblot. Positive CSF findings include all of the following: pleocytosis; evidence of intrathecal production of *B.burgdorferi* antibodies in CSF; and increased protein levels.

IV antibiotic therapy for Lyme Disease is considered not medically necessary in the following situations: patients with symptoms consistent with chronic fatigue syndrome or fibromyalgia; patients with seronegative Lyme disease in the absence of CSF antibodies; initial therapy in patients with Lyme arthritis without coexisting neurologic symptoms; patients with vague systemic symptoms without supporting serologic or CSF studies; patients with a positive ELISA test, unconfirmed by an immunoblot or Western blot test; patients with an isolated positive

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serologic test in the setting of multiple negative serologic studies; repeat or prolonged courses (greater than 4 weeks) of antibiotic therapy.

The following are considered investigational: Repeat PCR-based direct detection of *B. burgdorferi* as a justification for continuation of IV antibiotics beyond 1 month in patients with persistent symptoms or as a technique to follow therapeutic response; PCR-based direct detection of *B. burgdorferi* in urine samples; genotyping or phenotyping of *B. burgdorferi*; CPT codes 87475 and 87477.

Notification given 3/2/06. Effective date 5/8/06.

- 5/5/08 Item A.2 in the When Covered section revised to read, "Cranial neuropathy, other than uncomplicated cranial nerve palsy, with documented CSF abnormalities." Revised the last sentence in Item C. to read, "Documentation of Lyme arthritis requires either unequivocal serologic studies, or when serologic studies are equivocal, PCR-based direct detection of *B. burgdorferi* in the synovial fluid." Also added bullet to Item C. with the following statement: "Patients who have persistent or recurrent joint swelling after a recommended course of oral antibiotic therapy should be re-treated with another 4-week course of oral antibiotics or with a 2-4 week course of intravenous ceftriaxone. A second 4-week course of oral antibiotic therapy is recommended for the patient whose arthritis has substantively improved but has not yet completely resolved, reserving intravenous antibiotic therapy for those patients whose arthritis failed to improve at all or worsened. Clinicians should consider waiting several months before initiating re-treatment with antimicrobial agents because of the anticipated slow resolution of inflammation after treatment." The following statements added to the Not Covered section: "Cranial nerve palsy (e.g. Bell's palsy) without clinical evidence of meningitis" and "Antibiotic-refractory Lyme arthritis (unresponsive to 2 courses of oral antibiotics or to 1 course of oral and 1 course of intravenous antibiotic therapy)." Statement from the American Academy of Neurology added to Policy Guidelines section. References updated. Specialty Matched Consultant Advisory Panel review 3/31/08. Notification given 5/5/08. Effective date 8/11/08. (adn)
- 3/16/10 Description section revised (information describing the tests for diagnosis of LD updated). In the When Covered section: added the word "documented" to Items A.1. and A.3 and deleted the word "associated." The sentence following A.5. revised to read: 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. The last statement under Item A revised to read: PCR-based direct detection of *B. burgdorferi* in CSF samples may be considered medically necessary 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. In the When Not Covered section, added statement number 9 to Item A that reads: [IV antibiotic therapy for LD is considered not medically necessary in] patient with chronic (>6 months) subjective symptoms ("post-Lyme syndrome") after receiving recommended treatment regimens for documented Lyme disease. Updated the supporting rationale in the Policy Guidelines section. References updated. Specialty Matched Consultant Advisory Panel review 2/11/10. (adn)
- 6/22/10 Policy Number(s) removed (amw)
- 4/12/11 Added the following to the Description section: CXCL 13 is a B lymphocyte chemoattractant and has been reported to be elevated in acute neuroborreliosis, and a potential marker for successful treatment. Added Item F. to the NonCovered section: Determination of levels of the B lymphocyte chemoattractant CXCL 13 for diagnosis or monitoring treatment is considered **investigational**. Added the following rationale to the Policy Guidelines section: CXCL13 is a B lymphocyte chemoattractant that has been reported to be elevated in acute neuroborreliosis; thus it is a potential marker for successful treatment. However, data are limited. Additional research is necessary to determine diagnostic and treatment utility. Its use for the diagnosis of Lyme disease or monitoring treatment is considered investigational. Specialty Matched Consultant

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review 2/23/11. (adn)

- 3/30/12 Added the following to the Description section under Polymerase Chain Reaction (PCR): (but may not be indicated with recent history of tick bite or exposure). Added C6 peptide ELISA to the list of investigational diagnostic testing. Added “Patients with symptoms consistent with chronic fatigue syndrome or fibromyalgia, in the absence of objective clinical or laboratory evidence for Lyme disease” to When Intravenous Antibiotic Therapy and Testing for Lyme Disease is not covered. Policy Guidelines section extensively revised. Added reference. Specialty Matched Consultant review 2/29/12. (sk)

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