

MEDICAL POLICY

POLICY TITLE	INTRAVENOUS ANTIBIOTIC THERAPY FOR LYME DISEASE
POLICY NUMBER	MP 2.026

CLINICAL BENEFIT	<input checked="" type="checkbox"/> MINIMIZE SAFETY RISK OR CONCERN. <input checked="" type="checkbox"/> MINIMIZE HARMFUL OR INEFFECTIVE INTERVENTIONS. <input type="checkbox"/> ASSURE APPROPRIATE LEVEL OF CARE. <input type="checkbox"/> ASSURE APPROPRIATE DURATION OF SERVICE FOR INTERVENTIONS. <input checked="" type="checkbox"/> ASSURE THAT RECOMMENDED MEDICAL PREREQUISITES HAVE BEEN MET. <input type="checkbox"/> ASSURE APPROPRIATE SITE OF TREATMENT OR SERVICE.
Effective Date:	RETIRED 5/1/2026

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I. POLICY

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

Neuroborreliosis

A two (2)- to four (4)-week course of IV antibiotic therapy may be considered **medically necessary** in individuals 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; **or**
- Cranial neuropathy, other than uncomplicated cranial nerve palsy, with documented CSF abnormalities; **or**
- Encephalitis or encephalomyelitis with documented CSF abnormalities; **or**
- Radiculopathy; **or**
- Polyneuropathy.

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

Serologic documentation of infection requires:

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

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

- Pleocytosis; **and**
- Evidence of intrathecal production of *Borrelia burgdorferi* antibodies in CSF; **and**

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- Increased protein levels.

Lyme Carditis

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

Lyme Arthritis

A single two (2) - to four (4)-week course of IV antibiotic therapy may be considered **medically necessary** in the small subset of individuals with well-documented Lyme arthritis who have such severe arthritis that it requires the rapid response associated with IV antibiotics. Documentation of Lyme arthritis may include PCR-based direct detection of *B. burgdorferi* in the synovial tissue or fluid when results of serologic studies are equivocal.

Antibiotic Therapy

Intravenous antibiotic therapy is considered **investigational** in the following situations as there is insufficient evidence to support a general conclusion concerning the health outcomes or benefits associated with this procedure:

- Individuals with symptoms consistent with chronic fatigue syndrome or fibromyalgia, in the absence of objective clinical or laboratory evidence of Lyme disease; **or**
- Individuals with seronegative Lyme disease in the absence of CSF antibodies; **or**
- Initial therapy in individuals with Lyme arthritis without coexisting neurologic symptoms; **or**
- Cranial nerve palsy (e.g., Bell's palsy) without clinical evidence of meningitis; **or**
- Post-antibiotic 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); **or**
- Individuals with vague systemic symptoms without supporting serologic or CSF studies; **or**
- Individuals with a positive enzyme-linked immunosorbent assay (ELISA) test, unconfirmed by an immunoblot or Western blot test (see definition above); **or**
- Individuals with an isolated positive serologic test in the setting of multiple negative serologic studies; **or**
- Individuals 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 **investigational** as there is insufficient evidence to support a general conclusion concerning the health outcomes or benefits associated with this procedure

Cross-reference:

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G2143 Lyme Disease

II. PRODUCT VARIATIONS

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This policy is only applicable to certain programs and products administered by Capital Blue Cross and subject to benefit variations as discussed in Section VI. Please see additional information below.

FEP PPO - Refer to FEP Medical Policy Manual. The FEP Medical Policy manual can be found at:

<https://www.fepblue.org/benefit-plans/medical-policies-and-utilization-management-guidelines/medical-policies>

III. DESCRIPTION/BACKGROUND

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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 *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. Manifestations of the early disseminated disease may include lymphocytic meningitis, facial palsy, painful radiculoneuritis, atrioventricular (AV) block, or migratory musculoskeletal pain. Months to years later, the disease may be manifested by intermittent oligoarthritis, particularly involving the knee joint; chronic encephalopathy; spinal pain; or distal paresthesias. While most manifestations of Lyme disease can be adequately treated with oral antibiotics, intravenous (IV) antibiotics are indicated in some patients with disseminated Lyme disease. The following paragraphs describe the various manifestations of Lyme disease, therapies, and the various laboratory tests used to support the diagnosis of Lyme disease.

Manifestations

Erythema migrans

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

Neuroborreliosis

Lymphocytic meningitis, characterized by head and neck pain, may occur during the acute disseminated stage of the disease. In patients with meningitis, the cerebrospinal fluid (CSF) will typically show a lymphocytic pleocytosis (lymphocyte count greater than normal) with increased levels of protein and normal glucose levels. Intrathecal production of antibodies directed at spirochetal antigens is also typically present. Other manifestations of early disseminated disease can include cranial neuritis (including unilateral or bilateral facial palsy) and peripheral nervous system manifestations. Cranial neuritis, most frequently Bell palsy, may present early in

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the course of disseminated Lyme disease, occasionally before the development of antibodies. Peripheral nervous system manifestations of Lyme disease include paresthesias or radicular pain with only minimal sensory signs. Patients typically exhibit electromyographic or nerve conduction velocity abnormalities.

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

Lyme Carditis

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

Lyme Arthritis

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

Treatment of Lyme Disease

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

IV. RATIONALE

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Summary of Evidence

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

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antibiotics. The evidence is sufficient to determine that the technology is unlikely to improve the net health outcome.

V. DEFINITIONS

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ELISA TEST refers to Enzyme-Linked Immunosorbent Assay (ELISA). This test is the initial serologic test for LD.

VI. BENEFIT VARIATIONS

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The existence of this medical policy does not mean that this service is a covered benefit under the member's health benefit plan. Benefit determinations are based on the applicable health benefit plan language. Medical policies do not constitute a description of benefits. Members and providers should consult the member's health benefit plan for information or contact Capital Blue Cross for benefit information.

VII. DISCLAIMER

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Capital Blue Cross' medical policies are developed to assist in administering a member's benefits. These medical policies do not constitute medical advice and are subject to change. Treating providers are solely responsible for medical advice and treatment of members. Members should discuss any medical policy related to their coverage or condition with their provider and consult their benefit information to determine if the service is covered. If there is a discrepancy between this medical policy and a member's benefit information, the benefit information will govern. If a provider or a member has a question concerning the application of this medical policy to a specific member's plan of benefits, please contact Capital Blue Cross' Provider Services or Member Services. Capital Blue Cross considers the information contained in this medical policy to be proprietary and it may only be disseminated as permitted by law.

VIII. CODING INFORMATION

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Note: This list of codes may not be all-inclusive, and codes are subject to change at any time. The identification of a code in this section does not denote coverage as coverage is determined by the terms of member benefit information. In addition, not all covered services are eligible for separate reimbursement.

Covered when medically necessary:

Procedure Codes							
S5035	S9379	S9494	S9497	S9500	S9501	S9502	S9503
S9504	99601	99602					

Note: Refer to the Laboratory Service policies for testing related to Lyme disease.

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ICD-10-CM Diagnosis Code	Description
A69.20	Lyme disease, unspecified
A69.21	Meningitis due to Lyme disease
A69.22	Other neurologic disorders in Lyme disease
A69.23	Arthritis due to Lyme disease
A69.29	Other conditions associated with Lyme disease

IX. REFERENCES

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1. Steere AC. Lyme disease. *N Engl J Med*. Jul 12 2001; 345(2): 115-25. PMID 11450660
2. Institute of Medicine (IOM). *Critical Needs and Gaps in Understanding: Prevention, Amelioration, and Resolution of Lyme and Other Tick-Borne Diseases: The Short-Term and Long-Term Outcomes: Workshop Report*. Washington, DC: National Academies Press; 2011
3. Lantos PM, Rumbaugh J, Bockenstedt LK, et al. Clinical Practice Guidelines by the Infectious Diseases Society of America (IDSA), American Academy of Neurology (AAN), and American College of Rheumatology (ACR): 2020 Guidelines for the Prevention, Diagnosis and Treatment of Lyme Disease. *Clin Infect Dis*. Jan 23 2021; 72(1): e1-e48. PMID 33417672
4. Mead P, Petersen J, Hinckley A. Updated CDC Recommendation for Serologic Diagnosis of Lyme Disease. *MMWR Morb Mortal Wkly Rep*. Aug 16 2019; 68(32): 703. PMID 31415492
5. Centers for Disease Control and Prevention. Lyme Disease: Treatment. Updated May 15, 2024; <https://www.cdc.gov/lyme/treatment/index.html>
6. Sanchez E, Vannier E, Wormser GP, et al. Diagnosis, Treatment, and Prevention of Lyme Disease, Human Granulocytic Anaplasmosis, and Babesiosis: A Review. *JAMA*. Apr 26 2016; 315(16): 1767-77. PMID 27115378
7. Halperin JJ, Shapiro ED, Logigian E, et al. Practice parameter: treatment of nervous system Lyme disease (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology*. Jul 03 2007; 69(1): 91-102. PMID 17522387
8. Lantos PM, Auwaerter PG, Wormser GP. A systematic review of *Borrelia burgdorferi* morphologic variants does not support a role in chronic Lyme disease. *Clin Infect Dis*. Mar 2014; 58(5): 663-71. PMID 24336823
9. Solheim AM, Lorentzen AR, Dahlberg AO, et al. Six versus 2 weeks treatment with doxycycline in European Lyme neuroborreliosis: a multicentre, non-inferiority, double-blinded, randomised and placebo-controlled trial. *J Neurol Neurosurg Psychiatry*. Jul 27 2022. PMID 35896378
10. Berende A, ter Hofstede HJ, Vos FJ, et al. Randomized Trial of Longer-Term Therapy for Symptoms Attributed to Lyme Disease. *N Engl J Med*. Mar 31 2016; 374(13): 1209-20. PMID 27028911

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11. Fallon BA, Keilp JG, Corbera KM, et al. A randomized, placebo-controlled trial of repeated IV antibiotic therapy for Lyme encephalopathy. *Neurology*. Mar 25 2008; 70(13): 992-1003. PMID 17928580
12. Cameron D. Severity of Lyme disease with persistent symptoms. Insights from a double-blind placebo-controlled clinical trial. *Minerva Med*. Oct 2008; 99(5): 489-96. PMID 18971914
13. Oksi J, Nikoskelainen J, Hiekkänen H, et al. Duration of antibiotic treatment in disseminated Lyme borreliosis: a double-blind, randomized, placebo-controlled, multicenter clinical study. *Eur J Clin Microbiol Infect Dis*. Aug 2007; 26(8): 571-81. PMID 17587070
14. Kaplan RF, Trevino RP, Johnson GM, et al. Cognitive function in post-treatment Lyme disease: do additional antibiotics help?. *Neurology*. Jun 24 2003; 60(12): 1916-22. PMID 12821733
15. Klempner MS, Hu LT, Evans J, et al. Two controlled trials of antibiotic treatment in patients with persistent symptoms and a history of Lyme disease. *N Engl J Med*. Jul 12 2001; 345(2): 85-92. PMID 11450676
16. Krupp LB, Hyman LG, Grimson R, et al. Study and treatment of post Lyme disease (STOP-LD): a randomized double masked clinical trial. *Neurology*. Jun 24 2003; 60(12): 1923-30. PMID 12821734
17. Association of Public Health Laboratories. *Suggested Reporting Language, Interpretation and Guidance Regarding Lyme Disease Serologic Test Results*. May 2021
18. National Institute for Health and Care Excellence (NICE). *Lyme disease [NG95]*. 2018
19. Cameron DJ, Johnson LB, Maloney EL. Evidence assessments and guideline recommendations in Lyme disease: the clinical management of known tick bites, erythema migrans rashes and persistent disease. *Expert Rev Anti Infect Ther*. Sep 2014; 12(9): 1103-35. PMID 25077519
20. Blue Cross Blue Shield Association Medical Policy Reference Manual. 5.01.08, *Intravenous Antibiotic Therapy and Associated Diagnostic Testing for Lyme Disease*. November 2024

X. POLICY HISTORY

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MP 2.026	03/26/2020 Consensus Review. Policy statement unchanged, verbiage updated to match BCBSA. Variation, background, rationale, and references update. Coding reviewed.
	04/14/2021 Consensus Review. Policy statement unchanged. References updated.
	12/01/2022 Consensus Review. In policy statement changed “patients” to “members”, no change to intent. Updated cross-references, FEP, background, rationale, coding table and references.
	12/27/2023 Consensus Review. Editorial refinements to policy statements (members to individuals); intent unchanged. Updated references. No changes to coding.
	11/20/2024 Minor Review. Deleted PCR statement as testing is managed by a vendor. Updated NMN statements to INV. Clarifications made to the INV

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	sections, no change to intent. Updated background and references. No changes to coding.
	12/5/2025 Retirement review.

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