

MEDICAL POLICY	Lyme Disease
<p>Effective Date: 5/1/2021</p>  <p style="text-align: right;">5/1/2021</p>	<p>Medical Policy Number: 123</p> <p>Technology Assessment Committee Approved Date: 7/12; 12/13; 10/14; 7/15; 4/16</p> <p>Medical Policy Committee Approved Date: 5/17; 7/18; 8/19; 3/2020; 4/2021</p>
<p>Medical Officer Date</p>	

See Policy CPT CODE section below for any prior authorization requirements

SCOPE:

Providence Health Plan, Providence Health Assurance, Providence Plan Partners, and Ayin Health Solutions as applicable (referred to individually as “Company” and collectively as “Companies”).

APPLIES TO:

All lines of business

BENEFIT APPLICATION

Medicaid Members

Oregon: Services requested for Oregon Health Plan (OHP) members follow the OHP Prioritized List and Oregon Administrative Rules (OARs) as the primary resource for coverage determinations. Medical policy criteria below may be applied when there are no criteria available in the OARs and the OHP Prioritized List.

POLICY CRITERIA

Note: This policy does not address intravenous (IV) antibiotic treatment of Lyme disease. IV antibiotic treatment of Lyme disease is addressed in the Providence Health Plan pharmacy policy titled, “Parenteral Antibiotic Use in the Treatment of Lyme Disease.” These requests should be sent to PHP Pharmacy for review.

Diagnostic Testing

- I. Diagnostic testing for Lyme disease is considered **medically necessary and covered** when done in accordance with the Centers for Disease Control and Prevention (CDC) two-step laboratory testing process for Lyme disease. (See [Clinical Practice Guidelines](#) for full details.)
- II. Diagnostic testing for Lyme disease is considered **investigational and is not covered** when criterion I. above is not met, including but not limited to, the following tests which the CDC has determined to be invalid for diagnosing Lyme disease:

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- A. Capture assays for antigens in urine
- B. Culture, immunofluorescence staining, or cell sorting of cell wall-deficient or cystic forms of *B. burgdorferi*
- C. Lymphocyte transformation tests
- D. Quantitative CD57 lymphocyte assays
- E. "Reverse Western blots"
- F. In-house criteria for interpretation of immunoblots
- G. Measurements of antibodies in joint fluid (synovial fluid)
- H. IgM or IgG tests without a previous ELISA/EIA/IFA
- I. ZEUS ELISA™ Test Systems

Non-Antimicrobial Alternative Therapies

- III. All non-antimicrobial alternative therapies for Lyme disease are considered **investigational and are not covered**, including but not limited to:
 - A. Oxygen and reactive oxygen species
 - B. Energy and radiation
 - C. Heavy metals and chelation
 - D. Nutritional and herbal therapy
 - E. Biological and pharmacological therapy
 - F. Empirical anti-babesiosis therapy in the absence of documentation of active babesiosis
 - G. Anti-Bartonella therapies
 - H. Fever therapy (with or without malaria induction)
 - I. Intravenous immunoglobulin
 - J. Cholestyramine
 - K. Magnesium or bismuth injections

Link to [Policy Summary](#)

CPT CODES

All Lines of Business	
No Prior Authorization Required	
Lab Codes Used for Diagnosis:	
0041U	Borrelia burgdorferi, antibody detection of 5 recombinant protein groups, by immunoblot, IgM
0042U	Borrelia burgdorferi, antibody detection of 12 recombinant protein groups, by immunoblot, IgG
0043U	Tick-Borne Relapsing Fever Borrelia group, antibody detection to 4 recombinant protein groups, by immunoblot, IgM
0044U	Tick-Borne Relapsing Fever Borrelia group, antibody detection to 4 recombinant protein groups, by immunoblot, IgG
84181	Protein; Western Blot, with interpretation and report, blood or other body fluid

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84182	Protein; Western Blot, with interpretation and report, blood or other body fluid, immunological probe for band identification, each
86617	Antibody; <i>Borrelia burgdorferi</i> (Lyme disease) confirmatory test (eg, Western blot or immunoblot)
86618	Antibody; <i>Borrelia burgdorferi</i> (Lyme disease)
88346	Immunofluorescence, per specimen; initial single antibody stain procedure
88350	Immunofluorescence, per specimen; each additional single antibody stain procedure (List separately in addition to code for primary procedure)
Home Infusion Procedures:	
99601	Home infusion/specialty drug administration, per visit (up to 2 hours)
99602	Home infusion/specialty drug administration, per visit (up to 2 hours); each additional hour (List separately in addition to code for primary procedure)
Parenteral Antibiotic Therapy:	
96365	Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); initial, up to 1 hour
96366	Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); each additional hour (List separately in addition to code for primary procedure)
96367	Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); additional sequential infusion of a new drug/substance, up to 1 hour (List separately in addition to code for primary procedure)
96368	Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); concurrent infusion (List separately in addition to code for primary procedure)
96369	Subcutaneous infusion for therapy or prophylaxis (specify substance or drug); initial, up to 1 hour, including pump set-up and establishment of subcutaneous infusion site(s)
96370	Subcutaneous infusion for therapy or prophylaxis (specify substance or drug); each additional hour (List separately in addition to code for primary procedure)
96371	Subcutaneous infusion for therapy or prophylaxis (specify substance or drug); additional pump set-up with establishment of new subcutaneous infusion site(s) (List separately in addition to code for primary procedure)
S9494-S9504	Home infusion therapy

DESCRIPTION

According to the Centers for Disease Control and Prevention (CDC), “Lyme disease is caused by the bacterium *Borrelia burgdorferi* and is transmitted to humans through the bite of infected blacklegged ticks.”¹ Symptoms include fever, headache, fatigue, and a characteristic “bull’s-eye” skin rash called erythema migrans. Untreated Lyme disease can affect the joints, heart, and nervous system. Lyme disease is diagnosed based on a person’s exposure to infected ticks, symptoms, and physical findings (e.g., rash). Serologic testing may also be helpful in diagnosing Lyme disease if performed correctly using validated methods. Typically, Lyme disease can be successfully treated with a few weeks of antibiotics.

REVIEW OF EVIDENCE

A review of the Centers for Disease Control and Prevention (CDC), ECRI, Hayes, Cochrane, and PubMed databases was conducted regarding intravenous antibiotic therapy for the treatment of Lyme disease. Below is a summary of the available evidence identified through February 2021.

The criteria for the diagnosis of Lyme disease is based on the CDC recommended testing regimen for Lyme disease (see [Clinical Practice Guidelines](#) for full details).^{2,3} Therefore, an evidence review was only conducted regarding non-antibiotic therapies for Lyme disease.

Review

In 2015, Lantos et al. conducted a study to identify and characterize the range of unorthodox alternative therapies advertised to patients with a diagnosis of Lyme disease.⁴ A review of evidence was then conducted for each alternative therapy to assess whether a scientific basis had been established for the effectiveness of the therapy.

The authors identified several broad categories of unconventional therapies for Lyme disease. These are summarized in the table below.

Table 1. Examples of Alternative Therapies Marketed to Patients for the Treatment of Lyme Disease⁴

Categories of Therapy	Examples
Oxygen	<ul style="list-style-type: none"> - Hyperbaric oxygen - Hydrogen peroxide - Ozone
Energy and radiation	<ul style="list-style-type: none"> - Ultraviolet light - Photon therapy - “Cold” lasers - Saunas and steam rooms - “Rife” therapy (electromagnetic frequency treatments) - Magnets
Metal/chelation	<ul style="list-style-type: none"> - Mercury chelation and removal - Dimercaptosuccinic acid (DMSA) - 2,3-Dimercapto-1-propanesulfonic acid (DMPS) - Alpha lipoic acid (ALA) - Ethylene diamine tetraacetic acid (EDTA) - Removal of dental amalgam - Colloidal silver - Bismuth
Nutritional supplements	<ul style="list-style-type: none"> - Vitamins C and B12 - Herbs - Garlic, cilantro, Chlorella, Sarsaparilla, - Andrographis, Turmeric, Olive leaf, - Cat’s claw

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	<ul style="list-style-type: none"> - Burnt mugwort (moxibustion) - Glutathione - Fish oil - Magnesium - Salt
Biological and pharmacologic	<ul style="list-style-type: none"> - Urotherapy (urine ingestion) - Enemas - Bee venom - Hormonal therapy - Dihydroepiandrosterone, Pregnenolone, Cortisone, Hydrocortisone - Synthetic thyroid hormone - Lithium orotate - Olmesartan - Cholestyramine - Naltrexone - Sodium chlorite (bleach) - Intravenous immune globulin (IVIG) - Apheresis - Stem cell transplantation

The authors identified no medical literature or scientific studies supporting the efficacy of any of the treatments listed above. Additionally, very few of these treatments were ever evaluated in any scientific studies, and those that were evaluated were done so in poorly designed studies. The authors concluded that “(t)he efficacy of these unconventional treatments for Lyme disease is not supported by scientific evidence, and in many cases they are potentially harmful.”⁴

CLINICAL PRACTICE GUIDELINES

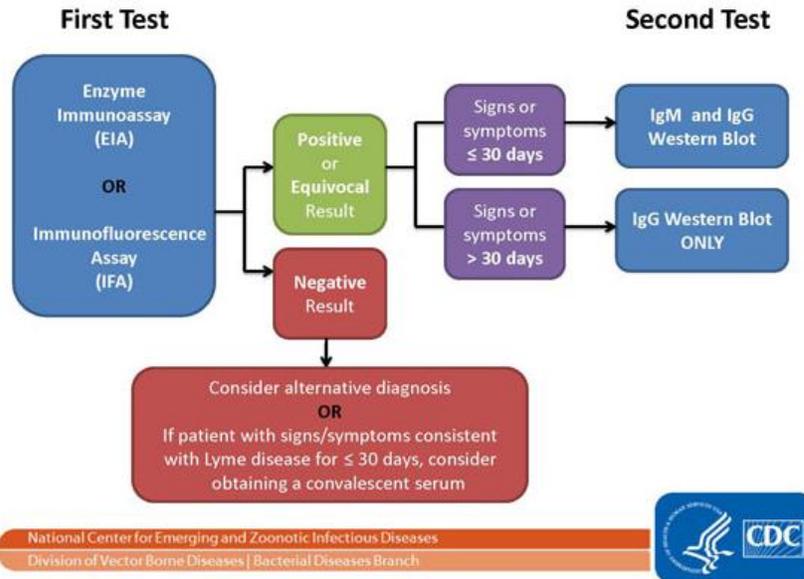
Centers for Disease Control and Prevention (CDC)

The Centers for Disease Control and Prevention (CDC) recommends a two-step serologic process for diagnosing Lyme disease²:

1. Enzyme immunoassay (EIA) or rarely, an indirect immunofluorescence assay (IFA). If this step is negative, no further testing is recommended. If this step is positive or indeterminate (equivocal), the second step is performed.
2. Immunoblot test, commonly, a “Western blot” test.

Results are considered positive only if the EIA/IFA and the immunoblot are both positive.

Two-Tiered Testing for Lyme Disease



These two steps are designed to be done together in order to accurately diagnose Lyme disease. The CDC does not recommend skipping a step, as doing so will increase the frequency of false positive results.

Some laboratories may offer Lyme disease testing using assays whose accuracy and clinical usefulness have not been adequately established.³ Examples of these unvalidated tests include:

- Capture assays for antigens in urine
- Culture, immunofluorescence staining, or cell sorting of cell wall-deficient or cystic forms of *B. burgdorferi*
- Lymphocyte transformation tests
- Quantitative CD57 lymphocyte assays
- “Reverse Western blots”
- In-house criteria for interpretation of immunoblots
- Measurements of antibodies in joint fluid (synovial fluid)
- IgM or IgG tests without a previous ELISA/EIA/IFA

Infectious Disease Society of America (IDSA)

The 2006 IDSA guideline for the diagnosis, management, and prevention of Lyme disease recommends against the use of the following therapies for Lyme disease⁵:

- Excessive doses of antimicrobials
- Multiple, repeated courses of antimicrobials for the same episode of Lyme disease or an excessive duration of antimicrobial therapy
- Combination antimicrobial therapy

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- Pulsed-dosing (i.e., antibiotic therapy on some days but not on other days)
- First-generation cephalosporins, benzathine penicillin G, fluoroquinolones, carbapenems, vancomycin, metronidazole, tinidazole, trimethoprim-sulfamethoxazole, amantadine, ketolides, isoniazid, or fluconazole
- Empirical anti-babesiosis therapy in the absence of documentation of active babesiosis
- Anti-Bartonella therapies
- Hyperbaric oxygen therapy
- Fever therapy (with or without malaria induction)
- Intravenous immunoglobulin
- Ozone
- Cholestyramine
- Intravenous hydrogen peroxide
- Vitamins or nutritional managements
- Magnesium or bismuth injections

CENTERS FOR MEDICARE & MEDICAID

As of 3/1/2021, no Centers for Medicare & Medicaid (CMS) coverage guidance was identified which addresses diagnostic testing or treatment of Lyme disease.

POLICY SUMMARY

The Centers for Disease Control and Prevention (CDC) recommends a two-step testing process for the accurate diagnosis of Lyme disease; therefore, any deviance from the CDC testing regimen or use of any invalid assay is considered investigational. Many unconventional therapies for the treatment of Lyme disease have been purported. Due to a lack of scientific evidence demonstrating the efficacy of these therapies, non-antimicrobial alternative therapies for Lyme disease are consider investigational.

INSTRUCTIONS FOR USE

Company Medical Policies serve as guidance for the administration of plan benefits. Medical policies do not constitute medical advice nor a guarantee of coverage. Company Medical Policies are reviewed annually and are based upon published, peer-reviewed scientific evidence and evidence-based clinical practice guidelines that are available as of the last policy update. The Companies reserve the right to determine the application of Medical Policies and make revisions to Medical Policies at any time. Providers will be given at least 60-days’ notice of policy changes that are restrictive in nature.

The scope and availability of all plan benefits are determined in accordance with the applicable coverage agreement. Any conflict or variance between the terms of the coverage agreement and Company Medical Policy will be resolved in favor of the coverage agreement.

REGULATORY STATUS

Mental Health Parity Statement

Coverage decisions are made on the basis of individualized determinations of medical necessity and the experimental or investigational character of the treatment in the individual case. In cases where medical necessity is not established by policy for specific treatment modalities, evidence not previously considered regarding the efficacy of the modality that is presented shall be given consideration to determine if the policy represents current standards of care.

REFERENCES

1. Centers for Disease Control and Prevention. Lyme Disease. <https://www.cdc.gov/lyme/index.html>. Published 2021. Accessed 3/1/2021.
2. Centers for Disease Control and Prevention. Two-Step Testing Process for Lyme Disease. <https://www.cdc.gov/lyme/diagnostesting/labtest/twostep/index.html>. Published 2019. Accessed 3/1/2021.
3. Centers for Disease Control and Prevention. Lyme Disease Laboratory Tests That Are Not Recommended. <https://www.cdc.gov/lyme/diagnostesting/labtest/otherlab/index.html>. Published 2018. Accessed 3/1/2021.
4. Lantos PM, Shapiro ED, Auwaerter PG, et al. Unorthodox alternative therapies marketed to treat Lyme disease. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America*. 2015;60(12):1776-1782
5. Wormser GP, Dattwyler RJ, Shapiro ED, et al. The clinical assessment, treatment, and prevention of lyme disease, human granulocytic anaplasmosis, and babesiosis: clinical practice guidelines by the Infectious Diseases Society of America. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America*. 2006;43(9):1089-1134