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:

See Policy CPT CODE section below for any prior authorization requirements
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 investigative 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

CPT CODES

<table>
<thead>
<tr>
<th>Lab Codes Used for Diagnosis:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Borrelia burgdorferi, antibody detection of 5 recombinant protein groups, by immunoblot, IgM</td>
</tr>
<tr>
<td>Borrelia burgdorferi, antibody detection of 12 recombinant protein groups, by immunoblot, IgG</td>
</tr>
<tr>
<td>Tick-Borne Relapsing Fever Borrelia group, antibody detection to 4 recombinant protein groups, by immunoblot, IgM</td>
</tr>
<tr>
<td>Tick-Borne Relapsing Fever Borrelia group, antibody detection to 4 recombinant protein groups, by immunoblot, IgG</td>
</tr>
<tr>
<td>Protein; Western Blot, with interpretation and report, blood or other body fluid</td>
</tr>
</tbody>
</table>
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 “bulls-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). 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. 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 Disease

<table>
<thead>
<tr>
<th>Categories of Therapy</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxygen</td>
<td>Hyperbaric oxygen</td>
</tr>
<tr>
<td></td>
<td>Hydrogen peroxide</td>
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<tr>
<td></td>
<td>Ozone</td>
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<tr>
<td>Energy and radiation</td>
<td>Ultraviolet light</td>
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<td></td>
<td>Photon therapy</td>
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<tr>
<td></td>
<td>“Cold” lasers</td>
</tr>
<tr>
<td></td>
<td>Saunas and steam rooms</td>
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<tr>
<td></td>
<td>“Rife” therapy (electromagnetic frequency treatments)</td>
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<tr>
<td></td>
<td>Magnets</td>
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<tr>
<td>Metal/chelation</td>
<td>Mercury chelation and removal</td>
</tr>
<tr>
<td></td>
<td>Dimercaptosuccinic acid (DMSA)</td>
</tr>
<tr>
<td></td>
<td>2,3-Dimercapto-1-propanesulfonic acid (DMPS)</td>
</tr>
<tr>
<td></td>
<td>Alpha lipoic acid (ALA)</td>
</tr>
<tr>
<td></td>
<td>Ethylene diamine tetraacetic acid (EDTA)</td>
</tr>
<tr>
<td></td>
<td>Removal of dental amalgam</td>
</tr>
<tr>
<td></td>
<td>Colloidal silver</td>
</tr>
<tr>
<td></td>
<td>Bismuth</td>
</tr>
<tr>
<td>Nutritional supplements</td>
<td>Vitamins C and B12</td>
</tr>
<tr>
<td></td>
<td>Herbs</td>
</tr>
<tr>
<td></td>
<td>Garlic, cilantro, Chlorella, Sarsaparilla, Andrographis, Turmeric, Olive leaf, Cat’s claw</td>
</tr>
</tbody>
</table>
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.”

**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 disease:

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 indeterminant (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.
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. 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 disease:

- 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
MEDICAL POLICY

Pentastigmine

Lyme Disease

- 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