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Section:	Prescription Drugs	**Effective Date:**	January 1, 2019
Subsection:	Anti-Infective Agents	**Original Policy Date:**	December 7, 2011
Subject:	IV Antibiotics Lyme Disease	**Page:**	1 of 9

Last Review Date: November 30, 2018

IV Antibiotics Lyme Disease

Description

IV Antibiotics for Lyme Disease (Ceftriaxone, Cefotaxime sodium, Doxycycline, Penicillin G potassium)

Background
Lyme disease is a tick-borne infectious disease caused by the *Borellia* species of spirochetes. Lyme disease is endemic to many regions throughout the United States and is the most commonly seen vector-borne infection. If detected at an early stage, Lyme disease is often treatable with only a small risk of further complications. However, if left untreated Lyme disease can lead to complications of the heart, joints, and central nervous system. In these cases it is important that antibiotics be administered as quickly as possible and guidelines recommend that parenteral, or intravenous, antibiotics are the agents of choice. Treatment of neuroborreliosis and Lyme carditis require 2 to 4 weeks of parenteral antibiotics (1).

In cases of early, uncomplicated Lyme disease, studies have shown that oral antibiotics are just as effective, if not more effective, than parenteral antibiotics. In addition, oral antibiotics are easier to administer and are often less expensive than their intravenous counterparts (1).

Regulatory Status
FDA-approved indications:

Ceftriaxone is indicated for the treatment of the following infections when caused by susceptible organisms (2):

- LOWER RESPIRATORY TRACT INFECTIONS caused by Streptococcus pneumoniae, Staphylococcus aureus, Haemophilus influenzae, Haemophilus parainfluenzae, Klebsiella pneumoniae, Escherichia coli, Enterobacter aerogenes, Proteus mirabilis or Serratia marcescens.
- ACUTE BACTERIAL OTITIS MEDIA caused by Streptococcus pneumoniae, Haemophilus influenzae (including beta-lactamase producing strains) or Moraxellacatarrhalis (including beta-lactamase producing strains).
- SKIN AND SKIN STRUCTURE INFECTIONS caused by Staphylococcus aureus, Staphylococcus epidermidis, Streptococcus pyogenes, Viridans group streptococci, Escherichia coli, Enterobacter cloacae, Klebsiella oxytoca, Klebsiella pneumoniae, Proteus mirabilis, Morganella morganii, Pseudomonas aeruginosa, Serratia marcescens, Acinetobacter calcoaceticus, Bacteroides fragilis or Peptostreptococcus species.
- URINARY TRACT INFECTIONS (complicated and uncomplicated) caused by Escherichia coli, Proteus mirabilis, Proteus vulgaris, Morganella morganii or Klebsiella pneumoniae.
- UNCOMPLICATED GONORRHEA (cervical/urethral and rectal) caused by Neisseria gonorrhoeae, including both penicillinase- and nonpenicillinase-producing strains, and pharyngeal gonorrhea caused by nonpenicillinase-producing strains of Neisseria gonorrhoeae.
- PELVIC INFLAMMATORY DISEASE caused by Neisseria gonorrhoeae. Ceftriaxone, like other cephalosporins, has no activity against Chlamydia trachomatis. Therefore, when cephalosporins are used in the treatment of patients with pelvic inflammatory disease and Chlamydia trachomatis is one of the suspected pathogens, appropriate antichlamydial coverage should be added.
- BACTERIAL SEPTICEMIA caused by Staphylococcus aureus, Streptococcus pneumoniae, Escherichia coli, Haemophilus influenzae or Klebsiella pneumoniae.
- BONE AND JOINT INFECTIONS caused by Staphylococcus aureus, Streptococcus pneumoniae, Escherichia coli, Proteus mirabilis, Klebsiella pneumoniae or Enterobacter species.
- INTRA-ABDOMINAL INFECTIONS caused by Escherichia coli, Klebsiella pneumoniae, Bacteroides fragilis, Clostridium species or Peptostreptococcus species.
- MENINGITIS caused by Haemophilus influenzae, Neisseria meningitidis or Streptococcus pneumoniae. Ceftriaxone has also been used successfully in a limited number of cases of meningitis and shunt infection caused by Staphylococcus epidermidis and Escherichia coli.

Off label indication for ceftriaxone: Lyme disease

Cefotaxime is indicated for the treatment of patients with serious infections caused by susceptible strains of the designated microorganisms in the diseases listed below (3):

- LOWER RESPIRATORY TRACT INFECTIONS, including pneumonia, caused by Streptococcus pneumoniae, Streptococcus pyogenes and other streptococci (excluding enterococci, e.g., Enterococcus faecalis), Staphylococcus aureus (penicillinase and non-penicillinase producing), Escherichia coli, Klebsiella species, Haemophilus influenzae (including ampicillin resistant strains), Haemophilus parainfluenzae, Proteus mirabilis, Serratia marcescens, Enterobacter species, indole positive Proteus and Pseudomonas species (including P. aeruginosa).
- GENITOURINARY INFECTIONS infections caused by Enterococcus species, Staphylococcus epidermidis, Staphylococcus aureus, (penicillinase and non-penicillinase producing), Citrobacter species, Enterobacter species, Escherichia coli, Klebsiella species, Proteus mirabilis, Proteus vulgaris, Providencia stuartii, Morganella morganii, Providencia rettgeri, Serratia marcescens and Pseudomonas species (including P. aeruginosa). Also, uncomplicated gonorrhea (cervical/urethral and rectal) caused by Neisseria gonorrhoeae, including penicillinase producing strains.
- GYNECOLOGIC INFECTIONS, including pelvic inflammatory disease, endometritis and pelvic cellulitis caused by Staphylococcus epidermidis, Streptococcus species, Enterococcus species, Enterobacter species, Klebsiella species, Escherichia coli, Proteus mirabilis, Bacteroides species (including Bacteroides fragilis), Clostridium species, and anaerobic cocci (including Peptostreptococcus species and Peptococcus species) and Fusobacterium species (including F. nucleatum). Cefotaxime, like other cephalosporins, has no activity against Chlamydia trachomatis. Therefore, when cephalosporins are used in the treatment of patients with pelvic inflammatory disease and C. trachomatis is one of the suspected pathogens, appropriate anti-chlamydial coverage should be added.
- BACTEREMIA/SEPTICEMIA caused by Escherichia coli, Klebsiella species, and Serratia marcescens, Staphylococcus aureus and Streptococcus species (including S. pneumonia).
- SKIN AND SKIN STRUCTURE INFECTIONS caused by Staphylococcus aureus (penicillinase and non-penicillinase producing), Staphylococcus epidermidis, Streptococcus pyogenes (Group A streptococci) and other streptococci, Enterococcus species, Acinetobacter species, Escherichia coli, Citrobacter species (including C. freundii), Enterobacter species, Klebsiella species, Proteus mirabilis, Proteus vulgaris, Morganella morganii, Providencia rettgeri, Pseudomonas species, Serratia marcescens,

Bacteroides species, and anaerobic cocci (including Peptostreptococcus species and Peptococcus species).

- INTRA-ABDOMINAL INFECTIONS including peritonitis caused by Streptococcus species, Escherichia coli, Klebsiella species, Bacteroides species, and anaerobic cocci (including Peptostreptococcus species and Peptococcus species) Proteus mirabilis, and Clostridium species.
- BONE AND/OR JOINT INFECTIONS caused by Staphylococcus aureus (penicillinase and non-penicillinase producing strains), Streptococcus species (including S. pyogenes), Pseudomonas species (including P. aeruginosa), and Proteus mirabilis.
- CENTRAL NERVOUS SYSTEM INFECTIONS, e.g., meningitis and ventriculitis, caused by Neisseria meningitidis, Haemophilus influenzae, Streptococcus pneumoniae, Klebsiella pneumoniae and Escherichia coli.

Cefotaxime is indicated for the prevention of patients with serious infections caused by susceptible strains of the designated microorganisms in the diseases listed below (3):

- PREOPERATIVELY reduces the incidence of certain infections in patients undergoing surgical procedures (e.g., abdominal or vaginal hysterectomy, gastrointestinal and genitourinary tract surgery) that may be classified as contaminated or potentially contaminated.
- CESAREAN SECTION, intraoperative (after clamping the umbilical cord) and postoperative

Off label indication for cefotaxime: Lyme disease

Doxycycline for Injection is indicated for the treatment of infections caused by the following microorganisms (4):

- Rickettsiae (Rocky Mountain spotted fever, typhus fever, and the typhus group. Q fever, rickettsial pox and tick fevers)
- Mycoplasma pneumoniae (PPLO, Eaton Agent)
- Agents of psittacosis and ornithosis
- Agents of lymphogranuloma venereum and granuloma inguinal
- The spirochetal agent of relapsing fever (Borrelia recurrentis)
- Haemophilus ducreyi (chancroid)
- Pasteurella pestis and Pasteurella tularensis
- Bartonella bacilliformis
- Bacteroides species
- Vibrio comma and Vibrio fetus

- Brucella species (in conjunction with streptomycin)
- The following gram-negative microorganisms when bacteriologic testing indicates appropriate susceptibility to the drug:
    - Escherichia coli
    - Enterobacter aerogenes
    - Shigella species
    - Mima species and Herellea species
    - Haemophilus influenzae (respiratory infections)
    - Klebsiella species (respiratory and urinary infections)
- The following gram-positive microorganisms when bacteriologic testing indicates appropriate susceptibility to the drug:
    - Streptococcus species
    - For upper respiratory infections due to group A beta-hemolytic streptococci, penicillin is the usual drug of choice, including prophylaxis of rheumatic fever
    - Diplococcus pneumoniae
    - Staphylococcus aureus, respiratory, skin and soft tissue infections. Tetracyclines are not the drugs of choice in the treatment of any type of staphylococcal infections
    - Anthrax due to Bacillus anthracis, including inhalational anthrax (post-exposure)
- When penicillin is contraindicated, doxycycline for injection is an alternative drug in the treatment of infections due to:
    - Neisseria gonorrhoeae and N. meningitidis
    - Treponema pallidum and Treponema pertenue (syphilis and yaws)
    - Listeria monocytogenes
    - Clostridium species
    - Fusobacterium fusiforme (Vincent's infection)
    - Actinomyces species.
- Trachoma

Off label indication for doxycycline for injection: Lyme disease

Penicillin G Potassium is approved for the treatment of patients with infections caused by susceptible strains of microorganisms in the following diseases (5):

- Septicemia
- Empyema
- Pneumonia
- Pericarditis

- Endocarditis
- Erysipelothrix endocarditis
- Fusospirochetosis
- Meningococcal meningitis and/or septicemia
- Gram-negative bacillary infections
- Meningitis
- Anthrax
- Actinomycosis
- Botulism
- Gas gangrene
- Tetanus
- Diptheria
- Lower respiratory tract infection
- Listeria infections
- Pasteurella infections
- Haverhill infections
- Rat bite fever
- Disseminated gonococcal infection
- Syphilis
- Bacteremia

Off label indication for penicillin G potassium: Lyme disease

Related policies

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Ceftriaxone, cefotaxime sodium, doxycycline for injection and penicillin G potassium may be considered **medically necessary** for the treatment of Lyme disease if the conditions indicated below are met.

Ceftriaxone, cefotaxime sodium, doxycycline for injection and penicillin G potassium may be considered **medically necessary** for the treatment of infections other than Lyme disease.

Ceftriaxone, cefotaxime sodium, doxycycline for injection and penicillin G potassium may be considered **investigational** for the treatment of Lyme disease if the conditions listed below are not met.

Prior-Approval Requirements

Diagnoses

Patient must have **ONE** of the following:

1. Any diagnosis other than Lyme disease

2. Diagnosis of Lyme disease

   AND ALL of the following:
   - A. Positive or indeterminate ELISA for Lyme Disease
   - B. Positive immunoblot as defined by CDC criteria, also known as a Western blot

   AND ONE of the following
   - A. Neuroborreliosis with objective neurologic complications
     - a. Neurological complications include:
       - i. Lymphocytic meningitis with documented cerebrospinal fluid (CSF) abnormalities
       - ii. Cranial neuropathy, other than uncomplicated cranial nerve palsy, with documented CSF abnormalities
       - iii. Encephalitis or encephalomyelitis with documented CSF abnormalities
       - iv. Radiculopathy
       - v. Polyneuropathy
   - B. Documented Lyme carditis
     - a. Documentation of Lyme carditis may include PCR-based direct detection of *B. burgdorferi* in the blood when results of serologic studies are equivocal
   - C. Documented Lyme arthritis that has not responded to a 4-week course of oral antibiotics

Prior – Approval *Renewal* Requirements

None

Policy Guidelines

Pre - PA Allowance

Duration 2 weeks

Prior - Approval Limits

Duration 2 weeks for Lyme disease
12 months for all diagnoses other than Lyme disease

Prior – Approval *Renewal* Limits

None

Rationale

Summary

Lyme disease is a tick-borne infectious disease caused by the *Borellia* species of spirochetes. Lyme disease is endemic to many regions throughout the United States and is the most commonly seen vector-borne infection. If detected at an early stage, Lyme disease is often treatable with only a small risk of further complications. Treatment of neuroborreliosis and Lyme carditis require 2 to 4 weeks of parenteral antibiotics. In cases of early, uncomplicated Lyme disease, studies have shown that oral antibiotics are just as effective, if not more effective, than parenteral antibiotics.

Prior approval is required to ensure the safe, clinically appropriate and cost effective use of IV antibiotics for Lyme disease while maintaining optimal therapeutic outcomes.

References

1. Wormser GP, Dattwyler, RJ, Shapiro ED et al. The clinical assessment, treatment, and prevention of Lyme disease, human granulocytic anaplasmosis, and babesiosis. Clinical Infectious Diseases. 2006;43(9):1089-1134.
2. Ceftriaxone [package insert]. Lake Forest, IL : Hospira, Inc.; June 2017.
3. Cefotaxime [package insert]. Baltimore, Maryland: Lupin Pharmaceuticals, Inc; July 2015.

4. Doxycycline for Injection [package insert]. Lake Zurich, IL: Fresenius Kabi, LLC; October 2015.
5. Penicillin G Potassium Injection [package insert]. Deerfield, IL: Baxter Healthcare Corporation; July 2018.

Policy History

Date	Action
December 2011	New Policy
December 2012	Annual review and update
June 2014	Annual editorial review and reference update
March 2016	Annual review and reference update
	Policy number changed from 5.03.15 to 5.01.15
December 2017	Annual editorial review and reference update
November 2018	Annual review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on November 30, 2018 and is effective January 1, 2019.