IV ANTIBIOTICS FOR LYME DISEASE
(Ceftriaxone, Cefotaxime sodium, Doxycycline, Penicillin G potassium)

RATIONALE FOR INCLUSION IN PA PROGRAM

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*. 
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- **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,
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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.
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(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)
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- 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
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- 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

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
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