



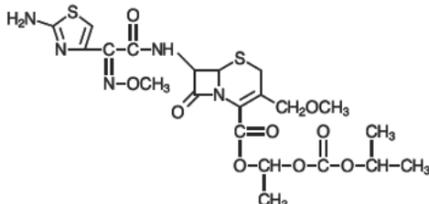
Cepodoxime Proxetil for Oral Suspension, USP

R_x only

To reduce the development of drug-resistant bacteria and maintain the effectiveness of Cepodoxime Proxetil for Oral Suspension, USP and other antibacterial drugs, Cepodoxime Proxetil for Oral Suspension, USP should be used only to treat or prevent infections that are proven or strongly suspected to be caused by bacteria.

For Oral Use Only DESCRIPTION

Cepodoxime proxetil is an orally administered, extended spectrum, semi-synthetic antibiotic of the cephalosporin class. The chemical name is (RS)-1-[isopropoxycarbonyloxy] ethyl (+)-(6R,7R)-7-[2-(2-amino-4-thiazolyl)-2-(1Z-methoxyimino)acetamido]-3-methoxymethyl-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylate. Its empirical formula is C₂₁H₂₇N₅O₉S₂ and its structural formula is represented below:



The molecular weight of cepodoxime proxetil is 557.6. Cepodoxime proxetil is a prodrug; its active metabolite is cepodoxime. All doses of cepodoxime proxetil in this insert are expressed in terms of the active cepodoxime moiety. The drug is supplied as flavored granules for oral suspension.

Each 5 mL of Cepodoxime Proxetil for Oral Suspension, USP contains cepodoxime proxetil equivalent to 50 mg or 100 mg of cepodoxime activity after constitution and the following inactive ingredients: anhydrous citric acid, aspartame, caramel flavoring, colloidal silicon dioxide, guar gum, magnesium stearate, silicon dioxide, sodium benzoate, sodium citrate, sorbitan trioleate, sucrose, strawberry flavoring, vanilla flavoring.

CLINICAL PHARMACOLOGY

Absorption and Excretion

Cepodoxime proxetil is a prodrug that is absorbed from the gastrointestinal tract and de-esterified to its active metabolite, cepodoxime. Following oral administration of 100 mg of cepodoxime proxetil to fasting subjects, approximately 50% of the administered cepodoxime dose was absorbed systemically. Over the recommended dosing range (100 to 400 mg), approximately 29 to 33% of the administered cepodoxime dose was excreted unchanged in the urine in 12 hours. There is minimal metabolism of cepodoxime *in vivo*.

Effects of Food

When a 200 mg dose of the suspension was taken with food, the extent of absorption (mean AUC) and mean peak plasma concentration in fed subjects were not significantly different from fasted subjects, but the rate of absorption was slower with food (48% increase in T_{max}).

Pharmacokinetics of Cepodoxime Proxetil Suspension

In adult subjects, a 100 mg dose of oral suspension produced an average peak cepodoxime concentration of approximately 1.5 mcg/mL (range: 1.1 to 2.1 mcg/mL), which is equivalent to that reported following administration of the 100 mg tablet. Time to peak plasma concentration and area under the plasma concentration-time curve (AUC) for the oral suspension were also equivalent to those produced with film-coated tablets in adults following a 100 mg oral dose.

The pharmacokinetics of cepodoxime were investigated in 29 patients aged 1 to 17 years. Each patient received a single, oral, 5 mg/kg dose of cepodoxime oral suspension. Plasma and urine samples were collected for 12 hours after dosing. The plasma levels reported from this study are as follows:

Cepodoxime Plasma Levels (mcg/mL) in Fasted Patients (1 to 17 Years of Age) After Suspension Administration

Dose (Cepodoxime Equivalents)	Time after Oral Ingestion						
	1hr	2hr	3hr	4hr	6hr	8hr	12hr
5 mg/kg*	1.4	2.1	2.1	1.7	0.90	0.40	0.090

* Dose did not exceed 200 mg.

Distribution

Protein binding of cepodoxime ranges from 22 to 33% in serum and from 21 to 29% in plasma.

Skin Blister

Following multiple-dose administration every 12 hours for 5 days of 200 mg or 400 mg cepodoxime proxetil, the mean maximum cepodoxime concentration in skin blister fluid averaged 1.6 and 2.8 mcg/mL, respectively. Skin blister fluid cepodoxime levels at 12 hours after dosing averaged 0.2 and 0.4 mcg/mL for the 200 mg and 400 mg multiple-dose regimens, respectively.

Tonsil Tissue

Following a single, oral 100 mg cepodoxime proxetil film-coated tablet, the mean maximum cepodoxime concentration in tonsil tissue averaged 0.24 mcg/g at 4 hours post-dosing and 0.09 mcg/g at 7 hours post-dosing. Equilibrium was achieved between plasma and tonsil tissue within 4 hours of dosing. No detection of cepodoxime in tonsillar tissue was reported 12 hours after dosing. These results demonstrated that concentrations of cepodoxime exceeded the MIC₉₀ of *S. pyogenes* for at least 7 hours after dosing of 100 mg of cepodoxime proxetil.

Lung Tissue

Following a single, oral 200 mg cepodoxime proxetil film-coated tablet, the mean maximum cepodoxime concentration in lung tissue averaged 0.63 mcg/g at 3 hours post-dosing, 0.52 mcg/g at 6 hours post-dosing, and 0.19 mcg/g at 12 hours post-dosing. The results of this study indicated that cepodoxime penetrated into lung tissue and produced sustained drug concentrations for at least 12 hours after dosing at levels that exceeded the MIC₉₀ for *S. pneumoniae* and *H. influenzae*.

CSF

Adequate data on CSF levels of cepodoxime are not available.

Effects of Decreased Renal Function

Elimination of cepodoxime is reduced in patients with moderate to severe renal impairment (<50 mL/min creatinine clearance). (See PRECAUTIONS and DOSAGE AND ADMINISTRATION.) In subjects with mild impairment of renal function (50 to 80 mL/min creatinine clearance), the average half-life of cepodoxime was 3.5 hours. In subjects with moderate (30 to 49 mL/min creatinine clearance) or severe renal impairment (5 to 29 mL/min creatinine clearance), the half-life increased to 5.9 and 9.8 hours, respectively. Approximately 23% of the administered dose was cleared from the body during a standard 3-hour hemodialysis procedure.

Effect of Hepatic Impairment (cirrhosis)

Absorption was somewhat diminished and elimination unchanged in patients with cirrhosis. The mean cepodoxime T_{1/2} and renal clearance in cirrhotic patients were similar to those derived in studies of healthy subjects. Ascites did not appear to affect values in cirrhotic subjects. No dosage adjustment is recommended in this patient population.

Pharmacokinetics in Elderly Subjects

Elderly subjects do not require dosage adjustments unless they have diminished renal function. (See PRECAUTIONS.) In healthy geriatric subjects, cepodoxime half-life in plasma averaged 4.2 hours (vs 3.3 in younger subjects) and urinary recovery averaged 21% after a 400 mg dose was administered every 12 hours. Other pharmacokinetic parameters (C_{max}, AUC, and T_{max}) were unchanged relative to those observed in healthy young subjects.

Microbiology

Mechanism of Action

Cepodoxime is a bactericidal agent that acts by inhibition of bacterial cell wall synthesis. Cepodoxime has activity in the presence of some beta-lactamases, both penicillinases and cephalosporinases, of Gram-negative and Gram-positive bacteria.

Mechanism of Resistance

Resistance to Cepodoxime is primarily through hydrolysis by beta-lactamase, alteration of penicillin-binding proteins (PBPs), and decreased permeability.

Cepodoxime has been shown to be active against most isolates of the following bacteria, both *in vitro* and in clinical infections as described in the Indications and Usage (1) section:

Gram-positive bacteria

Staphylococcus aureus (methicillin-susceptible strains, including those producing penicillinases)
Staphylococcus saprophyticus
Streptococcus pneumoniae (excluding penicillin-resistant isolates)
Streptococcus pyogenes

Gram-negative bacteria

Escherichia coli
Klebsiella pneumoniae
Proteus mirabilis
Haemophilus influenzae (including beta-lactamase producing isolates)
Moraxella catarrhalis

Other Gram-negative bacteria

Neisseria gonorrhoeae (including penicillinase-producing isolates)
The following *in vitro* data are available, but their clinical significance is unknown. At least 90 percent of the following microorganisms exhibit an *in vitro* minimum inhibitory concentration (MIC) less than or equal to the susceptible breakpoint for Cepodoxime. However, the efficacy of Cepodoxime in treating clinical infections due to these microorganisms has not been established in adequate and well-controlled clinical trials.

Gram-positive bacteria

Streptococcus agalactiae
Streptococcus spp. (Groups C, F, G)

Gram-negative bacteria

Citrobacter diversus
Klebsiella oxytoca
Proteus vulgaris
Providencia rettgeri
Haemophilus parainfluenzae

Anaerobic Gram-positive bacteria

Peptostreptococcus magnus

Susceptibility Test Methods

When available, the clinical microbiology laboratory should provide the results of *in vitro* susceptibility test results for antimicrobial drug products used in resident hospitals to the physician as periodic reports that describe the susceptibility profile of nosocomial and community-acquired pathogens. These reports should aid the physician in selecting an antibacterial drug product for treatment.

Diffusion techniques

Quantitative methods are used to determine antimicrobial minimal inhibitory concentrations (MICs). These MICs provide estimates of the susceptibility of bacteria to antimicrobial compounds. The MICs should be determined using a standardized test method.^{1,2} The MIC values should be interpreted according to criteria provided in Table 1.

Diffusion techniques

Quantitative methods that require measurement of zone diameters also provide reproducible estimates of the susceptibility of bacteria to antimicrobial compounds. The zone size provides an estimate of the susceptibility of bacteria to antimicrobial compounds. The zone size should be determined using a standardized test method.^{2,3} This procedure uses paper disks impregnated with 10 mcg Cepodoxime to test the susceptibility of microorganisms to Cepodoxime. The disk diffusion interpretive criteria are provided in Table 1.

Table 1. Susceptibility Test Interpretive Criteria for Cepodoxime²

Pathogen	Minimum Inhibitory Concentrations (mcg/mL)			Disk Diffusion Diameters (mm)		
	S	I	R	S	I	R
Enterobacteriaceae	≤ 2	4	≥ 8	≥ 21	18-20	≤ 17
<i>Haemophilus influenzae</i> ^a	≤ 2	-	≥ 21	-	-	-
<i>Streptococcus pneumoniae</i>	≤ 0.5	1	≥ 2	-	-	-
<i>Neisseria gonorrhoeae</i> ^a	≤ 0.5	-	≥ 29	-	-	-

^a The current absence of resistant isolates precludes defining any results other than "Susceptible." Isolates yielding MIC results other than "Susceptible" should be submitted to a reference laboratory for further testing.

Susceptibility of staphylococci to Cepodoxime may be deduced from testing only penicillin and either cefoxitin or oxacillin.

A report of *Susceptible* indicates that the antimicrobial is likely to inhibit growth of the pathogen if the antimicrobial compound reaches the concentration at the infection site necessary to inhibit growth of the pathogen. A report of *Intermediate* indicates that the result should be considered equivocal, and if the microorganism is not fully susceptible to alternative, clinically feasible drugs, the test should be repeated. This category implies possible clinical applicability in body sites where the drug is physiologically concentrated or in situations where a high dosage of drug can be used. This category also provides a buffer zone that prevents small uncontrolled technical factors from causing major discrepancies in interpretation. A report of *Resistant* indicates that the antimicrobial is not likely to inhibit growth of the pathogen if the antimicrobial compound reaches the concentrations usually achievable at the infection site; other therapy should be selected.

Quality Control

Standardized susceptibility test procedures require the use of laboratory controls to monitor and ensure the accuracy and precision of supplies and reagents used in the assay, and the techniques of the individual performing the test.^{1,2,3} Standard Cepodoxime powder should provide the following range of MIC values noted in Table 2. For the diffusion technique using the 10 mcg disk, the criteria in Table 2 should be achieved.

Table 2. Acceptable Quality Control Ranges for Cepodoxime

QC Strains	Minimum Inhibitory Concentrations (mcg/mL)	Disk Diffusion Zone diameters (mm)
<i>Escherichia coli</i> ATCC 25922	0.25 - 1	23 - 28
<i>Haemophilus influenzae</i> ATCC 49247	0.25 - 1	25 - 31
<i>Streptococcus pneumoniae</i> ATCC 49619	0.03 - 0.12	28 - 34
<i>Neisseria gonorrhoeae</i> ATCC 49226	0.03 - 0.12	35 - 43
<i>Staphylococcus aureus</i> ATCC 25923	1	19 - 25
<i>Staphylococcus aureus</i> ATCC 29213	1	-

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INDICATIONS AND USAGE

Cepodoxime proxetil is indicated for the treatment of patients with mild to moderate infections caused by susceptible strains of the designated microorganisms in the conditions listed below.

Recommended dosages, durations of therapy, and applicable patient populations vary among these indications. Please see DOSAGE AND ADMINISTRATION for a complete recommendation.

Acute otitis media caused by *Streptococcus pneumoniae* (excluding penicillin-resistant strains), *Streptococcus pyogenes*, *Haemophilus influenzae* (including beta-lactamase-producing strains), or *Moraxella (Branhamella) catarrhalis* (including beta-lactamase-producing strains).

Pharyngitis and/or tonsillitis caused by *Streptococcus pyogenes*.

NOTE: Only penicillin by the intramuscular route of administration has been shown to be effective in the prophylaxis of rheumatic fever. Cepodoxime proxetil is generally effective in the eradication of streptococci from the oropharynx. However, data establishing the efficacy of cepodoxime proxetil for the prophylaxis of subsequent rheumatic fever are not available.

Community-acquired pneumonia caused by *S. pneumoniae* or *H. influenzae* (including beta-lactamase-producing strains).

Acute bacterial exacerbation of chronic bronchitis caused by *S. pneumoniae*, *H. influenzae* (non-beta-lactamase-producing strains only), or *M. catarrhalis*. Data are insufficient at this time to establish efficacy in patients with acute bacterial exacerbations of chronic bronchitis caused by beta-lactamase-producing strains of *H. influenzae*.

Acute, uncomplicated urethral and cervical gonorrhea caused by *Neisseria gonorrhoeae* (including penicillinase-producing strains).

Acute, uncomplicated ano-rectal infections in women due to *Neisseria gonorrhoeae* (including penicillinase-producing strains).

NOTE: The efficacy of cepodoxime in treating male patients with rectal infections caused by *N. gonorrhoeae* has not been established. Data do not support the use of cepodoxime proxetil in the treatment of pharyngeal infections due to *N. gonorrhoeae* in men or women.

Uncomplicated skin and skin structure infections caused by *Staphylococcus aureus* (including penicillinase-producing strains) or *Streptococcus pyogenes*. Abscesses should be surgically drained as clinically indicated.

NOTE: In clinical trials, successful treatment of uncomplicated skin and skin structure infections was dose-related. The effective therapeutic dose for skin infections was higher than those used in other recommended indications. (See DOSAGE AND ADMINISTRATION.)

Acute maxillary sinusitis caused by *Haemophilus influenzae* (including beta-lactamase-producing strains), *Streptococcus pneumoniae*, and *Moraxella catarrhalis*.

Uncomplicated urinary tract infections (cystitis) caused by *Escherichia coli*, *Klebsiella pneumoniae*, *Proteus mirabilis*, or *Staphylococcus saprophyticus*.

NOTE: In considering the use of cepodoxime proxetil in the treatment of cystitis, cepodoxime proxetil's lower bacterial eradication rates should be weighed against the increased eradication rates and different safety profiles of some other classes of approved agents. (See CLINICAL STUDIES section.)

Appropriate specimens for bacteriological examination should be obtained in order to isolate and identify causative organisms and to determine their susceptibility to cepodoxime. Therapy may be instituted while awaiting the results of these studies. Once these results become available, antimicrobial therapy should be adjusted accordingly.

To reduce the development of drug-resistant bacteria and maintain the effectiveness of Cepodoxime Proxetil for Oral Suspension, USP and other antibacterial drugs, Cepodoxime Proxetil for Oral Suspension, USP should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

CONTRAINDICATIONS

Cepodoxime proxetil is contraindicated in patients with a known allergy to cepodoxime or to the cephalosporin group of antibiotics.

WARNINGS

BEFORE THERAPY WITH CEPDOXIME PROXETIL IS INSTITUTED, CAREFUL INQUIRY SHOULD BE MADE TO DETERMINE WHETHER THE PATIENT HAS HAD PREVIOUS HYPERSENSITIVITY REACTIONS TO CEPDOXIME, OTHER CEPHALOSPORINS, PENICILLINS, OR OTHER DRUGS. IF CEPDOXIME IS TO BE ADMINISTERED TO PENICILLIN SENSITIVE PATIENTS, CAUTION SHOULD BE EXERCISED BECAUSE CROSS HYPERSENSITIVITY AMONG BETA-LACTAM ANTIBIOTICS HAS BEEN CLEARLY DOCUMENTED AND MAY OCCUR IN UP TO

10% OF PATIENTS WITH A HISTORY OF PENICILLIN ALLERGY. IF AN ALLERGIC REACTION TO CEPDOXIME PROXETIL OCCURS, DISCONTINUE THE DRUG. SERIOUS ACUTE HYPERSENSITIVITY REACTIONS MAY REQUIRE TREATMENT WITH EPINEPHRINE AND OTHER EMERGENCY MEASURES, INCLUDING OXYGEN, INTRAVENOUS FLUIDS, INTRAVENOUS ANTISTAMINE, AND AIRWAY MANAGEMENT, AS CLINICALLY INDICATED.

Clostridium difficile associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, including cepodoxime proxetil for oral suspension, USP, and may range in severity from mild diarrhea to fatal colitis. Treatment with antibacterial agents alters the normal flora of the colon leading to overgrowth of *C. difficile*.

C. difficile produces toxins A and B which contribute to the development of CDAD. Hypertoxin producing strains of *C. difficile* cause increased morbidity and mortality, as these infections can be refractory to antimicrobial therapy and may require colectomy. CDAD must be considered in all patients who present with diarrhea following antibiotic use. Careful medical history is necessary since CDAD has been reported to occur over two months after the administration of antibacterial agents.

If CDAD is suspected or confirmed, ongoing antibiotic use not directed against *C. difficile* may need to be discontinued. Appropriate fluid and electrolyte management, protein supplementation, antibiotic treatment of *C. difficile*, and surgical evaluation should be instituted as clinically indicated.

A concerted effort to monitor for *C. difficile* in cepodoxime-treated patients with diarrhea was undertaken because of an increased incidence of diarrhea associated with *C. difficile* in early trials in normal subjects. *C. difficile* organisms or toxin was reported in 10% of the cepodoxime-treated adult patients with diarrhea; however, no specific diagnosis of pseudomembranous colitis was made in these patients.

In post-marketing experience outside the United States, reports of pseudomembranous colitis associated with the use of cepodoxime proxetil have been received.

PRECAUTIONS

General

In patients with transient or persistent reduction in urinary output due to renal insufficiency, the total daily dose of cepodoxime proxetil should be reduced because high and prolonged serum antibiotic concentrations can occur in such individuals following usual doses. Cepodoxime, like other cephalosporins, should be administered with caution to patients receiving concurrent treatment with potent diuretics. (See DOSAGE AND ADMINISTRATION.)

As with other antibiotics, prolonged use of cepodoxime proxetil may result in overgrowth of non-susceptible organisms. Repeated evaluation of the patient's condition is essential. If superinfection occurs during therapy, appropriate measures should be taken.

Prescribing Cepodoxime Proxetil for Oral Suspension, USP in the absence of a proven or strongly suspected bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.

Information for Patients

Patients should be counseled that antibacterial drugs including Cepodoxime Proxetil for Oral Suspension, USP should only be used to treat bacterial infections. They do not treat viral infections (e.g., the common cold). When Cepodoxime Proxetil for Oral Suspension, USP is prescribed to treat a bacterial infection, patients should be told that although it is common to feel better early in the course of therapy, the medication should be taken exactly as directed. Skipping doses or not completing the full course of therapy may (1) decrease the effectiveness of the immediate treatment and (2) increase the likelihood that bacteria will develop resistance and will not be treatable by Cepodoxime Proxetil for Oral Suspension, USP or other antibacterial drugs in the future.

Diarrhea is a common problem caused by antibiotics which usually ends when the antibiotic is discontinued. Sometimes after starting treatment with antibiotics, patients can develop watery and bloody stools (with or without stomach cramps and fever) even as late as two or more months after having taken the last dose of the antibiotic. If this occurs, patients should contact their physician as soon as possible.

Phenylketonurics

Cepodoxime proxetil for oral suspension contains phenylalanine 17 mg per 5 mL (1 teaspoonful) constituted suspension for both the 50 mg/5 mL and 100 mg/5 mL strengths.

Drug Interactions

Antacids

Concomitant administration of high doses of antacids (sodium bicarbonate and aluminum hydroxide) or H₂ blockers reduces peak plasma levels by 24% to 42% and the extent of absorption by 27% to 32%, respectively. The rate of absorption is not altered by these concomitant medications. Oral anti-cholinergics (e.g., propantheline) delay peak plasma levels (47% increase in T_{max}), but do not affect the extent of absorption (AUC).

Probenecid

As with other beta-lactam antibiotics, renal excretion of cepodoxime was inhibited by probenecid and resulted in an approximately 31% increase in AUC and 20% increase in peak cepodoxime plasma levels.

Nephrotoxic drugs

Although nephrotoxicity has not been noted when cepodoxime proxetil was given alone, close monitoring of renal function is advised when cepodoxime proxetil is administered concomitantly with compounds of known nephrotoxic potential.

Drug/Laboratory Test Interactions

Cephalosporins, including cepodoxime proxetil, are known to occasionally induce a positive direct Coombs' test.

Carcinogenesis, Mutagenesis, Impairment of Fertility

Long-term animal carcinogenesis studies of cepodoxime proxetil have not been performed.

Mutagenesis studies of cepodoxime, including the Ames test both with and without metabolic activation, the chromosome aberration test, the unscheduled DNA synthesis assay, mitotic recombination and gene conversion, the forward gene mutation assay and the *in vivo* micronucleus test, were all negative. No untoward effects on fertility or reproduction were noted when 100 mg/kg/day or less (2 times the human dose based on mg/m²) was administered orally to rats.

Pregnancy

Teratogenic Effects

Pregnancy Category B

Cepodoxime proxetil was neither teratogenic nor embryocidal when administered to rats during organogenesis at doses up to 100 mg/kg/day (2 times the human dose based on mg/m²) or to rabbits at doses up to 30 mg/kg/day (1 to 2 times the human dose based on mg/m²).

There are, however, no adequate and well-controlled studies of cepodoxime proxetil use in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Labor and Delivery

Cepodoxime proxetil has not been studied for use during labor and delivery. Treatment should only be given if clearly needed.

Nursing Mothers

Cepodoxime is excreted in human milk. In a study of 3 lactating women, levels of cepodoxime in human milk were 0%, 2% and 6% of concomitant serum levels at 4 hours following a 200 mg oral dose of cepodoxime proxetil. At 6 hours post-dosing, levels were 0%, 9% and 16% of concomitant serum levels. Because of the potential for serious reactions in nursing infants, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric Use

Safety and efficacy in infants less than 2 months of age have not been established.

Geriatric Use

Of the 3338 patients in multiple-dose clinical studies of cepodoxime proxetil film-coated tablets, 521 (16%) were 65 and over, while 214 (6%) were 75 and over. No overall differences in effectiveness or safety were observed between the elderly and younger patients. In healthy geriatric subjects with normal renal function, cepodoxime half-life in plasma averaged 4.2 hours and urinary recovery averaged 21% after a 400 mg dose was given every 12 hours for 15 days.

Other pharmacokinetic parameters were unchanged relative to those observed in healthy younger subjects.

Dose adjustment in elderly patients with normal renal function is not necessary.

ADVERSE REACTIONS

Clinical Trials

Granules for Oral Suspension (Multiple Dose)

In clinical trials using multiple doses of cepodoxime proxetil granules for oral suspension, 2128 pediatric patients (93% of whom were less than 12 years of age) were treated with the recommended dosages of cepodoxime (10 mg/kg/day

(Continued)

3. Clinical and Laboratory Standards Institute (CLSI). *Performance Standards for Antimicrobial Disk Diffusion Susceptibility Tests; Approved Standard – Eleventh Edition* CLSI document M02-A11, Clinical and Laboratory Standards Institute, 950 West Valley Road, Suite 2500, Wayne, Pennsylvania 19087, USA, 2012.

CLINICAL TRIALS**Cystitis**

In two double-blind, 2:1 randomized, comparative trials performed in adults in the United States, cefpodoxime proxetil was compared to other beta-lactam antibiotics. In these studies, the following bacterial eradication rates were obtained at 5 to 9 days after therapy:

Pathogen	Cefpodoxime	Comparator
<i>E. coli</i>	200/243 (82%)	99/123 (80%)
Other pathogens <i>K. pneumoniae</i> <i>P. mirabilis</i> <i>S. saprophyticus</i>	34/42 (81%)	23/28 (82%)
TOTAL	234/285 (82%)	122/151 (81%)

In these studies, clinical cure rates and bacterial eradication rates for cefpodoxime proxetil were comparable to the comparator agents; however, the clinical cure rates and bacteriologic eradication rates were lower than those observed with some other classes of approved agents for cystitis.

Acute Otitis Media Studies

In controlled studies of acute otitis media performed in the United States, where significant rates of beta-lactamase-producing organisms were found, cefpodoxime proxetil was compared to cefixime. In these studies, using very strict evaluability criteria and microbiologic and clinical response criteria at the 4 to 21 day post-therapy follow-up, the following presumptive bacterial eradication/clinical success outcomes (cured and improved) were obtained.

Pathogen	Cefpodoxime Proxetil 5 mg/kg Q 12 h x 5 d	Cefixime
<i>S. pneumoniae</i>	88/122 (72%)	72/124 (58%)
<i>H. influenzae</i>	50/76 (66%)	61/81 (75%)
<i>M. catarrhalis</i>	22/39 (56%)	23/41 (56%)
<i>S. pyogenes</i>	20/25 (80%)	13/23 (57%)
Clinical success rate	171/254 (67%)	165/258 (64%)

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