HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use CEFUROXIME AXETIL TABLETS safely and effectively. See full prescribing information for CEFUROXIME AXETIL TABLETS.

CEFUROXIME AXETIL tablets, for oral use

Initial U.S. Approval: 1987

DOSAGE FORMS AND STRENGTHS

Tablets: 250 mg and 500 mg (3)

CONTRAINDICATIONS

 Known hypersensitivity to cefuroxime axetil tablets or other cephalosporins (4)

WARNINGS AND PRECAUTIONS

Serious hypersensitivity (anaphylactic) reactions: In the event of a serious reaction, discontinue cefuroxime axetil tablets and institute appropriate therapy. (5.1)

Clostridium difficile-associated diarrhea (CDAD): If diarrhea occurs, evaluate patients for CDAD. (5.2)

ADVERSE REACTIONS

The most common adverse reactions (5%) for cefuroxime axetil tablets are diarrhea, nausea/vomiting, urinary-tract infection and vaginitis (early Lyme disease). (5.1)

To report SUSPECTED ADVERSE REACTIONS, contact Lupin Pharmaceuticals Inc. or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch

DRUG INTERACTIONS

Oral Contraceptives: Effects on gut flora may lower estrogen reabsorption and reduce efficacy of oral contraceptives. (7.1)

DOSAGE FORMS AND STRENGTHS

Tablets: 250 mg and 500 mg (3)

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DRUG INTERACTIONS

Oral Contraceptives: Effects on gut flora may lower estrogen reabsorption and reduce efficacy of oral contraceptives. (7.1)
2.1 Important Administration Instructions

2 DOSAGE AND ADMINISTRATION

contribute to the empiric selection of therapy. In the absence of such data, local epidemiology and susceptibility patterns may guide selection or modification of antibacterial therapy. 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.

1 INDICATIONS AND USAGE

1.2 Acute Bacterial Otitis Media

Cefuroxime axetil tablets are indicated for the treatment of pediatric patients (who can swallow tablets whole) with acute bacterial otitis media caused by susceptible strains of Streptococcus pneumoniae, Haemophilus influenzae (including β-lactamase–producing strains), Moraxella catarrhalis (including β-lactamase–producing strains), or Strepococcus pyogenes.

1.3 Acute Bacterial Maxillary Sinusitis

Cefuroxime axetil tablets are indicated for the treatment of adult and pediatric patients (13 years and older) with mild-to-moderate acute bacterial maxillary sinusitis caused by susceptible strains of Streptococcus pneumoniae or Haemophilus influenzae (non-β-lactamase–producing strains only).

1.4 Acute Bacterial Exacerbations of Chronic Bronchitis

Cefuroxime axetil tablets are indicated for the treatment of adult patients and pediatric patients (aged 13 years and older) with mild-to-moderate acute bacterial exacerbations of chronic bronchitis caused by susceptible strains of Streptococcus pneumoniae, Haemophilus influenzae (β-lactamase–producing strains), or Streptococcus pyogenes.

1.5 Uncomplicated Skin and Skin-Structure Infections

Cefuroxime axetil tablets are indicated for the treatment of adult patients and pediatric patients (aged 13 years and older) with uncomplicated skin and skin-structure infections caused by susceptible strains of Staphylococcus aureus (including β-lactamase–producing strains) or Streptococcus pyogenes.

1.6 Uncomplicated Urinary Tract Infections

Cefuroxime axetil tablets are indicated for the treatment of adult patients and pediatric patients (aged 13 years and older) with uncomplicated urinary tract infections caused by susceptible strains of Escherichia coli or Klebsiella pneumoniae.

1.7 Uncomplicated Gonorrhea

Cefuroxime axetil tablets are indicated for the treatment of adult patients and pediatric patients (aged 13 years and older) with uncomplicated gonorrhea, urethral and endocervical, caused by penicillinase producing and non-penicillinase–producing susceptible strains of Neisseria gonorrhoeae and uncomplicated gonorrhea, rectal, in females, caused by non-penicillinase–producing susceptible strains of Neisseria gonorrhoeae.

1.8 Early Lyme Disease (erythema migrans)

Cefuroxime axetil tablets are indicated for the treatment of adult patients and pediatric patients (aged 13 years and older) with early Lyme disease (erythema migrans) caused by susceptible strain of Borrelia burgdorferi.

1.10 Usage

To reduce the development of drug-resistant bacteria and maintain the effectiveness of cefuroxime axetil and other antibacterial drugs, cefuroxime axetil 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.

11 DESCRIPTION

2.1 Important Administration Instructions

• Cefuroxime axetil tablets and cefuroxime axetil for oral suspension are not bioequivalent and are therefore not substitutable on a milligram-per-milligram basis (see CLINICAL PHARMACOLOGY (12.3)).

• Administer cefuroxime axetil tablets as described in the appropriate dosage guidelines (see DOSAGE AND ADMINISTRATION (2.2)).

• Administer cefuroxime axetil tablets with or without food.
Pediatric patients (aged 13 years and older) who cannot swallow the cefuroxime axetil tablets whole should receive cefuroxime axetil for oral suspension because the tablet has a strong, persistent bitter taste when crushed [see DOSAGE AND ADMINISTRATION (2.2)].

2.2 Dosage for Cefuroxime Axetil Tablets

Administer cefuroxime axetil tablets as described in the dosage guidelines table below with or without food.

### Table 1. Adult Patients and Pediatric Patients Dosage Guidelines for Cefuroxime Axetil Tablets

<table>
<thead>
<tr>
<th>Infection</th>
<th>Dosage</th>
<th>Duration (Days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults and Adolescents (13 years and older)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pharyngitis/tonsillitis (mild to moderate)</td>
<td>250 mg every 12 hours</td>
<td>10</td>
</tr>
<tr>
<td>Acute bacterial maxillary sinusitis (mild to moderate)</td>
<td>250 mg every 12 hours</td>
<td>10</td>
</tr>
<tr>
<td>Acute bacterial exacerbation of chronic bronchitis (mild to moderate)</td>
<td>250 or 500 mg every 12 hours</td>
<td>10*</td>
</tr>
<tr>
<td>Uncomplicated skin and skin-structure infections</td>
<td>250 or 500 mg every 12 hours</td>
<td>10</td>
</tr>
<tr>
<td>Uncomplicated urinary tract infection</td>
<td>250 mg every 12 hours</td>
<td>10</td>
</tr>
<tr>
<td>Uncomplicated gonorrhea</td>
<td>1,000 mg</td>
<td>single dose</td>
</tr>
<tr>
<td>Early Lyme disease</td>
<td>500 mg every 12 hours</td>
<td>20</td>
</tr>
<tr>
<td>Pediatric Patients younger than 13 years (who can swallow tablets whole)†</td>
<td>250 mg every 12 hours</td>
<td>10</td>
</tr>
<tr>
<td>Acute bacterial otitis media</td>
<td>250 mg every 12 hours</td>
<td>10</td>
</tr>
<tr>
<td>Acute bacterial maxillary sinusitis</td>
<td>250 mg every 12 hours</td>
<td>10</td>
</tr>
</tbody>
</table>

* The safety and effectiveness of cefuroxime axetil administered for less than 10 days in patients with acute exacerbations of chronic bronchitis have not been established.

† When crushed, the tablet has a strong, persistent bitter taste. Therefore, patients who cannot swallow the tablet whole should receive the oral suspension.

2.5 Dosage in Patients with Impaired Renal Function

A dosage interval adjustment is required for patients whose creatinine clearance is less than 30 mL/min, as listed in Table 4 below, because cefuroxime is eliminated primarily by the kidney [see CLINICAL PHARMACOLOGY (12.3)].

### Table 4. Dosing in Adults with Renal Impairment

<table>
<thead>
<tr>
<th>Creatinine Clearance (mL/min)</th>
<th>Recommended Dosage</th>
<th>Dosage</th>
<th>Duration (Days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;30</td>
<td>No dosage adjustment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10 to 30</td>
<td>Standard individual dose given every 24 hours</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10 (without hemodialysis)</td>
<td>Standard individual dose given every 48 hours</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hemodialysis</td>
<td>A single additional standard dose should be given at the end of each dialysis</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

3 DOSAGE FORMS AND STRENGTHS

Cefuroxime axetil tablets USP are off-white, capsule-shaped, film-coated tablets available in the following strengths:
- 250 mg of cefuroxime (as cefuroxime axetil) are white to off-white, capsule-shaped, film-coated tablets with “LUPIN” debossed on one side and “301” on the other side.
- 500 mg of cefuroxime (as cefuroxime axetil) are white to off-white, capsule-shaped, film-coated tablets with “LUPIN” debossed on one side and “302” on the other side.

4 CONTRAINDICATIONS

Cefuroxime axetil is contraindicated in patients with a known hypersensitivity (e.g., anaphylaxis) to cefuroxime axetil or to other β-lactam antibacterial drugs (e.g., penicillin and cephalosporin).

5 WARNINGS AND PRECAUTIONS

5.1 Anaphylactic Reactions

Serious and occasionally fatal hypersensitivity (anaphylactic) reactions have been reported in patients on β-lactam antibacterials. These reactions are more likely to occur in individuals with a history of β-lactam hypersensitivity and/or a history of sensitivity to multiple allergens. There have been reports of individuals with a history of penicillin hypersensitivity who have experienced severe reactions when treated with cephalosporins. Cefuroxime axetil is contraindicated in patients with a known hypersensitivity to cefuroxime axetil or other β-lactam antibacterial drugs (see CONTRAINDICATIONS (4)). Before initiating therapy with cefuroxime axetil, inquire about previous hypersensitivity reactions to penicillin, cephalosporin, or other allergens. If an allergic reaction occurs, discontinue cefuroxime axetil and institute appropriate therapy.

5.2 Clostridium difficile-Associated Diarrhea

Clostridium difficile-associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, including cefuroxime axetil, 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. Hypersensitivity 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 antibacterial use. Careful medical history is necessary since CDAD has been reported to occur over 2 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.

5.3 Potential for Microbial Overgrowth

The possibility of superinfections with fungal or bacterial pathogens should be considered during therapy.

5.4 Development of Drug-Resistant Bacteria

Prescribing cefuroxime axetil either 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.

5.6 Interference with Glucose Tests

A false-positive result for glucose in the urine may occur with copper reduction tests, and a false-negative result for blood/plasma glucose may occur with ferricyanide tests in subjects receiving cefuroxime axetil [see DRUG INTERACTIONS (7.4)].

6 ADVERSE REACTIONS

The following serious and otherwise important adverse reactions is described in greater detail in the Warnings and Precautions section of the label:

Anaphylactic Reactions [see WARNINGS AND PRECAUTIONS (5.1)]
6.1 Clinical Trials Experience
Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared with rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Tablets
Multiple-Dose Dosing Regimens with 7 to 10 Days’ Duration: In multiple-dose clinical trials, 912 subjects were treated with cefuroxime axetil (125 to 500 mg twice daily). It is noted that 125 mg twice daily is not an approved dosage. Twenty (2.2%) subjects discontinued medication due to adverse reactions. Seventeen (85%) of the 20 subjects who discontinued therapy did so because of gastrointestinal disturbances, including diarrhea, nausea, vomiting, and abdominal pain. The percentage of subjects treated with cefuroxime axetil who discontinued study drug because of adverse reactions was similar at daily doses of 1,000, 500, and 250 mg (2.3%, 2.1%, and 2.2%, respectively). However, the incidence of gastrointestinal adverse reactions increased with the higher recommended doses.

The adverse reactions in Table 5 are for subjects (n = 912) treated with cefuroxime axetil in multiple-dose clinical trials.

Table 5. Adverse Reactions (≥1%) after Multiple-Dose Regimens with Cefuroxime Axetil Tablets

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>Cefuroxime Axetil Tablets (n = 912)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood and lymphatic system disorders</td>
<td></td>
</tr>
<tr>
<td>Eosinophilia</td>
<td>1%</td>
</tr>
<tr>
<td>Gastrointestinal disorders</td>
<td></td>
</tr>
<tr>
<td>Diarrhea</td>
<td>4%</td>
</tr>
<tr>
<td>Nausea/Vomiting</td>
<td>3%</td>
</tr>
<tr>
<td>Investigations</td>
<td></td>
</tr>
<tr>
<td>Transient elevation in AST</td>
<td>2%</td>
</tr>
<tr>
<td>Transient elevation in ALT</td>
<td>2%</td>
</tr>
<tr>
<td>Transient elevation in LDH</td>
<td>1%</td>
</tr>
</tbody>
</table>

The following adverse reactions occurred in less than 1% but greater than 0.1% of subjects (n = 912) treated with cefuroxime axetil in multiple-dose clinical trials.

Immune System Disorders: Hives, swollen tongue.
Metabolism and Nutrition Disorders: Anorexia.
Nervous System Disorders: Headache.
Cardiac Disorders: Chest pain.
Respiratory Disorders: Shortness of breath.
Gastrointestinal Disorders: Abdominal pain, abdominal cramps, flatulence, indigestion, mouth ulcers.
Skin and Subcutaneous Tissue Disorders: Rash, itch.
Renal and Urinary Disorders: Dysuria.
Reproductive and Breast Disorders: Vaginitis, vulvar itch.
General Disorders and Administration Site Conditions: Chills, sleepiness, thirst.
Investigations: Positive Coombs’ test.

Early Lyme Disease with 20-Day Regimen: Two multicenter trials assessed cefuroxime axetil tablets 500 mg twice daily for 20 days. The most common drug-related adverse experiences were diarrhea (10.6%), Jarisch-Herxheimer reaction (5.6%), and vaginitis (5.4%). Other adverse experiences occurred with frequencies comparable to those reported with 7 to 10 days’ dosing.

Single-Dose Regimen for Uncomplicated Gonorrhea: In clinical trials using a single 1,000-mg dose of cefuroxime axetil tablets, 1,061 subjects were treated for uncomplicated gonorrhea. The adverse reactions in Table 6 were for subjects treated with a single dose of 1,000 mg cefuroxime axetil tablets in U.S. clinical trials.

Table 6. Adverse Reactions (≥1%) after Single-Dose Regimen with 1,000-mg Cefuroxime Axetil Tablets for Uncomplicated Gonorrhea

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>Cefuroxime Axetil Tablets (n = 1,061)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastrointestinal disorders</td>
<td></td>
</tr>
<tr>
<td>Nausea/Vomiting</td>
<td>7%</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>4%</td>
</tr>
</tbody>
</table>

The following adverse reactions occurred in less than 1% but greater than 0.1% of subjects (n = 1,061) treated with a single dose of cefuroxime axetil tablets 1,000 mg for uncomplicated gonorrhoea in U.S. clinical trials.

Infections and Infestations: Vaginal candidiasis.
Nervous System Disorders: Headache, dizziness, somnolence.
Cardiac Disorders: Tightness/pain in chest, tachycardia.
Gastrointestinal Disorders: Abdominal pain, dyspepsia.
Skin and Subcutaneous Tissue Disorders: Erythema, rash, pruritus.
Musculoskeletal and Connective Tissue Disorders: Muscle cramps, muscle stiffness, muscle spasm of neck, lockjaw-type reaction.
Renal and Urinary Disorders: Bleeding/pain in urethra, kidney pain.
Reproductive System and Breast Disorders: Vaginal itch, vaginal discharge.

6.2 Postmarketing Experience
The following adverse reactions have been identified during post-approval use of cefuroxime axetil. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Blood and Lymphatic System Disorders
Hemolytic anemia, leukopenia, pancytopenia, thrombocytopenia.
Gastrointestinal Disorders
Pseudomembranous colitis [see WARNINGS AND PRECAUTIONS (5.2)]
Hepatobiliary Disorders
Hepatic impairment including hepatitis and cholestasis, jaundice.
Immunologic System Disorders
Anaphylaxis, serum sickness-like reaction.
Investigations
Increased prothrombin time.
Nervous System Disorders
Cefuroxime axetil is in the amorphous form and has the following structural formula: $\text{RS}-7-[\text{Z}(-)\text{-methyl-oxime}], 1\text{-acetate 3-carbamate}$. Its molecular formula is $\text{C}_{30}\text{H}_{27}\text{N}_{2}\text{O}_{5}\text{S}$, and it has a molecular weight of 510.48.

7 DESCRIPTION

Cefuroxime axetil tablets USP contain cefuroxime as cefuroxime axetil. Cefuroxime axetil is a semisynthetic, cephalosporin antibacterial drug for oral administration. The chemical name of cefuroxime axetil (1-(acetyloxy) ethyl ester of cefuroxime) is (RS)-1-hydroxyethyl (8R,7R)-7-[2-(2-furyl)glyoxyl-amido]-3-(hydroxymethyl)-8-oxo-5-thia-1-azabicyclo[4.2.0]-oct-2-ene-2-carboxylate, 7-hydroxyethyl (6R)-7-$\text{RS}$-$\text{Z}$-methyl-oxime, 1-acetate 3-carbamate. Its molecular formula is $\text{C}_{30}\text{H}_{27}\text{N}_{2}\text{O}_{5}\text{S}$, and it has a molecular weight of 510.48.

Cefuroxime axetil is in the amorphous form and has the following structural formula:
Cefuroxime axetil tablets USP are film-coated and contain the equivalent of 250 or 500 mg of cefuroxime as cefuroxime axetil. Cefuroxime axetil tablets USP contain the inactive ingredients: colloidal silicon dioxide, croscarmellose sodium, hydroxypropyl cellulose, microcrystalline cellulose, propylparaben, polyethylene glycol, sodium lauryl sulfate, talc and titanium dioxide.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action
Cefuroxime axetil is an antibacterial drug [see CLINICAL PHARMACOLOGY (12.4)].

12.3 Pharmacokinetics

Absorption
After oral administration, cefuroxime axetil is absorbed from the gastrointestinal tract and rapidly hydrolyzed by nonspecific esterases in the intestinal mucosa and blood to cefuroxime. Serum pharmacokinetic parameters for cefuroxime following administration of cefuroxime axetil tablets to adults are shown in Table 8.

<table>
<thead>
<tr>
<th>Dose (mg)</th>
<th>Peak Plasma Concentration (mcg/mL)</th>
<th>Time of Peak (h)</th>
<th>Mean Elimination Half-life (h)</th>
<th>AUC (mcg·h/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>125 mg</td>
<td>2.1</td>
<td>2.2</td>
<td>1.2</td>
<td>50.0</td>
</tr>
<tr>
<td>250 mg</td>
<td>4.1</td>
<td>2.5</td>
<td>1.2</td>
<td>12.9</td>
</tr>
<tr>
<td>500 mg</td>
<td>7.0</td>
<td>3.0</td>
<td>1.2</td>
<td>27.4</td>
</tr>
<tr>
<td>1,000 mg</td>
<td>13.6</td>
<td>2.5</td>
<td>1.3</td>
<td>50.0</td>
</tr>
</tbody>
</table>

* Mean values of 12 healthy adult volunteers.
† Drug administered immediately after a meal.

Food Effect: Absorption of the tablet is greater when taken after food (absolute bioavailability increases from 37% to 52%). Despite this difference in absorption, the clinical and bacteriologic responses of subjects were independent of food intake at the time of tablet administration in 2 trials where this was assessed.

All pharmacokinetic and clinical effectiveness and safety trials in pediatric subjects using the suspension formulation were conducted in the fed state. No data are available on the absorption kinetics of the suspension formulation when administered to fasted pediatric subjects.

Loss of Bioequivalence: Oral suspension was not bioequivalent to tablets when tested in healthy adults. The tablet and oral suspension formulations are NOT substitutable on a milligram-per-milligram basis. The area under the curve for the suspension averaged 91% of that for the tablet, and the peak plasma concentration for the suspension averaged 71% of the peak plasma concentration of the tablet. Therefore, the safety and effectiveness of both the tablet and oral suspension formulations were established in separate clinical trials.

Distribution
Cefuroxime is distributed throughout the extracellular fluids. Approximately 50% of serum cefuroxime is bound to protein.

Metabolism
The axetil moiety is metabolized to acetaldehyde and acetic acid.

Excretion
Cefuroxime is excreted unchanged in the urine; in adults, approximately 50% of the administered dose is recovered in the urine within 12 hours. The pharmacokinetics of cefuroxime in pediatric subjects have not been studied. Until further data are available, the renal elimination of cefuroxime axetil established in adults should not be extrapolated to pediatric subjects.

Specific Populations

Renal Impairment: In a trial of 28 adults with normal renal function or severe renal impairment (creatinine clearance <30 mL/min), the elimination half-life was prolonged in relation to severity of renal impairment. Prolongation of the dosage interval is recommended in adult patients with creatinine clearance <30 mL/min [see DOSAGE AND ADMINISTRATION (2.5)].

Geriatric Patients: In a trial of 20 elderly subjects (mean age = 83.9 years) having a mean creatinine clearance of 34.9 mL/min, the mean serum elimination half-life was prolonged to 3.5 hours; however, despite the lower elimination of cefuroxime in geriatric patients, dosage adjustment based on age is not necessary [see USE IN SPECIFIC POPULATIONS (8.5)].

Drug Interactions
Concomitant administration of probenecid with cefuroxime axetil tablets increases the cefuroxime area under the serum concentration versus time curve and maximum serum concentration by 50% and 21%, respectively.

12.4 Microbiology

Mechanism of Action
Cefuroxime axetil is a bactericidal agent that acts by inhibition of bacterial cell wall synthesis. Cefuroxime axetil has activity in the presence of some β-lactamases, both penicillinases and cephalosporinases, of gram-negative and gram-positive bacteria.

Mechanism of Resistance
Resistance to cefuroxime axetil is primarily through hydrolysis by β-lactamase, alteration of penicillin-binding protein (PBPs), decreased permeability, and the presence of bacterial efflux pumps.

Susceptibility to cefuroxime axetil will vary with geography and time; local susceptibility data should be consulted, if available. Beta-lactamase-negative, ampicillin-resistant (BLNAR) isolates of H. influenzae should be considered resistant to cefuroxime axetil.

Cefuroxime axetil has been shown to be active against most isolates of the following bacteria, both in
### Susceptibility Test Methods

When available, the clinical microbiology laboratory should provide the results of in vitro susceptibility tests for antimicrobial drug products used in local hospitals and practice areas 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.

**Dilution Techniques:** Quantitative methods are used to determine antimicrobial MICs. These MICs provide reproducible estimates of the susceptibility of bacteria to antimicrobial compounds. The MICs should be determined using a standardized test method (broth or agar). The MIC values should be interpreted according to criteria provided in Table 10.

**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. This procedure uses paper disks impregnated with 30 mcg cefuroxime axetil to test the susceptibility of microorganisms to cefuroxime axetil. The disk diffusion interpretive criteria are provided in Table 10.

### Table 10. Susceptibility Test Interpretive Criteria for Cefuroxime Axetil

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Minimum Inhibitory Concentrations (mcg/mL)</th>
<th>Disk Diffusion Zone Diameters (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Susceptible</td>
<td>Intermediate</td>
</tr>
<tr>
<td>Enteroxacteriaceae</td>
<td>≤4</td>
<td>8 to 16</td>
</tr>
<tr>
<td>Haemophilus spp.</td>
<td>≤4</td>
<td>8</td>
</tr>
<tr>
<td>Moraxella catarrhalis</td>
<td>≤4</td>
<td>8</td>
</tr>
<tr>
<td>Streptococcus pneumonia</td>
<td>≤1</td>
<td>2</td>
</tr>
</tbody>
</table>

* For Enteroxacteriaceae, Haemophilus spp., and Moraxella catarrhalis, susceptibility interpretive criteria are based on a dose of 500 mg every 12 hours in patients with normal renal function.

### Susceptibility of Staphylococcus to Cefuroxime
Susceptibility of Staphylococcus to cefuroxime may be deduced from testing penicillin and either cefoxitin or oxacillin.

### Susceptibility of Streptococcus Pyogenes
Susceptibility of Streptococcus pyogenes may be deduced from testing penicillin.

A report of “Susceptible” indicates that the antimicrobial drug is likely to inhibit growth of the pathogen if the antimicrobial drug reaches the concentration usually achievable at the site of infection. 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 drug is not likely to inhibit growth of the pathogen if the antimicrobial drug reaches the concentration 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. The QC ranges for MIC and disk diffusion testing using the 30 mcg disk are provided in Table 11.

### Table 11. Acceptable Quality Control (QC) Ranges for Cefuroxime Axetil

<table>
<thead>
<tr>
<th>QC Strain</th>
<th>Minimum Inhibitory Concentrations (mcg/mL)</th>
<th>Disk Diffusion Zone Diameters (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Escherichia coli ATCC 25922</td>
<td>2 to 8</td>
<td>20 to 26</td>
</tr>
<tr>
<td>Staphylococcus aureus ATCC 25923</td>
<td>5 to 2</td>
<td>27 to 35</td>
</tr>
<tr>
<td>Staphylococcus aurum ATCC 259213</td>
<td>0.25 to 1</td>
<td>-</td>
</tr>
<tr>
<td>Haemophilus influenzae ATCC 49766</td>
<td>0.25 to 1</td>
<td>28 to 36</td>
</tr>
<tr>
<td>Neisseria gonorrhoea ATCC 49226</td>
<td>0.25 to 1</td>
<td>33 to 41</td>
</tr>
</tbody>
</table>
14 CLINICAL STUDIES

14.1 Acute Bacterial Maxillary Sinusitis

One adequate and well-controlled trial was performed in subjects with acute bacterial maxillary sinusitis. In this trial, each subject had a maxillary sinus aspirate collected by sinus puncture before treatment was initiated for presumptive acute bacterial sinusitis. All subjects had radiographic and clinical evidence of acute maxillary sinusitis. In the trial, the clinical effectiveness of cefuroxime axetil in treating acute maxillary sinusitis was comparable to an oral antimicrobial agent containing a specific β-lactamase inhibitor. However, microbiology data demonstrated cefuroxime axetil to be effective in treating acute bacterial maxillary sinusitis due to Streptococcus pneumoniae or non-β-lactamase–producing Haemophilus influenzae. Insufficient numbers of β-lactamase–producing Haemophilus influenzae and Moraxella catarrhalis isolates were obtained in this trial to adequately evaluate the effectiveness of cefuroxime axetil in treating acute bacterial maxillary sinusitis due to these 2 organisms.

This trial randomized 317 adult subjects, 132 subjects in the U. S. and 185 subjects in South America. Table 12 shows the results of the intent-to-treat analysis.

### Table 12. Clinical Effectiveness of Cefuroxime Axetil Tablets in the Treatment of Acute Bacterial Maxillary Sinusitis

<table>
<thead>
<tr>
<th>U.S. Subjects†</th>
<th>South American Subjects‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cefuroxime Axetil Tablets 250 mg Twice Daily(Control) (n = 49)</td>
<td>Cefuroxime Axetil Tablets 250 mg Twice Daily(Control) (n = 49)</td>
</tr>
<tr>
<td>Clinical success (cure + improvement)</td>
<td>65%</td>
</tr>
<tr>
<td>Clinical cure</td>
<td>53%</td>
</tr>
<tr>
<td>Clinical improvement</td>
<td>12%</td>
</tr>
</tbody>
</table>

* 95% confidence interval around the success difference [-0.08, +0.32].
† 95% confidence interval around the success difference [-0.10, +0.16].

In this trial and in a supporting maxillary puncture trial, 15 evaluable subjects had non-β-lactamase–producing Haemophilus influenzae as the identified pathogen. Of these, 67% (10/15) had this pathogen eradicated. Eighteen (18) evaluable subjects had Streptococcus pneumoniae as the identified pathogen. Of these, 83% (15/18) had this pathogen eradicated.

14.2 Early Lyme Disease

Two adequate and well-controlled trials were performed in subjects with early Lyme disease. All subjects presented with physician-documented erythema migrans, with or without systemic manifestations of infection. Subjects were assessed at 1 month posttreatment for success in treating early Lyme disease (Part I) and at 1 year posttreatment for success in preventing the progression to the sequelae of late Lyme disease (Part II).

A total of 355 adult subjects (181 treated with cefuroxime axetil and 174 treated with doxycycline) were randomized in the 2 trials, with diagnosis of early Lyme disease confirmed in 79% (281/355). The clinical and laboratory data reflected the entire patient population for the 2 trials. Clinical data for evaluable subjects in the “validated” patient subset are shown in Table 13.

#### Table 13. Clinical Effectiveness of Cefuroxime Axetil Tablets Compared with Doxycycline in the Treatment of Early Lyme Disease

<table>
<thead>
<tr>
<th>Part I</th>
<th>(1 Month after 20 Days of Treatment)</th>
<th>Part II</th>
<th>(1 Year after 20 Days of Treatment)†</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cefuroxime Axetil Tablets 500 mg Twice Daily/Doxycycline 100 mg 3 Times Daily (n = 125)</td>
<td>Cefuroxime Axetil Tablets 500 mg Twice Daily/Doxycycline 100 mg 3 Times Daily (n = 105)</td>
<td></td>
</tr>
<tr>
<td>Satisfactory clinical outcome§</td>
<td>91%</td>
<td>93%</td>
<td>84%</td>
</tr>
<tr>
<td>Clinical cure/success</td>
<td>72%</td>
<td>73%</td>
<td>75%</td>
</tr>
<tr>
<td>Clinical improvement</td>
<td>19%</td>
<td>19%</td>
<td>10%</td>
</tr>
</tbody>
</table>

* 95% confidence interval around the satisfactory difference [-0.08, +0.65].
† 95% confidence interval around the satisfactory difference for Part II (-0.13, +0.07).
§ Satisfactory clinical outcome includes cure + improvement (Part I) and success + improvement (Part II).

Cefuroxime axetil and doxycycline were effective in prevention of the development of sequelae of late Lyme disease.

While the incidence of drug-related gastrointestinal adverse reactions was similar in the 2 treatment groups (cefuroxime axetil - 13%; doxycycline - 11%), the incidence of drug-related diarrhea was higher in the cefuroxime axetil arm versus the doxycycline arm (11% versus 3%, respectively).

15 REFERENCES

3. Clinical and Laboratory Standards Institute (CLSI). Performance Standards for Antimicrobial Susceptibility Testing; Twenty-Fifth Informational Supplement. 2015. CLSI document M100-S25, Clinical and Laboratory Standards Institute, 950 West Valley Road, Suite 2500, Wayne, Pennsylvania 19087, USA.
16 HOW SUPPLIED/STORAGE AND HANDLING
Cefuroxime axetil tablets USP, 250 mg of cefuroxime (as cefuroxime axetil), are white to off-white, capsule-shaped, film-coated tablets with “LUPIN” debossed on one side and “302” on the other side, supplied in bottles of 20 and 60.
20s Bottle NDC 68180-302-20
60s Bottle NDC 68180-302-60
Cefuroxime axetil tablets USP, 500 mg of cefuroxime (as cefuroxime axetil), are white to off-white, capsule-shaped, film-coated tablets with “LUPIN” debossed on one side and “303” on the other side, supplied in bottles of 20 and 60.
20s Bottle NDC 68180-303-20
60s Bottle NDC 68180-303-60
Store the tablets at 20 to 25°C (68 to 77°F) [See USP Controlled Room Temperature]. Replace cap securely after each opening.

17 PATIENT COUNSELING INFORMATION

Allergic Reactions
Inform patients that cefuroxime axetil is a cephalosporin that can cause allergic reactions in some individuals [see WARNINGS AND PRECAUTIONS (5.1)].

Clostridium difficile-Associated Diarrhea
Inform patients that diarrhea is a common problem caused by antibacterials, and it usually ends when the antibacterial is discontinued. Sometimes after starting treatment with antibacterials, patients can develop watery and bloody stools (with or without stomach cramps and fever) even as late as 2 or more months after having taken the last dose of the antibacterial. If this occurs, advise patients to contact their physician as soon as possible.

Crushing Tablets
Instruct patients to swallow the tablet whole, without crushing the tablet. Patients who cannot swallow the tablet whole should receive the oral suspension.

Drug Resistance
Inform patients that antibacterial drugs, including cefuroxime axetil, should only be used to treat bacterial infections. They do not treat viral infections (e.g., the common cold). When cefuroxime axetil is prescribed to treat a bacterial infection, inform patients 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 cefuroxime axetil or other antibacterial drugs in the future.

Manufactured for:
Lupin Pharmaceuticals, Inc.
Baltimore, Maryland 21202
United States.
Manufactured by:
Lupin Limited
Mandideep 462 046
INDIA.
Revised: January 2018
ID#:254015
Cefuroxime Axetil Tablets USP, 250 mg
Bottle of 20s
NDC 68180-302-20

Cefuroxime Axetil Tablets USP, 500 mg
Bottle of 20s
NDC 68180-303-20
**Route of Administration**

ORAL

**Active Ingredient/Active Moiety**

<table>
<thead>
<tr>
<th>Ingredient Name</th>
<th>Basis of Strength</th>
<th>Strength</th>
</tr>
</thead>
<tbody>
<tr>
<td>CEFUROXIME AXETIL (UNII: Z49QDT0J8Z) (CEFUROXIME - UNII:O1R9FJ93ED)</td>
<td>CEFUROXIME</td>
<td>250 mg</td>
</tr>
</tbody>
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**Inactive Ingredients**

<table>
<thead>
<tr>
<th>Ingredient Name</th>
<th>Strength</th>
</tr>
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<tbody>
<tr>
<td>CELULLOSE, MICROCRYSTALLINE (UNII: OP1R32D61U)</td>
<td></td>
</tr>
<tr>
<td>CROSCARMELLOSE SODIUM (UNII: MDGOL18468)</td>
<td></td>
</tr>
<tr>
<td>HYROMELLOSE 1918 (5 MPA.S) (UNII: 36SGP6210W)</td>
<td></td>
</tr>
<tr>
<td>HYROMELLOSE 1918 (5 MPA.S) (UNII: 875577171T)</td>
<td></td>
</tr>
<tr>
<td>POLYETHYLENE GLYCOL 4000 (UNII: R868R82K15)</td>
<td></td>
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<td>PROPYLGLYCOL (UNII: 6DC9Q167V3)</td>
<td></td>
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<tr>
<td>SILICON DIOXIDE (UNII: ETJ7Z6XBU4)</td>
<td></td>
</tr>
<tr>
<td>SODIUM LAURYL SULFATE (UNII: 368GB5141J)</td>
<td></td>
</tr>
<tr>
<td>TALC (UNII: 7SEV7J4R1U)</td>
<td></td>
</tr>
<tr>
<td>TITANIUM DIOXIDE (UNII: 15FIX9V2JP)</td>
<td></td>
</tr>
</tbody>
</table>

**Product Characteristics**

- **Color**: WHITE (white to off white)
- **Shape**: OVAL (capsule shaped)
- **Size**: 15mm
- **Flavor**: Imprint Code: LUPIN;302

**Packaging**

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<tr>
<th>#</th>
<th>Item Code</th>
<th>Package Description</th>
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<th>Marketing End Date</th>
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<tr>
<td>1</td>
<td>NDC:68180-302-20</td>
<td>20 in 1 BOTTLE; Type 0: Not a Combination Product</td>
<td>07/25/2003</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>NDC:68180-302-60</td>
<td>60 in 1 BOTTLE; Type 0: Not a Combination Product</td>
<td>07/25/2003</td>
<td></td>
</tr>
</tbody>
</table>

**Marketing Information**

<table>
<thead>
<tr>
<th>Marketing Category</th>
<th>Application Number or Monograph Citation</th>
<th>Marketing Start Date</th>
<th>Marketing End Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>ANDA</td>
<td>ANDA065135</td>
<td>07/25/2003</td>
<td></td>
</tr>
</tbody>
</table>