CEFUROXIME AXETIL- cefuroxime axetil tablet
Lupin Pharmaceuticals, Inc.

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

RECENT MAJOR CHANGES

Indications and Usage, Acute Bacterial Exacerbations
of Chronic Bronchitis and Secondary Bacterial Infections
of Acute Bronchitis: Secondary Bacterial Infections of Acute Bronchitis
11/2016

Dosage and Administration, Dosage for CEFTIN Tablets:
Secondary Bacterial Infections of Acute Bronchitis
11/2016

INDICATIONS AND USAGE
Cefuroxime axetil tablets are a cephalosporin antibacterial drug indicated for the treatment of the following infections due to susceptible bacteria:

- Pharyngitis/tonsillitis (adults and pediatric patients 13 years and older)
- Acute bacterial maxillary sinusitis (adults and pediatric patients 13 years and older)
- Acute bacterial exacerbations of chronic bronchitis (adults and pediatric patients 13 years and older)
- Uncomplicated skin and skin-structure infections (adults and pediatric patients 13 years and older)
- Uncomplicated urinary tract infections (adults and pediatric patients 13 years and older)
- Uncomplicated gonorrhea (adults and pediatric patients 13 years and older)
- Early Lyme disease (adults and pediatric patients 13 years and older)

To reduce the development of drug-resistant bacteria and maintain the effectiveness of cefuroxime axetil tablets and other antibacterial drugs, cefuroxime axetil tablets should be used only to treat or prevent infections that are proven or strongly suspected to be caused by bacteria.

CONTRAINDICATIONS
- Oral contraceptives: Effects on gut flora may lower estrogen reabsorption and reduce efficacy of oral contraceptives.
- Drugs that reduce gastric acidity: May lower the exposure to cefuroxime axetil tablets and other antibacterial drugs.

WARNINGS AND PRECAUTIONS
- Serum hyperosmolality (hypernatremia): In the event of a serious reaction, discontinue cefuroxime axetil tablets and institute appropriate therapy.
- Clostridium difficile-associated diarrhea (CDAD): If diarrhea occurs, evaluate patients for CDAD.

ADVERSE REACTIONS
- The most common adverse reactions (≥3%) for cefuroxime axetil tablets are diarrhea, nausea/vomiting, lichen planus-like reactions and vaginitis.

Dosage and Administration

Dosage adjustment is required for patients with impaired renal function. Administer cefuroxime axetil tablets as described in the dosage guidelines.

DOSAGE FORMS AND STRENGTHS
Tablets: 250 mg and 500 mg.

Table: Adults: 250 mg every 12 hours

Acute bacterial maxillary sinusitis (mild to moderate) 250 mg every 12 hours
10
Acute bacterial exacerbation of chronic bronchitis (mild to moderate) 250 mg every 12 hours
10
Uncomplicated skin and skin-structure infections 250 or 500 mg every 12 hours
10
Uncomplicated urinary tract infections 250 mg every 12 hours
7 to 10
Uncomplicated gonorrhea 1,000 mg single dose
20
Early Lyme disease 500 mg every 12 hours

Pediatric Patients younger than 13 years (who can swallow tablets whole)
Acute bacterial otitis media 250 mg every 12 hours

Acute bacterial maxillary sinusitis 250 mg every 12 hours

DOSAGE FORMS AND STRENGTHS

Tablets: 250 mg and 500 mg (3)

CONTRAINDICATIONS

Known hypersensitivity (e.g., anaphylaxis) to cefuroxime axetil tablets or other cephalosporins.

WARNINGS AND PRECAUTIONS

- Serum hyperosmolality (hypernatremia): In the event of a serious reaction, discontinue cefuroxime axetil tablets and institute appropriate therapy.
- Clostridium difficile-associated diarrhea (CDAD): If diarrhea occurs, evaluate patients for CDAD.

ADVERSE REACTIONS

The most common adverse reactions (≥3%) for cefuroxime axetil tablets are diarrhea, nausea/vomiting, lichen planus-like reactions and vaginitis.

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 12/2018

FULL PRESCRIBING INFORMATION: CONTENTS*

1 INDICATIONS AND USAGE
1.1 Pharyngitis/Tonsillitis
1.2 Acute Bacterial Otitis Media
1.3 Acute Bacterial Maxillary Sinusitis
1.4 Acute Bacterial Exacerbations of Chronic Bronchitis
1.5 Uncomplicated Skin and Skin-Structure Infections
1.6 Uncomplicated Urinary Tract Infections
1.7 Uncomplicated Gonorrhea
1.8 Early Lyme Disease (erythema migrans)
1.10 Usage

2 DOSAGE AND ADMINISTRATION
2.1 Important Administration Instructions
2.2 Dosage for Cefuroxime Axetil Tablets
2.3 Duration

3 DOSAGE FORMS AND STRENGTHS

4 CONTRAINDICATIONS

5 WARNINGS AND PRECAUTIONS
5.1 Anaphylactic Reactions
5.2 Clostridium difficile-Associated Diarrhea
5.3 Potential for Microbial Overgrowth
5.4 Development of Drug-Resistant Bacteria
5.6 Interference with Glucose Tests

6 ADVERSE REACTIONS
6.1 Clinical Trials Experience
6.2 Postmarketing Experience

7 DRUG INTERACTIONS
7.1 Oral Contraceptives
7.2 Drugs that Reduce Gastric Acidity
7.3 Probenecid
2.1 Important Administration Instructions

2.2 DOSAGE AND ADMINISTRATION

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

When culture and susceptibility information are available, they should be considered in selecting or modifying 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.

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.

2.2.1 Administration of Tablets

Administer cefuroxime axetil tablets with or without food. Tablets should be swallowed whole. Do not crush tablets.

1.10 Usage

Usage

Usage

Usage

Usage

Usage

Usage

Usage

Usage

Usage

Usage

Usage

Usage

Usage
Anaphylactic Reactions

Warnings and Precautions section of the label:

The following serious and otherwise important adverse reaction is described in greater detail in the
ADVERSE REACTIONS

5.1 Anaphylactic Reactions

Serious and occasionally fatal hyperreactivity (anaphylactic) reactions have been reported in patients

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.

5.3 Potential for Microbial Overgrowth

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

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 test in subjects receiving
cefuroxime axetil [see DRUG INTERACTIONS (7.4)].

6 ADVERSE REACTIONS

The following serious and otherwise important adverse reaction 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>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>Cefuroxime Axetil Tablets (n = 912)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Blood and lymphatic system disorders</strong></td>
<td></td>
</tr>
<tr>
<td>Eosinophilia</td>
<td>1%</td>
</tr>
<tr>
<td><strong>Gastrointestinal disorders</strong></td>
<td></td>
</tr>
<tr>
<td>Diarrhea</td>
<td>4%</td>
</tr>
<tr>
<td>Nausea/Vomiting</td>
<td>3%</td>
</tr>
<tr>
<td><strong>Investigations</strong></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 System 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>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>Cefuroxime Axetil Tablets (n = 1,061)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gastrointestinal disorders</strong></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 gonorrhea 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.

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.

Immune 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:

\[
C_{11}H_{14}N_2O_7S, \text{ with a molecular weight of 510.48.}
\]

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-acetylloxoy)ethyl ester of cefuroxime) is (RS)-1-hydroxyseryl (5R,7R)-7-[(2-furyl)methoxy]-3-(3-hydroxyethyl)-1,3-oxo-5-thia-1,3-azabicyclo[4.2.0]oct-2-ene-2-carboxylate, 7-(Z)-(O-methyl-oxime), 1-acetate 3-carbamate. Its molecular formula is C_{36}H_{42}N_2O_7S, 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, hydrogenated vegetable oil, hypromellose, microcrystalline cellulose, propylene glycol, 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 8. Pharmacokinetics of Cefuroxime Administered in the Postprandial State as Cefuroxime Axetil Tablets to Adults

<table>
<thead>
<tr>
<th>Dose (mg)</th>
<th>Peak Plasma Concentration (mg/mL)</th>
<th>Time of Peak Plasma Concentration (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>6.7</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.

Lack 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 tablets. 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. Although 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
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 interpreted according to criteria provided in Table 10.

Dilution Techniques: Quantitative methods using standardized 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 10. Susceptibility Test Interpretive Criteria for Cefuroxime Axetil

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Minimum Inhibitory Concentrations (mcg/mL)Disk Diffusion Zone Diameters (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(S) Susceptible</td>
</tr>
<tr>
<td>Enterobacteriaceae</td>
<td>≤4</td>
</tr>
<tr>
<td>Haemophilus spp.</td>
<td>≤4</td>
</tr>
<tr>
<td>Moraxella catarrhalis</td>
<td>≤4</td>
</tr>
<tr>
<td>Streptococcus pneumoniae</td>
<td>≤1</td>
</tr>
</tbody>
</table>

* For Enterobacteriaceae, 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 may be deduced from testing penicillin and either cefoxitin or oxacillin.

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 concentrations 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 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 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. The QC ranges for MIC and disk diffusion testing using the 30 mcg disk are provided in Table 11.
13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Although lifetime studies in animals have not been performed to evaluate carcinogenic potential, no mutagenic activity was found for cefuroxime axetil in a battery of bacterial mutation tests. Positive results were obtained in an in vivo chromosome aberration assay; however, negative results were found in an in vivo micronucleus test at doses up to 1.5 g/kg. Reproduction studies in rats at doses up to 1,000 mg/kg/day (9 times the recommended maximum human dose based on body surface area) have revealed no impairment of fertility.

14 CLINICAL STUDIES

14.1 Acute 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 maxillary 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 only 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>
<thead>
<tr>
<th>Clinical Effectiveness of Cefuroxime Axetil Tablets in the Treatment of Acute Bacterial Maxillary Sinusitis</th>
<th>U.S. Subjects</th>
<th>South American Subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cefuroxime Axetil Tablets</td>
<td>Cefuroxime Axetil Tablets</td>
<td>Cefuroxime Axetil Tablets</td>
</tr>
<tr>
<td>(n = 49)</td>
<td>(n = 43)</td>
<td>(n = 49)</td>
</tr>
<tr>
<td>Clinical success (cure + improvement)</td>
<td>63%</td>
<td>53%</td>
</tr>
<tr>
<td>Clinical cure</td>
<td>53%</td>
<td>44%</td>
</tr>
<tr>
<td>Clinical improvement</td>
<td>12%</td>
<td>9%</td>
</tr>
</tbody>
</table>

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 sequela 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 diagnosis of early Lyme disease in these subjects was validated by 1) blinded expert reading of a color slide of a skin lesion and immunoblot ["Western blot"] of the presence of antibodies specific to Borrelia burgdorferi, the etiologic agent of Lyme disease. The efficacy data in Table 13 are specific to this "validated" patient subset, while the safety data below refer to the entire patient population for the 2 trials. Clinical data for evaluable subjects in the "validated" patient subset are shown in Table 13.

<table>
<thead>
<tr>
<th>Clinical Effectiveness of Cefuroxime Axetil Tablets Compared with Doxycycline in the Treatment of Early Lyme Disease</th>
<th>Part I (1 Month after 20 Days of Treatment)</th>
<th>Part II (1 Year after 20 Days of Treatment)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cefuroxime Axetil Tablets (n = 125)</td>
<td>Cefuroxime Axetil Tablets (n = 105)</td>
<td></td>
</tr>
<tr>
<td>Satisfactory clinical outcome†</td>
<td>91%</td>
<td>93%</td>
</tr>
<tr>
<td>Clinical cure/success</td>
<td>72%</td>
<td>73%</td>
</tr>
<tr>
<td>Clinical improvement</td>
<td>19%</td>
<td>19%</td>
</tr>
</tbody>
</table>

† 95% confidence interval around the satisfactory difference [-0.08, +0.05].
‡ 95% confidence interval around the satisfactory difference [-0.03, +0.03].
§ 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 (13% versus 3%, respectively).

15 REFERENCES

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 their 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
### 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>
</table>

### Inactive Ingredients

<table>
<thead>
<tr>
<th>Ingredient Name</th>
<th>Strength</th>
</tr>
</thead>
<tbody>
<tr>
<td>CELLULOSE, MICROCRYSTALLINE (UNII: OP1R32D61U)</td>
<td></td>
</tr>
<tr>
<td>CROSCARMELLOSE SODIUM (UNII: M21501L88)</td>
<td></td>
</tr>
<tr>
<td>HYDROXYPROLose 1918 (5 MPA.S) (UNII: 3S5PF2120W)</td>
<td></td>
</tr>
<tr>
<td>HYDROXYPROLose 1918 (5 MPA.S) (UNII: R75371T74)</td>
<td></td>
</tr>
<tr>
<td>POLYETHYLENE GLYCOL 4000 (UNII: 880890801)</td>
<td></td>
</tr>
<tr>
<td>PROPYLENE GLYCOL (UNII: 5DF6Q67V73)</td>
<td></td>
</tr>
<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>
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</tr>
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</table>

### Product Characteristics

<table>
<thead>
<tr>
<th>Color</th>
<th>Shape</th>
<th>Size</th>
<th>Flavor</th>
<th>Imprint Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>WHITE (white to off white)</td>
<td>OVAL (capsule-shaped)</td>
<td>19mm</td>
<td></td>
<td>LUPIN;303</td>
</tr>
</tbody>
</table>

### Packaging

<table>
<thead>
<tr>
<th>#</th>
<th>Item Code</th>
<th>Package Description</th>
<th>Marketing Start Date</th>
<th>Marketing End Date</th>
</tr>
</thead>
<tbody>
<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>07/25/2003</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>07/25/2003</td>
</tr>
</tbody>
</table>

### Marketing Information

<table>
<thead>
<tr>
<th>Marketing Category</th>
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<th>Marketing End Date</th>
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<tbody>
<tr>
<td>ANDA</td>
<td>ANDA06535 I5B5</td>
<td>07/25/2003</td>
<td>07/25/2003</td>
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### CEFUROXIME AXETIL

**cefuroxime axetil tablet**

**Product Information**

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<thead>
<tr>
<th>Product Type</th>
<th>NDC Code</th>
<th>Item Code (Source)</th>
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<tbody>
<tr>
<td>HUMAN PRESCRIPTION DRUG</td>
<td>68180-303-0</td>
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</tr>
</tbody>
</table>

**Labeler** - Lupin Pharmaceuticals, Inc. (881551871)

**Registrant** - LUPIN LIMITED (675923163)

**Establishment**

<table>
<thead>
<tr>
<th>Name</th>
<th>Address</th>
<th>INSEE</th>
<th>Business Operations</th>
</tr>
</thead>
<tbody>
<tr>
<td>LUPIN LIMITED</td>
<td>72550 4600</td>
<td>72550 4600</td>
<td>MANUFACTURE(68180-302, 68180-303), PACK(68180-302, 68180-303)</td>
</tr>
</tbody>
</table>

**Revised:** 12/2018