

## HIGHLIGHTS OF PRESCRIBING INFORMATION

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

CEFTIN (cefuroxime axetil) tablets, for oral use  
CEFTIN (cefuroxime axetil) for oral suspension  
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 (1.4)-Removed	11/2016
Dosage and Administration, Dosage for CEFTIN Tablets: Secondary Bacterial Infections of Acute Bronchitis (2.2)-Removed	11/2016
Dosage and Administration, Preparation and Administration of CEFTIN for Oral Suspension (2.4)	10/2017

### INDICATIONS AND USAGE

CEFTIN is a cephalosporin antibacterial drug indicated for the treatment of the following infections due to susceptible bacteria: (1)

- Pharyngitis/tonsillitis (adults and pediatric patients) (1.1)
- Acute bacterial otitis media (pediatric patients) (1.2)
- Acute bacterial maxillary sinusitis (adults and pediatric patients) (1.3)
- Acute bacterial exacerbations of chronic bronchitis (adults and pediatric patients 13 years and older) (1.4)
- Uncomplicated skin and skin-structure infections (adults and pediatric patients 13 years and older) (1.5)
- Uncomplicated urinary tract infections (adults and pediatric patients 13 years and older) (1.6)
- Uncomplicated gonorrhea (adults and pediatric patients 13 years and older) (1.7)
- Early Lyme disease (adults and pediatric patients 13 years and older) (1.8)
- Impetigo (pediatric patients) (1.9)

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

### DOSAGE AND ADMINISTRATION

- Tablets and oral suspension are not bioequivalent and are therefore not substitutable on a milligram-per-milligram basis. (2.1)
- Administer tablets with or without food. (2.2)
- Administer oral suspension with food. (2.3)
- Administer CEFTIN tablets or CEFTIN for oral suspension as described in the dosage guidelines. (2.2, 2.3, 2.4)
- Dosage adjustment is required for patients with impaired renal function. (2.5)

Adult Patients and Pediatric Patients Dosage Guidelines for CEFTIN Tablets		
Infection	Dosage	Duration (Days)
<b>Adults and Adolescents (13 years and older)</b>		
Pharyngitis/tonsillitis (mild to moderate)	250 mg every 12 hours	10
Acute bacterial maxillary sinusitis (mild to moderate)	250 mg every 12 hours	10
Acute bacterial exacerbations of chronic	250 or 500 mg	10

bronchitis (mild to moderate)	every 12 hours	
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
Early Lyme disease	500 mg every 12 hours	20
<b>Pediatric Patients younger than 13 years (who can swallow tablets whole)</b>		
Acute bacterial otitis media	250 mg every 12 hours	10
Acute bacterial maxillary sinusitis	250 mg every 12 hours	10

### Pediatric Patients (3 Months to 12 Years) Dosage Guidelines for CEFTIN for Oral Suspension

Infection	Recommended Daily Dose <sup>a</sup>	Maximum Daily Dose	Duration (Days)
Pharyngitis/tonsillitis	20 mg/kg	500 mg	10
Acute bacterial otitis media	30 mg/kg	1,000 mg	10
Acute bacterial maxillary sinusitis (mild to moderate)	30 mg/kg	1,000 mg	10
Impetigo	30 mg/kg	1,000 mg	10

<sup>a</sup> Total daily dose given twice daily divided in equal doses.

### DOSAGE FORMS AND STRENGTHS

- Tablets: 250 mg and 500 mg (3)
- For oral suspension: 125 mg/5 mL and 250 mg/5 mL (3)

### CONTRAINDICATIONS

Known hypersensitivity (e.g., anaphylaxis) to CEFTIN or to other  $\beta$ -lactams (e.g., penicillins and cephalosporins). (4)

### WARNINGS AND PRECAUTIONS

- Serious hypersensitivity (anaphylactic) reactions: In the event of a serious reaction, discontinue CEFTIN 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 ( $\geq 3\%$ ) for CEFTIN tablets are diarrhea, nausea/vomiting, Jarisch-Herxheimer reaction, and vaginitis (early Lyme disease). (6.1)

The most common adverse reactions ( $\geq 2\%$ ) for CEFTIN for oral suspension are diarrhea, dislike of taste, diaper rash, and nausea/vomiting. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact GlaxoSmithKline at 1-888-825-5249 or FDA at 1-800-FDA-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch).

### DRUG INTERACTIONS

- Oral Contraceptives: Effects on gut flora may lower estrogen reabsorption and reduce efficacy of oral contraceptives. (7.1)
- Drugs that reduce gastric acidity may lower the bioavailability of CEFTIN. (7.2)
- Coadministration with probenecid increases systemic exposure to CEFTIN and is therefore not recommended. (7.3)

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Revised: 10/2017

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## 1 FULL PRESCRIBING INFORMATION

### 2 1 INDICATIONS AND USAGE

#### 3 1.1 Pharyngitis/Tonsillitis

4 CEFTIN tablets are indicated for the treatment of adult patients and pediatric patients (13 years  
5 and older) with mild-to-moderate pharyngitis/tonsillitis caused by susceptible strains of  
6 *Streptococcus pyogenes*.

7 CEFTIN for oral suspension is indicated for the treatment of pediatric patients aged 3 months to  
8 12 years with mild-to-moderate pharyngitis/tonsillitis caused by susceptible strains of  
9 *Streptococcus pyogenes*.

#### 10 Limitations of Use

- 11 • The efficacy of CEFTIN in the prevention of rheumatic fever was not established in clinical  
12 trials.
- 13 • The efficacy of CEFTIN in the treatment of penicillin-resistant strains of *Streptococcus*  
14 *pyogenes* has not been demonstrated in clinical trials.

#### 15 1.2 Acute Bacterial Otitis Media

16 CEFTIN tablets are indicated for the treatment of pediatric patients (who can swallow tablets  
17 whole) with acute bacterial otitis media caused by susceptible strains of *Streptococcus*  
18 *pneumoniae*, *Haemophilus influenzae* (including  $\beta$ -lactamase-producing strains), *Moraxella*  
19 *catarrhalis* (including  $\beta$ -lactamase-producing strains), or *Streptococcus pyogenes*.

20 CEFTIN for oral suspension is indicated for the treatment of pediatric patients aged 3 months to  
21 12 years with acute bacterial otitis media caused by susceptible strains of *Streptococcus*  
22 *pneumoniae*, *Haemophilus influenzae* (including  $\beta$ -lactamase-producing strains), *Moraxella*  
23 *catarrhalis* (including  $\beta$ -lactamase-producing strains), or *Streptococcus pyogenes*.

#### 24 1.3 Acute Bacterial Maxillary Sinusitis

25 CEFTIN tablets are indicated for the treatment of adult and pediatric patients (13 years and  
26 older) with mild-to-moderate acute bacterial maxillary sinusitis caused by susceptible strains of

27 *Streptococcus pneumoniae* or *Haemophilus influenzae* (non- $\beta$ -lactamase-producing strains  
28 only).

29 CEFTIN for oral suspension is indicated for the treatment of pediatric patients aged 3 months to  
30 12 years with mild-to-moderate acute bacterial maxillary sinusitis caused by susceptible strains  
31 of *Streptococcus pneumoniae* or *Haemophilus influenzae* (non- $\beta$ -lactamase-producing strains  
32 only).

### 33 Limitations of Use

34 The effectiveness of CEFTIN for sinus infections caused by  $\beta$ -lactamase-producing  
35 *Haemophilus influenzae* or *Moraxella catarrhalis* in patients with acute bacterial maxillary  
36 sinusitis was not established due to insufficient numbers of these isolates in the clinical trials  
37 [see *Clinical Studies (14.1)*].

#### 38 **1.4 Acute Bacterial Exacerbations of Chronic Bronchitis**

39 CEFTIN tablets are indicated for the treatment of adult patients and pediatric patients (aged 13  
40 and older) with mild-to-moderate acute bacterial exacerbations of chronic bronchitis caused by  
41 susceptible strains of *Streptococcus pneumoniae*, *Haemophilus influenzae* ( $\beta$ -lactamase-negative  
42 strains), or *Haemophilus parainfluenzae* ( $\beta$ -lactamase-negative strains).

#### 43 **1.5 Uncomplicated Skin and Skin-Structure Infections**

44 CEFTIN tablets are indicated for the treatment of adult patients and pediatric patients (aged 13  
45 and older) with uncomplicated skin and skin-structure infections caused by susceptible strains of  
46 *Staphylococcus aureus* (including  $\beta$ -lactamase-producing strains) or *Streptococcus pyogenes*.

#### 47 **1.6 Uncomplicated Urinary Tract Infections**

48 CEFTIN tablets are indicated for the treatment of adult patients and pediatric patients (aged 13  
49 and older) with uncomplicated urinary tract infections caused by susceptible strains of  
50 *Escherichia coli* or *Klebsiella pneumoniae*.

#### 51 **1.7 Uncomplicated Gonorrhea**

52 CEFTIN tablets are indicated for the treatment of adult patients and pediatric patients (aged 13  
53 and older) with uncomplicated gonorrhea, urethral and endocervical, caused by penicillinase-  
54 producing and non-penicillinase-producing susceptible strains of *Neisseria gonorrhoeae* and  
55 uncomplicated gonorrhea, rectal, in females, caused by non-penicillinase-producing susceptible  
56 strains of *Neisseria gonorrhoeae*.

#### 57 **1.8 Early Lyme Disease (erythema migrans)**

58 CEFTIN tablets are indicated for the treatment of adult patients and pediatric patients (aged 13  
59 and older) with early Lyme disease (erythema migrans) caused by susceptible strains of *Borrelia*  
60 *burgdorferi*.

61 **1.9 Impetigo**

62 CEFTIN for oral suspension is indicated for the treatment of pediatric patients aged 3 months to  
63 12 years with impetigo caused by susceptible strains of *Staphylococcus aureus* (including  $\beta$ -  
64 lactamase-producing strains) or *Streptococcus pyogenes*.

65 **1.10 Usage**

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

72 **2 DOSAGE AND ADMINISTRATION**

73 **2.1 Important Administration Instructions**

- 74 • CEFTIN tablets and CEFTIN for oral suspension are not bioequivalent and are therefore not  
75 substitutable on a milligram-per-milligram basis [see *Clinical Pharmacology* (12.3)].
- 76 • Administer CEFTIN tablets or oral suspension as described in the appropriate dosage  
77 guidelines [see *Dosage and Administration* (2.2, 2.3, 2.4)].
- 78 • Administer CEFTIN tablets with or without food.
- 79 • Administer CEFTIN for oral suspension with food.
- 80 • Pediatric patients (aged 13 years and older) who cannot swallow the CEFTIN tablets whole  
81 should receive CEFTIN for oral suspension because the tablet has a strong, persistent bitter  
82 taste when crushed [see *Dosage and Administration* (2.2)].

83 **2.2 Dosage for CEFTIN Tablets**

84 Administer CEFTIN tablets as described in the dosage guidelines table below with or without  
85 food.

86 **Table 1. Adult Patients and Pediatric Patients Dosage Guidelines for CEFTIN Tablets**

<b>Infection</b>	<b>Dosage</b>	<b>Duration (Days)</b>
<b>Adults and Adolescents (13 years and older)</b>		
Pharyngitis/tonsillitis (mild to moderate)	250 mg every 12 hours	10
Acute bacterial maxillary sinusitis (mild to moderate)	250 mg every 12 hours	10
Acute bacterial exacerbations of chronic bronchitis (mild to moderate)	250 or 500 mg every 12 hours	10 <sup>a</sup>
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
Early Lyme disease	500 mg every 12 hours	20
<b>Pediatric Patients younger than 13 years (who can swallow tablets whole)<sup>b</sup></b>		
Acute bacterial otitis media	250 mg every 12 hours	10
Acute bacterial maxillary sinusitis	250 mg every 12 hours	10

87 <sup>a</sup> The safety and effectiveness of CEFTIN administered for less than 10 days in patients with  
 88 acute exacerbations of chronic bronchitis have not been established.

89 <sup>b</sup> When crushed, the tablet has a strong, persistent bitter taste. Therefore, patients who cannot  
 90 swallow the tablet whole should receive the oral suspension.

91 **2.3 Dosage for CEFTIN for Oral Suspension**

92 Administer CEFTIN for oral suspension as described in the dosage guidelines table below with  
 93 food.

94 **Table 2. Pediatric Patients (3 Months to 12 Years) Dosage Guidelines for CEFTIN for Oral**  
 95 **Suspension**

<b>Infection</b>	<b>Recommended Daily Dose<sup>a</sup></b>	<b>Maximum Daily Dose</b>	<b>Duration (Days)</b>
Pharyngitis/tonsillitis	20 mg/kg	500 mg	10
Acute bacterial otitis media	30 mg/kg	1,000 mg	10
Acute bacterial maxillary sinusitis	30 mg/kg	1,000 mg	10
Impetigo	30 mg/kg	1,000 mg	10

96 <sup>a</sup> Recommended daily dose given twice daily divided in equal doses.

97 **2.4 Preparation and Administration of CEFTIN for Oral Suspension**

98 Prepare a suspension at the time of dispensing as follows:

- 99 1. Shake the bottle to loosen the powder.
- 100 2. Remove the cap.
- 101 3. Add the total amount of cold water for reconstitution (Table 3) and replace the cap.
- 102 4. Invert the bottle and vigorously rock the bottle from side to side so that water rises through
- 103 the powder.

- 104 5. Once the sound of the powder against the bottle disappears, turn the bottle upright and  
 105 vigorously shake it in a diagonal direction for at least one minute.
- 106 6. After reconstitution, wait one hour before administering suspension to a patient.

107 **Table 3. Amount of Water Required for Reconstitution of Labeled Volumes of CEFTIN for**  
 108 **Oral Suspension**

Oral Suspension	Amount of Water Required for Reconstitution	Labeled Volume after Reconstitution
125 mg/5 mL	37 mL	100 mL
250 mg/5 mL	19 mL	50 mL
	35 mL	100 mL

- 109 • Shake the oral suspension well before each use.
- 110 • Replace cap securely after each opening.
- 111 • Store the reconstituted suspension refrigerated between 2° and 8°C (36° and 46°F).
- 112 • Discard the reconstituted suspension after 10 days.

113 **2.5 Dosage in Patients with Impaired Renal Function**

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

117 **Table 4. Dosing in Adults with Renal Impairment**

Creatinine Clearance (mL/min)	Recommended Dosage
≥30	No dosage adjustment
10 to <30	Standard individual dose given every 24 hours
<10 (without hemodialysis)	Standard individual dose given every 48 hours
Hemodialysis	A single additional standard dose should be given at the end of each dialysis

118 **3 DOSAGE FORMS AND STRENGTHS**

119 CEFTIN tablets are white, capsule-shaped, film-coated tablets available in the following  
 120 strengths:

- 121 • 250 mg of cefuroxime (as cefuroxime axetil) with "GX ES7" engraved on one side and blank  
 122 on the other side.
- 123 • 500 mg of cefuroxime (as cefuroxime axetil) with "GX EG2" engraved on one side and blank  
 124 on the other side.

125 CEFTIN for oral suspension is provided as dry, white to off-white, tutti-frutti–flavored powder.  
 126 When reconstituted as directed, the suspension provides the equivalent of 125 mg or 250 mg of

127 cefuroxime (as cefuroxime axetil) per 5 mL.

## 128 **4 CONTRAINDICATIONS**

129 CEFTIN is contraindicated in patients with a known hypersensitivity (e.g., anaphylaxis) to  
130 CEFTIN or to other  $\beta$ -lactam antibacterial drugs (e.g., penicillins and cephalosporins).

## 131 **5 WARNINGS AND PRECAUTIONS**

### 132 **5.1 Anaphylactic Reactions**

133 Serious and occasionally fatal hypersensitivity (anaphylactic) reactions have been reported in  
134 patients on  $\beta$ -lactam antibacterials. These reactions are more likely to occur in individuals with a  
135 history of  $\beta$ -lactam hypersensitivity and/or a history of sensitivity to multiple allergens. There  
136 have been reports of individuals with a history of penicillin hypersensitivity who have  
137 experienced severe reactions when treated with cephalosporins. CEFTIN is contraindicated in  
138 patients with a known hypersensitivity to CEFTIN or other  $\beta$ -lactam antibacterial drugs [*see*  
139 *Contraindications (4)*]. Before initiating therapy with CEFTIN, inquire about previous  
140 hypersensitivity reactions to penicillins, cephalosporins, or other allergens. If an allergic reaction  
141 occurs, discontinue CEFTIN and institute appropriate therapy.

### 142 **5.2 *Clostridium difficile*-Associated Diarrhea**

143 *Clostridium difficile*-associated diarrhea (CDAD) has been reported with use of nearly all  
144 antibacterial agents, including CEFTIN, and may range in severity from mild diarrhea to fatal  
145 colitis. Treatment with antibacterial agents alters the normal flora of the colon leading to  
146 overgrowth of *C. difficile*.

147 *C. difficile* produces toxins A and B which contribute to the development of CDAD. Hypertoxin-  
148 producing strains of *C. difficile* cause increased morbidity and mortality, as these infections can  
149 be refractory to antimicrobial therapy and may require colectomy. CDAD must be considered in  
150 all patients who present with diarrhea following antibiotic use. Careful medical history is  
151 necessary since CDAD has been reported to occur over 2 months after the administration of  
152 antibacterial agents.

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

### 157 **5.3 Potential for Microbial Overgrowth**

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

160 **5.4 Development of Drug-Resistant Bacteria**

161 Prescribing CEFTIN either in the absence of a proven or strongly suspected bacterial infection or  
162 a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the  
163 development of drug-resistant bacteria.

164 **5.5 Phenylketonuria**

165 CEFTIN for oral suspension 125 mg/5 mL contains phenylalanine 11.8 mg per 5 mL  
166 (1 teaspoonful) of reconstituted suspension. CEFTIN for oral suspension 250 mg/5 mL contains  
167 phenylalanine 25.2 mg per 5 mL (1 teaspoonful) of reconstituted suspension.

168 **5.6 Interference with Glucose Tests**

169 A false-positive result for glucose in the urine may occur with copper reduction tests, and a  
170 false-negative result for blood/plasma glucose may occur with ferricyanide tests in subjects  
171 receiving CEFTIN [*see Drug Interactions (7.4)*].

172 **6 ADVERSE REACTIONS**

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

175 Anaphylactic Reactions [*see Warnings and Precautions (5.1)*]

176 **6.1 Clinical Trials Experience**

177 Because clinical trials are conducted under widely varying conditions, adverse reaction rates  
178 observed in the clinical trials of a drug cannot be directly compared with rates in the clinical  
179 trials of another drug and may not reflect the rates observed in practice.

180 Tablets

181 *Multiple-Dose Dosing Regimens with 7 to 10 Days' Duration:* In multiple-dose clinical trials,  
182 912 subjects were treated with CEFTIN (125 to 500 mg twice daily). It is noted that 125 mg  
183 twice daily is not an approved dosage. Twenty (2.2%) subjects discontinued medication due to  
184 adverse reactions. Seventeen (85%) of the 20 subjects who discontinued therapy did so because  
185 of gastrointestinal disturbances, including diarrhea, nausea, vomiting, and abdominal pain. The  
186 percentage of subjects treated with CEFTIN who discontinued study drug because of adverse  
187 reactions was similar at daily doses of 1,000, 500, and 250 mg (2.3%, 2.1%, and 2.2%,  
188 respectively). However, the incidence of gastrointestinal adverse reactions increased with the  
189 higher recommended doses.

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

192 **Table 5. Adverse Reactions ( $\geq 1\%$ ) after Multiple-Dose Regimens with CEFTIN Tablets**

Adverse Reaction	CEFTIN (n = 912)
<b>Blood and lymphatic system disorders</b>	
Eosinophilia	1%
<b>Gastrointestinal disorders</b>	
Diarrhea	4%
Nausea/Vomiting	3%
<b>Investigations</b>	
Transient elevation in AST	2%
Transient elevation in ALT	2%
Transient elevation in LDH	1%

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

195 *Immune System Disorders:* Hives, swollen tongue.

196 *Metabolism and Nutrition Disorders:* Anorexia.

197 *Nervous System Disorders:* Headache.

198 *Cardiac Disorders:* Chest pain.

199 *Respiratory Disorders:* Shortness of breath.

200 *Gastrointestinal Disorders:* Abdominal pain, abdominal cramps, flatulence, indigestion,  
 201 mouth ulcers.

202 *Skin and Subcutaneous Tissue Disorders:* Rash, itch.

203 *Renal and Urinary Disorders:* Dysuria.

204 *Reproductive System and Breast Disorders:* Vaginitis, vulvar itch.

205 *General Disorders and Administration Site Conditions:* Chills, sleepiness, thirst.

206 *Investigations:* Positive Coombs' test.

207 *Early Lyme Disease with 20-Day Regimen:* Two multicenter trials assessed CEFTIN 500 mg  
 208 twice daily for 20 days. The most common drug-related adverse experiences were diarrhea  
 209 (10.6%), Jarisch-Herxheimer reaction (5.6%), and vaginitis (5.4%). Other adverse experiences  
 210 occurred with frequencies comparable to those reported with 7 to 10 days' dosing.

211 *Single-Dose Regimen for Uncomplicated Gonorrhea:* In clinical trials using a single 1,000-mg  
 212 dose of CEFTIN, 1,061 subjects were treated for uncomplicated gonorrhea.

213 The adverse reactions in Table 6 were for subjects treated with a single dose of 1,000 mg  
 214 CEFTIN in U.S. clinical trials.

215 **Table 6. Adverse Reactions ( $\geq 1\%$ ) after Single-Dose Regimen with 1,000-mg CEFTIN**  
 216 **Tablets for Uncomplicated Gonorrhea**

Adverse Reaction	CEFTIN (n = 1,061)
<b>Gastrointestinal disorders</b>	
Nausea/Vomiting	7%
Diarrhea	4%

217 The following adverse reactions occurred in less than 1% but greater than 0.1% of subjects  
 218 (n = 1,061) treated with a single dose of CEFTIN 1,000 mg for uncomplicated gonorrhea in U.S.  
 219 clinical trials.

220 *Infections and Infestations:* Vaginal candidiasis.

221 *Nervous System Disorders:* Headache, dizziness, somnolence.

222 *Cardiac Disorders:* Tightness/pain in chest, tachycardia.

223 *Gastrointestinal Disorders:* Abdominal pain, dyspepsia.

224 *Skin and Subcutaneous Tissue Disorders:* Erythema, rash, pruritus.

225 *Musculoskeletal and Connective Tissue Disorders:* Muscle cramps, muscle stiffness,  
 226 muscle spasm of neck, lockjaw-type reaction.

227 *Renal and Urinary Disorders:* Bleeding/pain in urethra, kidney pain.

228 *Reproductive System and Breast Disorders:* Vaginal itch, vaginal discharge.

229 Oral Suspension

230 In clinical trials using multiple doses of CEFTIN, pediatric subjects (96.7% were younger than  
 231 12 years) were treated with CEFTIN (20 to 30 mg/kg/day divided twice daily up to a maximum  
 232 dose of 500 or 1,000 mg/day, respectively). Eleven (1.2%) U.S. subjects discontinued medication  
 233 due to adverse reactions. The discontinuations were primarily for gastrointestinal disturbances,  
 234 usually diarrhea or vomiting. Thirteen (1.4%) U.S. pediatric subjects discontinued therapy due to  
 235 the taste and/or problems with drug administration.

236 The adverse reactions in Table 7 are for U.S. subjects (n = 931) treated with CEFTIN in  
 237 multiple-dose clinical trials.

238 **Table 7. Adverse Reactions ( $\geq 1\%$ ) after Multiple-Dose Regimens with CEFTIN for Oral**  
 239 **Suspension**

Adverse Reaction	CEFTIN (n = 931)
<b>Gastrointestinal disorders</b>	
Diarrhea	9%
Dislike of taste	5%
Nausea/vomiting	3%
<b>Skin and subcutaneous tissue disorders</b>	
Diaper rash	3%

240 The following adverse reactions occurred in less than 1% but greater than 0.1% of U.S. subjects  
 241 (n = 931) treated with CEFTIN for oral suspension in multiple-dose clinical trials.

242 *Infections and Infestations:* Gastrointestinal infection, candidiasis, viral illness, upper respiratory  
 243 infection, sinusitis, urinary tract infection.

244 *Blood and Lymphatic System Disorders:* Eosinophilia.

245 *Psychiatric Disorders:* Hyperactivity, irritable behavior.

246 *Gastrointestinal Disorders:* Abdominal pain, flatulence, ptyalism.

247 *Skin and Subcutaneous Tissue Disorders:* Rash.

248 *Musculoskeletal and Connective Tissue Disorders:* Joint swelling, arthralgia.

249 *Reproductive System and Breast Disorders:* Vaginal irritation.

250 *General Disorders and Administration Site Conditions:* Cough, fever.

251 *Investigations:* Elevated liver enzymes, positive Coombs' test.

## 252 **6.2 Postmarketing Experience**

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

### 257 Blood and Lymphatic System Disorders

258 Hemolytic anemia, leukopenia, pancytopenia, thrombocytopenia.

### 259 Gastrointestinal Disorders

260 Pseudomembranous colitis [see *Warnings and Precautions (5.2)*].

### 261 Hepatobiliary Disorders

262 Hepatic impairment including hepatitis and cholestasis, jaundice.

### 263 Immune System Disorders

264 Anaphylaxis, serum sickness-like reaction.

265 Investigations

266 Increased prothrombin time.

267 Nervous System Disorders

268 Seizure, encephalopathy.

269 Renal and Urinary Disorders

270 Renal dysfunction.

271 Skin and Subcutaneous Tissue Disorders

272 Angioedema, erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis,  
273 urticaria.

274 **7 DRUG INTERACTIONS**

275 **7.1 Oral Contraceptives**

276 Cefuroxime axetil may affect the gut flora, leading to lower estrogen reabsorption and reduced  
277 efficacy of combined oral estrogen/progesterone contraceptives. Counsel patients to consider  
278 alternate supplementary (non-hormonal) contraceptive measures during treatment.

279 **7.2 Drugs that Reduce Gastric Acidity**

280 Drugs that reduce gastric acidity may result in a lower bioavailability of CEFTIN compared with  
281 administration in the fasting state. Administration of drugs that reduce gastric acidity may negate  
282 the food effect of increased absorption of CEFTIN when administered in the postprandial state.  
283 Administer CEFTIN at least 1 hour before or 2 hours after administration of short-acting  
284 antacids. Histamine-2 (H<sub>2</sub>) antagonists and proton pump inhibitors should be avoided.

285 **7.3 Probenecid**

286 Concomitant administration of probenecid with cefuroxime axetil tablets increases serum  
287 concentrations of cefuroxime [*see Clinical Pharmacology (12.3)*]. Coadministration of  
288 probenecid with cefuroxime axetil is not recommended.

289 **7.4 Drug/Laboratory Test Interactions**

290 A false-positive reaction for glucose in the urine may occur with copper reduction tests (e.g.,  
291 Benedict's or Fehling's solution), but not with enzyme-based tests for glycosuria. As a  
292 false-negative result may occur in the ferricyanide test, it is recommended that either the glucose  
293 oxidase or hexokinase method be used to determine blood/plasma glucose levels in patients  
294 receiving cefuroxime axetil. The presence of cefuroxime does not interfere with the assay of  
295 serum and urine creatinine by the alkaline picrate method.

296 **8 USE IN SPECIFIC POPULATIONS**

297 **8.1 Pregnancy**

298 Pregnancy Category B. There are no adequate and well-controlled studies in pregnant women.  
299 Because animal reproduction studies are not always predictive of human response, CEFTIN  
300 should be used during pregnancy only if clearly needed.

301 Reproduction studies have been performed in mice at doses up to 3,200 mg/kg/day (14 times the  
302 recommended maximum human dose based on body surface area) and in rats at doses up to  
303 1,000 mg/kg/day (9 times the recommended maximum human dose based on body surface area)  
304 and have revealed no evidence of impaired fertility or harm to the fetus due to cefuroxime axetil.

305 **8.3 Nursing Mothers**

306 Because cefuroxime is excreted in human milk, caution should be exercised when CEFTIN is  
307 administered to a nursing woman.

308 **8.4 Pediatric Use**

309 The safety and effectiveness of CEFTIN have been established for pediatric patients aged  
310 3 months to 12 years for acute bacterial maxillary sinusitis based upon its approval in adults. Use  
311 of CEFTIN in pediatric patients is supported by pharmacokinetic and safety data in adults and  
312 pediatric patients, and by clinical and microbiological data from adequate and well-controlled  
313 trials of the treatment of acute bacterial maxillary sinusitis in adults and of acute otitis media  
314 with effusion in pediatric patients. It is also supported by postmarketing adverse events  
315 surveillance. [*See Indications and Usage (1), Dosage and Administration (2), Adverse Reactions*  
316 *(6), Clinical Pharmacology (12.3).*]

317 **8.5 Geriatric Use**

318 Of the total number of subjects who received CEFTIN in 20 clinical trials, 375 were aged 65 and  
319 older while 151 were aged 75 and older. No overall differences in safety or effectiveness were  
320 observed between these subjects and younger adult subjects. Reported clinical experience has  
321 not identified differences in responses between the elderly and younger adult patients, but  
322 greater sensitivity of some older individuals cannot be ruled out.

323 Cefuroxime is substantially excreted by the kidney, and the risk of adverse reactions may be  
324 greater in patients with impaired renal function. Because elderly patients are more likely to have  
325 decreased renal function, care should be taken in dose selection, and it may be useful to monitor  
326 renal function.

327 **8.6 Renal Impairment**

328 Reducing the dosage of CEFTIN is recommended for adult patients with severe renal  
329 impairment (creatinine clearance <30 mL/min) [*see Dosage and Administration (2.5), Clinical*  
330 *Pharmacology (12.3)*].

331 **10 OVERDOSAGE**

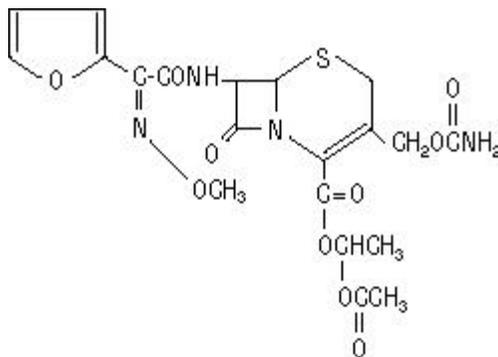
332 Overdosage of cephalosporins can cause cerebral irritation leading to convulsions or  
333 encephalopathy. Serum levels of cefuroxime can be reduced by hemodialysis and peritoneal  
334 dialysis.

335 **11 DESCRIPTION**

336 CEFTIN tablets and CEFTIN for oral suspension contain cefuroxime as cefuroxime axetil.  
337 CEFTIN is a semisynthetic, cephalosporin antibacterial drug for oral administration.

338 The chemical name of cefuroxime axetil (1-(acetyloxy) ethyl ester of cefuroxime) is (RS)-1-  
339 hydroxyethyl (6R,7R)-7-[2-(2-furyl)glyoxyl-amido]-3-(hydroxymethyl)-8-oxo-5-thia-1-  
340 azabicyclo[4.2.0]-oct-2-ene-2-carboxylate, 7<sup>2</sup>-(Z)-(O-methyl-oxime), 1-acetate 3-carbamate. Its  
341 molecular formula is C<sub>20</sub>H<sub>22</sub>N<sub>4</sub>O<sub>10</sub>S, and it has a molecular weight of 510.48.

342 Cefuroxime axetil is in the amorphous form and has the following structural formula:



343

344 Tablets are film-coated and contain the equivalent of 250 or 500 mg of cefuroxime as  
345 cefuroxime axetil. Tablets contain the inactive ingredients colloidal silicon dioxide,  
346 croscarmellose sodium, hydrogenated vegetable oil, hypromellose, methylparaben,  
347 microcrystalline cellulose, propylene glycol, propylparaben, sodium benzoate, sodium lauryl  
348 sulfate, and titanium dioxide.

349 Oral suspension, when reconstituted with water, provides the equivalent of 125 mg or 250 mg of  
350 cefuroxime (as cefuroxime axetil) per 5 mL. Oral suspension contains the inactive ingredients  
351 acesulfame potassium, aspartame, povidone K30, stearic acid, sucrose, tutti-frutti flavoring, and  
352 xanthan gum.

353 **12 CLINICAL PHARMACOLOGY**

354 **12.1 Mechanism of Action**

355 CEFTIN is an antibacterial drug [see *Clinical Pharmacology (12.4)*].

356 **12.3 Pharmacokinetics**

357 Absorption

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

362 **Table 8. Pharmacokinetics of Cefuroxime Administered in the Postprandial State as**  
363 **CEFTIN Tablets to Adults<sup>a</sup>**

<b>Dose<sup>b</sup> (Cefuroxime Equivalent)</b>	<b>Peak Plasma Concentration (mcg/mL)</b>	<b>Time of Peak Plasma Concentration (h)</b>	<b>Mean Elimination Half-life (h)</b>	<b>AUC (mcg•h/mL)</b>
125 mg	2.1	2.2	1.2	6.7
250 mg	4.1	2.5	1.2	12.9
500 mg	7.0	3.0	1.2	27.4
1,000 mg	13.6	2.5	1.3	50.0

364 <sup>a</sup> Mean values of 12 healthy adult volunteers.

365 <sup>b</sup> Drug administered immediately after a meal.

366 *Food Effect:* Absorption of the tablet is greater when taken after food (absolute bioavailability  
367 increases from 37% to 52%). Despite this difference in absorption, the clinical and bacteriologic  
368 responses of subjects were independent of food intake at the time of tablet administration in  
369 2 trials where this was assessed.

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

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

379 Distribution

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

382 Metabolism

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

384 Excretion

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

389 Specific Populations

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

394 *Pediatric Patients:* Serum pharmacokinetic parameters for cefuroxime in pediatric subjects  
395 administered CEFTIN for oral suspension are shown in Table 9.

396 **Table 9. Pharmacokinetics of Cefuroxime Administered in the Postprandial State as**  
397 **CEFTIN for Oral Suspension to Pediatric Subjects<sup>a</sup>**

<b>Dose<sup>b</sup> (Cefuroxime Equivalent)</b>	<b>n</b>	<b>Peak Plasma Concentration (mcg/mL)</b>	<b>Time of Peak Plasma Concentration (h)</b>	<b>Mean Elimination Half-life (h)</b>	<b>AUC (mcg•h/mL)</b>
10 mg/kg	8	3.3	3.6	1.4	12.4
15 mg/kg	12	5.1	2.7	1.9	22.5
20 mg/kg	8	7.0	3.1	1.9	32.8

398 <sup>a</sup> Mean age = 23 months.

399 <sup>b</sup> Drug administered with milk or milk products.

400 *Geriatric Patients:* In a trial of 20 elderly subjects (mean age = 83.9 years) having a mean  
401 creatinine clearance of 34.9 mL/min, the mean serum elimination half-life was prolonged to  
402 3.5 hours; however, despite the lower elimination of cefuroxime in geriatric patients, dosage  
403 adjustment based on age is not necessary [see *Use in Specific Populations (8.5)*].

404 Drug Interactions

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

408 **12.4 Microbiology**

409 Mechanism of Action

410 Cefuroxime axetil is a bactericidal agent that acts by inhibition of bacterial cell wall synthesis.  
411 Cefuroxime axetil has activity in the presence of some  $\beta$ -lactamases, both penicillinases and  
412 cephalosporinases, of gram-negative and gram-positive bacteria.

413 Mechanism of Resistance

414 Resistance to cefuroxime axetil is primarily through hydrolysis by  $\beta$ -lactamase, alteration of  
415 penicillin-binding proteins (PBPs), decreased permeability, and the presence of bacterial efflux  
416 pumps.

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

420 Cefuroxime axetil has been shown to be active against most isolates of the following bacteria,  
421 both in vitro and in clinical infections [see *Indications and Usage (1)*]:

- 422 • Gram-positive bacteria
- 423     *Staphylococcus aureus* (methicillin-susceptible isolates only)
- 424     *Streptococcus pneumoniae*
- 425     *Streptococcus pyogenes*
- 426 • Gram-negative bacteria
- 427     *Escherichia coli*<sup>a</sup>
- 428     *Klebsiella pneumoniae*<sup>a</sup>
- 429     *Haemophilus influenzae*
- 430     *Haemophilus parainfluenzae*
- 431     *Moraxella catarrhalis*
- 432     *Neisseria gonorrhoeae*

433 <sup>a</sup> Most extended spectrum  $\beta$ -lactamase (ESBL)-producing and carbapenemase-producing  
434 isolates are resistant to cefuroxime axetil.

- 435 • Spirochetes
- 436     *Borrelia burgdorferi*

437 The following in vitro data are available, but their clinical significance is unknown. At least  
438 90 percent of the following microorganisms exhibit an in vitro minimum inhibitory concentration  
439 (MIC) less than or equal to the susceptible breakpoint for cefuroxime axetil of 1 mcg/mL.  
440 However, the efficacy of cefuroxime axetil in treating clinical infections due to these  
441 microorganisms has not been established in adequate and well-controlled clinical trials.

- 442 • Gram-positive bacteria
- 443     *Staphylococcus epidermidis* (methicillin-susceptible isolates only)
- 444     *Staphylococcus saprophyticus* (methicillin-susceptible isolates only)
- 445     *Streptococcus agalactiae*
- 446 • Gram-negative bacteria
- 447     *Morganella morganii*
- 448     *Proteus inconstans*
- 449     *Proteus mirabilis*

450 *Providencia rettgeri*

451 • Anaerobic bacteria

452 *Peptococcus niger*

453 Susceptibility Test Methods

454 When available, the clinical microbiology laboratory should provide the results of in vitro  
455 susceptibility tests for antimicrobial drug products used in local hospitals and practice areas to  
456 the physician as periodic reports that describe the susceptibility profile of nosocomial and  
457 community-acquired pathogens. These reports should aid the physician in selecting an  
458 antibacterial drug product for treatment.

459 *Dilution Techniques:* Quantitative methods are used to determine antimicrobial MICs. These  
460 MICs provide reproducible estimates of the susceptibility of bacteria to antimicrobial  
461 compounds. The MICs should be determined using a standardized test method (broth or agar).<sup>1,2</sup>  
462 The MIC values should be interpreted according to criteria provided in Table 10.<sup>2,3</sup>

463 *Diffusion Techniques:* Quantitative methods that require measurement of zone diameters also  
464 provide reproducible estimates of the susceptibility of bacteria to antimicrobial compounds. The  
465 zone size provides an estimate of the susceptibility of bacteria to antimicrobial compounds. The  
466 zone size should be determined using a standardized test method.<sup>4</sup> This procedure uses paper  
467 disks impregnated with 30 mcg cefuroxime axetil to test the susceptibility of microorganisms to  
468 cefuroxime axetil. The disk diffusion interpretive criteria are provided in Table 10.<sup>3</sup>

469 **Table 10. Susceptibility Test Interpretive Criteria for Cefuroxime Axetil**

Pathogen	Minimum Inhibitory Concentrations (mcg/mL)			Disk Diffusion Zone Diameters (mm)		
	(S) Susceptible	(I) Intermediate	(R) Resistant	(S) Susceptible	(I) Intermediate	(R) Resistant
<i>Enterobacteriaceae</i> <sup>a</sup>	≤4	8 - 16	≥32	≥23	15 - 22	≤14
<i>Haemophilus</i> spp. <sup>a,b</sup>	≤4	8	≥16	≥20	17 - 19	≤16
<i>Moraxella</i> <i>catarrhalis</i> <sup>a</sup>	≤4	8	≥16	-	-	-
<i>Streptococcus</i> <i>pneumoniae</i>	≤1	2	≥4	-	-	-

470 <sup>a</sup> For *Enterobacteriaceae*, *Haemophilus* spp., and *Moraxella catarrhalis*, susceptibility  
471 interpretive criteria are based on a dose of 500 mg every 12 hours in patients with normal  
472 renal function.

473 <sup>b</sup> *Haemophilus* spp. includes only isolates of *H. influenzae* and *H. parainfluenzae*.

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

476 Susceptibility of *Streptococcus pyogenes* may be deduced from testing penicillin.<sup>3</sup>

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

488 *Quality Control:* Standardized susceptibility test procedures require the use of laboratory  
 489 controls to monitor and ensure the accuracy and precision of supplies and reagents used in the  
 490 assay, and the techniques of the individual performing the test.<sup>1,2,4</sup> The QC ranges for MIC and  
 491 disk diffusion testing using the 30-mcg disk are provided in Table 11.<sup>3</sup>

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

QC Strain	Minimum Inhibitory Concentrations (mcg/mL)	Disk Diffusion Zone Diameters (mm)
<i>Escherichia coli</i> ATCC 25922	2 to 8	20 to 26
<i>Staphylococcus aureus</i> ATCC 25923	-	27 to 35
<i>Staphylococcus aureus</i> ATCC 29213	0.5 to 2	-
<i>Streptococcus pneumoniae</i> ATCC 49619	0.25 to 1	-
<i>Haemophilus influenzae</i> ATCC 49766	0.25 to 1	28 to 36
<i>Neisseria gonorrhoeae</i> ATCC 49226	0.25 to 1	33 to 41

493 ATCC = American Type Culture Collection.

## 494 13 NONCLINICAL TOXICOLOGY

### 495 13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

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

502 **14 CLINICAL STUDIES**

503 **14.1 Acute Bacterial Maxillary Sinusitis**

504 One adequate and well-controlled trial was performed in subjects with acute bacterial maxillary  
505 sinusitis. In this trial, each subject had a maxillary sinus aspirate collected by sinus puncture  
506 before treatment was initiated for presumptive acute bacterial sinusitis. All subjects had  
507 radiographic and clinical evidence of acute maxillary sinusitis. In the trial, the clinical  
508 effectiveness of CEFTIN in treating acute maxillary sinusitis was comparable to an oral  
509 antimicrobial agent containing a specific  $\beta$ -lactamase inhibitor. However, microbiology data  
510 demonstrated CEFTIN to be effective in treating acute bacterial maxillary sinusitis due only to  
511 *Streptococcus pneumoniae* or non- $\beta$ -lactamase-producing *Haemophilus influenzae*. Insufficient  
512 numbers of  $\beta$ -lactamase-producing *Haemophilus influenzae* and *Moraxella catarrhalis* isolates  
513 were obtained in this trial to adequately evaluate the effectiveness of CEFTIN in treating acute  
514 bacterial maxillary sinusitis due to these 2 organisms.

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

517 **Table 12. Clinical Effectiveness of CEFTIN Tablets in the Treatment of Acute Bacterial**  
518 **Maxillary Sinusitis**

	U.S. Subjects <sup>a</sup>		South American Subjects <sup>b</sup>	
	CEFTIN 250 mg Twice Daily (n = 49)	Control <sup>c</sup> (n = 43)	CEFTIN 250 mg Twice Daily (n = 49)	Control <sup>c</sup> (n = 43)
Clinical success (cure + improvement)	65%	53%	77%	74%
Clinical cure	53%	44%	72%	64%
Clinical improvement	12%	9%	5%	10%

519 <sup>a</sup> 95% confidence interval around the success difference [-0.08, +0.32].

520 <sup>b</sup> 95% confidence interval around the success difference [-0.10, +0.16].

521 <sup>c</sup> Control was an antibacterial drug containing a  $\beta$ -lactamase inhibitor.

522 In this trial and in a supporting maxillary puncture trial, 15 evaluable subjects had non-  
523  $\beta$ -lactamase-producing *Haemophilus influenzae* as the identified pathogen. Of these, 67%  
524 (10/15) had this pathogen eradicated. Eighteen (18) evaluable subjects had *Streptococcus*  
525 *pneumoniae* as the identified pathogen. Of these, 83% (15/18) had this pathogen eradicated.

526 **14.2 Early Lyme Disease**

527 Two adequate and well-controlled trials were performed in subjects with early Lyme disease. All  
528 subjects presented with physician-documented erythema migrans, with or without systemic  
529 manifestations of infection. Subjects were assessed at 1 month posttreatment for success in

530 treating early Lyme disease (Part I) and at 1 year posttreatment for success in preventing the  
 531 progression to the sequelae of late Lyme disease (Part II).

532 A total of 355 adult subjects (181 treated with cefuroxime axetil and 174 treated with  
 533 doxycycline) were randomized in the 2 trials, with diagnosis of early Lyme disease confirmed in  
 534 79% (281/355). The clinical diagnosis of early Lyme disease in these subjects was validated by  
 535 1) blinded expert reading of photographs, when available, of the pretreatment erythema migrans  
 536 skin lesion, and 2) serologic confirmation (using enzyme-linked immunosorbent assay [ELISA]  
 537 and immunoblot assay [“Western” blot]) of the presence of antibodies specific to *Borrelia*  
 538 *burgdorferi*, the etiologic agent of Lyme disease. The efficacy data in Table 13 are specific to  
 539 this “validated” patient subset, while the safety data below reflect the entire patient population  
 540 for the 2 trials. Clinical data for evaluable subjects in the “validated” patient subset are shown in  
 541 Table 13.

542 **Table 13. Clinical Effectiveness of CEFTIN Tablets Compared with Doxycycline in the**  
 543 **Treatment of Early Lyme Disease**

	Part I (1 Month after 20 Days of Treatment) <sup>a</sup>		Part II (1 Year after 20 Days of Treatment) <sup>b</sup>	
	CEFTIN 500 mg Twice Daily (n = 125)	Doxycycline 100 mg 3 Times Daily (n = 108)	CEFTIN 500 mg Twice Daily (n = 105 <sup>c</sup> )	Doxycycline 100 mg 3 Times Daily (n = 83 <sup>c</sup> )
Satisfactory clinical outcome <sup>d</sup>	91%	93%	84%	87%
Clinical cure/success	72%	73%	73%	73%
Clinical improvement	19%	19%	10%	13%

544 <sup>a</sup> 95% confidence interval around the satisfactory difference for Part I (-0.08, +0.05).

545 <sup>b</sup> 95% confidence interval around the satisfactory difference for Part II (-0.13, +0.07).

546 <sup>c</sup> n’s include subjects assessed as unsatisfactory clinical outcomes (failure + recurrence) in  
 547 Part I (CEFTIN - 11 [5 failure, 6 recurrence]; doxycycline - 8 [6 failure, 2 recurrence]).

548 <sup>d</sup> Satisfactory clinical outcome includes cure + improvement (Part I) and success +  
 549 improvement (Part II).

550 CEFTIN and doxycycline were effective in prevention of the development of sequelae of late  
 551 Lyme disease.

552 While the incidence of drug-related gastrointestinal adverse reactions was similar in the  
 553 2 treatment groups (cefuroxime axetil - 13%; doxycycline - 11%), the incidence of drug-related  
 554 diarrhea was higher in the cefuroxime axetil arm versus the doxycycline arm (11% versus 3%,  
 555 respectively).

556 **15 REFERENCES**

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572 Valley Road, Suite 2500, Wayne, Pennsylvania 19087, USA.

573 **16 HOW SUPPLIED/STORAGE AND HANDLING**

574 CEFTIN tablets, 250 mg of cefuroxime (as cefuroxime axetil), are white, capsule-shaped,  
575 film-coated tablets engraved with "GX ES7" on one side and blank on the other side as follows:

576 20 Tablets/Bottle           NDC 0173-0387-00

577 CEFTIN tablets, 500 mg of cefuroxime (as cefuroxime axetil), are white, capsule-shaped,  
578 film-coated tablets engraved with "GX EG2" on one side and blank on the other side as follows:

579 20 Tablets/Bottle           NDC 0173-0394-00

580 **Store the tablets between 15° and 30°C (59° and 86°F). Replace cap securely after each**  
581 **opening.**

582 CEFTIN for oral suspension is provided as dry, white to off-white, tutti-frutti–flavored powder.  
583 When reconstituted as directed, the suspension provides the equivalent of 125 mg or 250 mg of  
584 cefuroxime (as cefuroxime axetil) per 5 mL. It is supplied in amber glass bottles as follows:

585 **125 mg/5 mL:**

586 100-mL Suspension       NDC 0173-0740-00

587 **250 mg/5 mL:**

588 50-mL Suspension       NDC 0173-0741-10

589 100-mL Suspension       NDC 0173-0741-00

590 **Before reconstitution, store dry powder between 2° and 30°C (36° and 86°F).**  
591 **After reconstitution, immediately store suspension refrigerated between 2° and 8°C (36°**  
592 **and 46°F). DISCARD AFTER 10 DAYS.**

## 593 **17 PATIENT COUNSELING INFORMATION**

### 594 Allergic Reactions

595 Inform patients that CEFTIN is a cephalosporin that can cause allergic reactions in some  
596 individuals [*see Warnings and Precautions (5.1)*].

### 597 Clostridium difficile-Associated Diarrhea

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

### 603 Phenylketonuria

604 Inform patients and caregivers that CEFTIN for oral suspension contains phenylalanine (a  
605 component of aspartame) [*see Warnings and Precautions (5.5)*].

### 606 Crushing Tablets

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

### 609 Oral Suspension

610 Instruct patients to shake the oral suspension well before each use, store in the refrigerator, and  
611 discard after 10 days. The oral suspension should be taken with food.

### 612 Drug Resistance

613 Inform patients that antibacterial drugs, including CEFTIN, should only be used to treat bacterial  
614 infections. They do not treat viral infections (e.g., the common cold). When CEFTIN is  
615 prescribed to treat a bacterial infection, inform patients that although it is common to feel better  
616 early in the course of therapy, the medication should be taken exactly as directed. Skipping doses  
617 or not completing the full course of therapy may: (1) decrease the effectiveness of the immediate  
618 treatment, and (2) increase the likelihood that bacteria will develop resistance and will not be  
619 treatable by CEFTIN or other antibacterial drugs in the future.

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