

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

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 and secondary bacterial infections of acute 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)
Adults and Adolescents (13 years and older)		
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
Secondary bacterial infections of acute bronchitis	250 or 500 mg every 12 hours	5 to 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
Early Lyme disease	500 mg every 12 hours	20
Pediatric Patients younger than 13 years (who can swallow tablets whole)		
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 ^a	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

^a 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 β -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.

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)
- Co-administration with probenecid increases systemic exposure to CEFTIN and is therefore not recommended. (7.3)

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 8/2015

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 and Secondary Bacterial Infections of Acute 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)
- 1.9 Impetigo
- 1.10 Usage

2 DOSAGE AND ADMINISTRATION

- 2.1 Important Administration Instructions
- 2.2 Dosage for CEFTIN Tablets
- 2.3 Dosage for CEFTIN for Oral Suspension
- 2.4 Preparation and Administration of CEFTIN for Oral Suspension
- 2.5 Dosage in Patients with Impaired Renal Function

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
- 5.5 Phenylketonuria
- 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
- 7.4 Drug/Laboratory Test Interactions
- 8 USE IN SPECIFIC POPULATIONS**
- 8.1 Pregnancy
- 8.3 Nursing Mothers
- 8.4 Pediatric Use
- 8.5 Geriatric Use
- 8.6 Renal Impairment

- 10 OVERDOSAGE**
- 11 DESCRIPTION**
- 12 CLINICAL PHARMACOLOGY**
- 12.1 Mechanism of Action
- 12.3 Pharmacokinetics
- 12.4 Microbiology
- 13 NONCLINICAL TOXICOLOGY**
- 13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
- 14 CLINICAL STUDIES**
- 14.1 Acute Bacterial Maxillary Sinusitis
- 14.2 Early Lyme Disease
- 14.3 Secondary Bacterial Infections of Acute Bronchitis
- 15 REFERENCES**
- 16 HOW SUPPLIED/STORAGE AND HANDLING**
- 17 PATIENT COUNSELING INFORMATION**
- *Sections or subsections omitted from the full prescribing information are not listed.

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 β -lactamase-producing strains), *Moraxella*
19 *catarrhalis* (including β -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 β -lactamase-producing strains), *Moraxella*
23 *catarrhalis* (including β -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- β -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- β -lactamase-producing strains
32 only).

33 Limitations of Use

34 The effectiveness of CEFTIN for sinus infections caused by β -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 and Secondary** 39 **Bacterial Infections of Acute Bronchitis**

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

45 **1.5 Uncomplicated Skin and Skin-structure Infections**

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

49 **1.6 Uncomplicated Urinary Tract Infections**

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

53 **1.7 Uncomplicated Gonorrhea**

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

59 **1.8 Early Lyme Disease (erythema migrans)**

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

63 **1.9 Impetigo**

64 CEFTIN for oral suspension is indicated for the treatment of pediatric patients aged 3 months to
65 12 years with impetigo caused by susceptible strains of *Staphylococcus aureus* (including β -
66 lactamase-producing strains) or *Streptococcus pyogenes*.

67 **1.10 Usage**

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

74 **2 DOSAGE AND ADMINISTRATION**

75 **2.1 Important Administration Instructions**

- 76 • CEFTIN tablets and CEFTIN for oral suspension are not bioequivalent and are therefore not
77 substitutable on a milligram-per-milligram basis [see *Clinical Pharmacology (12.3)*].
- 78 • Administer CEFTIN tablets or oral suspension as described in the appropriate dosage
79 guidelines [see *Dosage and Administration (2.2, 2.3, 2.4)*].
- 80 • Administer CEFTIN tablets with or without food.
- 81 • Administer CEFTIN for oral suspension with food.

- 82 • Pediatric patients (aged 13 years and older) who cannot swallow the CEFTIN tablets whole
83 should receive CEFTIN for oral suspension because the tablet has a strong, persistent bitter
84 taste when crushed [*see Dosage and Administration (2.2)*].

85 2.2 Dosage for CEFTIN Tablets

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

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

Infection	Dosage	Duration (Days)
Adults and Adolescents (13 years and older)		
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 ^a
Secondary bacterial infections of acute bronchitis	250 or 500 mg every 12 hours	5 to 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
Early Lyme disease	500 mg every 12 hours	20
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

89 ^a The safety and effectiveness of CEFTIN administered for less than 10 days in patients with
90 acute exacerbations of chronic bronchitis have not been established.

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

93 2.3 Dosage for CEFTIN for Oral Suspension

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

96 **Table 2. Pediatric Patients (3 months to 12 years) Dosage Guidelines for CEFTIN for Oral**
 97 **Suspension**

Infection	Recommended Daily Dose^a	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	30 mg/kg	1,000 mg	10
Impetigo	30 mg/kg	1,000 mg	10

98 ^a Recommended daily dose given twice daily divided in equal doses.

99 **2.4 Preparation and Administration of CEFTIN for Oral Suspension**

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

- 101 1. Shake the bottle to loosen the powder.
- 102 2. Remove the cap.
- 103 3. Add the total amount of water for reconstitution (Table 3) and replace the cap.
- 104 4. Invert the bottle and vigorously rock the bottle from side to side so that water rises through
105 the powder.
- 106 5. Once the sound of the powder against the bottle disappears, turn the bottle upright and
107 vigorously shake it in a diagonal direction.

108 **Table 3. Amount of Water Required for Reconstitution of Labeled Volumes of CEFTIN for**
 109 **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

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

114 **2.5 Dosage in Patients with Impaired Renal Function**

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

118 **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

119 **3 DOSAGE FORMS AND STRENGTHS**

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

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

126 CEFTIN for oral suspension is provided as dry, white to off-white, tutti-frutti–flavored powder.
127 When reconstituted as directed, the suspension provides the equivalent of 125 mg or 250 mg of
128 cefuroxime (as cefuroxime axetil) per 5 mL.

129 **4 CONTRAINDICATIONS**

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

132 **5 WARNINGS AND PRECAUTIONS**

133 **5.1 Anaphylactic Reactions**

134 Serious and occasionally fatal hypersensitivity (anaphylactic) reactions have been reported in
135 patients on β-lactam antibacterials. These reactions are more likely to occur in individuals with a
136 history of β-lactam hypersensitivity and/or a history of sensitivity to multiple allergens. There
137 have been reports of individuals with a history of penicillin hypersensitivity who have
138 experienced severe reactions when treated with cephalosporins. CEFTIN is contraindicated in
139 patients with a known hypersensitivity to CEFTIN or other β-lactam antibacterial drugs [*see*
140 *Contraindications (4)*].

141 Before initiating therapy with CEFTIN, inquire about previous hypersensitivity reactions to
142 penicillins, cephalosporins, or other allergens. If an allergic reaction occurs, discontinue CEFTIN
143 and institute appropriate therapy.

144 **5.2 Clostridium difficile-associated Diarrhea**

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

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

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

159 **5.3 Potential for Microbial Overgrowth**

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

162 **5.4 Development of Drug-resistant Bacteria**

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

166 **5.5 Phenylketonuria**

167 CEFTIN for oral suspension 125 mg/5 mL contains phenylalanine 11.8 mg per 5 mL
168 (1 teaspoonful) of reconstituted suspension. CEFTIN for oral suspension 250 mg/5 mL contains
169 phenylalanine 25.2 mg per 5 mL (1 teaspoonful) of reconstituted suspension.

170 **5.6 Interference with Glucose Tests**

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

174 **6 ADVERSE REACTIONS**

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

177 Anaphylactic Reactions [see Warnings and Precautions [5.1]]

178 **6.1 Clinical Trials Experience**

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

182 Tablets

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

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

194 **Table 5. Adverse Reactions (≥1%) after Multiple-dose Regimens with CEFTIN Tablets**

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

195

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

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

199 *Metabolism and Nutrition Disorders:* Anorexia.

200 *Nervous System Disorders:* Headache.

201 *Cardiac Disorders:* Chest pain.

202 *Respiratory Disorders:* Shortness of breath.

203 *Gastrointestinal Disorders:* Abdominal pain, abdominal cramps, flatulence,
204 indigestion, mouth ulcers.

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

206 *Renal and Urinary Disorders:* Dysuria.

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

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

209 *Investigations:* Positive Coombs' test.

210 *5-Day Regimen:* In clinical trials using CEFTIN 250 mg twice daily in the treatment of
211 secondary bacterial infections of acute bronchitis, 399 subjects were treated for 5 days and
212 402 subjects were treated for 10 days. No difference in the occurrence of adverse reactions was
213 found between the 2 regimens.

214 *Early Lyme Disease with 20-Day Regimen:* Two multicenter trials assessed CEFTIN 500 mg
215 twice daily for 20 days. The most common drug-related adverse experiences were diarrhea
216 (10.6%), Jarisch-Herxheimer reaction (5.6%), and vaginitis (5.4%). Other adverse experiences
217 occurred with frequencies comparable to those reported with 7 to 10 days' dosing.

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

220 The adverse reactions in Table 6 were for subjects treated with a single dose of 1,000 mg
221 CEFTIN in US clinical trials.

222

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

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

225
 226 The following adverse reactions occurred in less than 1% but greater than 0.1% of subjects
 227 (n = 1,061) treated with a single dose of CEFTIN 1,000 mg for uncomplicated gonorrhea in US
 228 clinical trials.

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

238 **Oral Suspension**

239 In clinical trials using multiple doses of CEFTIN, pediatric subjects (96.7% were younger than
 240 12 years) were treated with CEFTIN (20 to 30 mg/kg/day divided twice daily up to a maximum
 241 dose of 500 or 1,000 mg/day, respectively). Eleven (1.2%) US subjects discontinued medication
 242 due to adverse reactions. The discontinuations were primarily for gastrointestinal disturbances,
 243 usually diarrhea or vomiting. Thirteen (1.4%) US pediatric subjects discontinued therapy due to
 244 the taste and/or problems with drug administration.

245 The adverse reactions in Table 7 are for US subjects (n = 931) treated with CEFTIN in
 246 multiple-dose clinical trials.

247 **Table 7. Adverse Reactions ($\geq 1\%$) after Multiple-dose Regimens with CEFTIN for Oral**
 248 **Suspension**

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

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

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

253 *Blood and Lymphatic System Disorders:* Eosinophilia.

254 *Psychiatric Disorders:* Hyperactivity, irritable behavior.

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

256 *Skin and Subcutaneous Tissue Disorders:* Rash.

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

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

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

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

261 **6.2 Postmarketing Experience**

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

266 Blood and Lymphatic System Disorders

267 Hemolytic anemia, leukopenia, pancytopenia, thrombocytopenia.

268 Gastrointestinal Disorders

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

270 Hepatobiliary Disorders

271 Hepatic impairment including hepatitis and cholestasis, jaundice.

272 Immune System Disorders

273 Anaphylaxis, serum sickness-like reaction.

274 Investigations

275 Increased prothrombin time.

276 Nervous System Disorders

277 Seizure, encephalopathy.

278 Renal and Urinary Disorders

279 Renal dysfunction.

280 Skin and Subcutaneous Tissue Disorders

281 Angioedema, erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis,
282 urticaria.

283 **7 DRUG INTERACTIONS**

284 **7.1 Oral Contraceptives**

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

288 **7.2 Drugs that Reduce Gastric Acidity**

289 Drugs that reduce gastric acidity may result in a lower bioavailability of CEFTIN compared with
290 administration in the fasting state. Administration of drugs that reduce gastric acidity may negate
291 the food effect of increased absorption of CEFTIN when administered in the postprandial state.
292 Administer CEFTIN at least 1 hour before or 2 hours after administration of short-acting
293 antacids. Histamine-2 (H₂) antagonists and proton pump inhibitors should be avoided.

294 **7.3 Probenecid**

295 Concomitant administration of probenecid with cefuroxime axetil tablets increases serum
296 concentrations of cefuroxime [see *Clinical Pharmacology (12.3)*]. Co-administration of
297 probenecid with cefuroxime axetil is not recommended.

298 **7.4 Drug/Laboratory Test Interactions**

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

305 **8 USE IN SPECIFIC POPULATIONS**

306 **8.1 Pregnancy**

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

310 Reproduction studies have been performed in mice at doses up to 3,200 mg/kg/day (14 times the
311 recommended maximum human dose based on body surface area) and in rats at doses up to
312 1,000 mg/kg/day (9 times the recommended maximum human dose based on body surface area)
313 and have revealed no evidence of impaired fertility or harm to the fetus due to cefuroxime axetil.

314 **8.3 Nursing Mothers**

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

317 **8.4 Pediatric Use**

318 The safety and effectiveness of CEFTIN have been established for pediatric patients aged
319 3 months to 12 years for acute bacterial maxillary sinusitis based upon its approval in adults. Use
320 of CEFTIN in pediatric patients is supported by pharmacokinetic and safety data in adults and
321 pediatric patients, and by clinical and microbiological data from adequate and well-controlled
322 trials of the treatment of acute bacterial maxillary sinusitis in adults and of acute otitis media
323 with effusion in pediatric patients. It is also supported by postmarketing adverse events
324 surveillance. [*See Indications and Usage (1), Dosage and Administration (2), Adverse Reactions*
325 *(6), Clinical Pharmacology (12.3).*]

326 **8.5 Geriatric Use**

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

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

336 **8.6 Renal Impairment**

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

340 **10 OVERDOSAGE**

341 Overdosage of cephalosporins can cause cerebral irritation leading to convulsions or
342 encephalopathy. Serum levels of cefuroxime can be reduced by hemodialysis and peritoneal
343 dialysis.

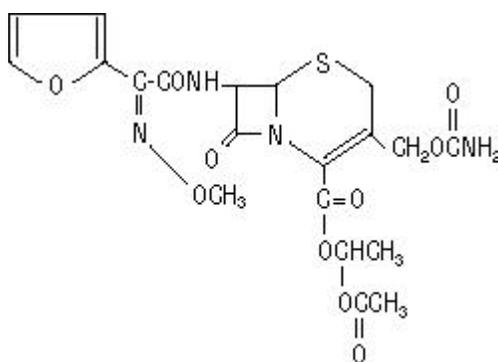
344 **11 DESCRIPTION**

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

347 The chemical name of cefuroxime axetil (1-(acetyloxy) ethyl ester of cefuroxime) is (RS)-1-
348 hydroxyethyl (6R,7R)-7-[2-(2-furyl)glyoxyl-amido]-3-(hydroxymethyl)-8-oxo-5-thia-1-
349 azabicyclo[4.2.0]-oct-2-ene-2-carboxylate, 7²-(Z)-(O-methyl-oxime), 1-acetate 3-carbamate. Its
350 molecular formula is C₂₀H₂₂N₄O₁₀S, and it has a molecular weight of 510.48.

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

352



353

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

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

363 **12 CLINICAL PHARMACOLOGY**

364 **12.1 Mechanism of Action**

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

366 **12.3 Pharmacokinetics**

367 Absorption

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

372 **Table 8. Pharmacokinetics of Cefuroxime Administered in the Postprandial State as**
373 **CEFTIN Tablets to Adults^a**

Dose^b (Cefuroxime Equivalent)	Peak Plasma Concentration (mcg/mL)	Time of Peak Plasma Concentration (h)	Mean Elimination Half-life (h)	AUC (mcg•h/mL)
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

374 ^a Mean values of 12 healthy adult volunteers.

375 ^b Drug administered immediately after a meal.

376 *Food Effect:* Absorption of the tablet is greater when taken after food (absolute bioavailability
377 increases from 37% to 52%). Despite this difference in absorption, the clinical and bacteriologic
378 responses of subjects were independent of food intake at the time of tablet administration in
379 2 trials where this was assessed.

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

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

389 Distribution

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

392 Metabolism

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

394 **Excretion**

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

399 **Specific Populations**

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

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

406 **Table 9. Pharmacokinetics of Cefuroxime Administered in the Postprandial State as**
407 **CEFTIN for Oral Suspension to Pediatric Subjects^a**

Dose^b (Cefuroxime Equivalent)	n	Peak Plasma Concentration (mcg/mL)	Time of Peak Plasma Concentration (h)	Mean Elimination Half-life (h)	AUC (mcg•h/mL)
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

408 ^a Mean age = 23 months.

409 ^b Drug administered with milk or milk products.

410 *Geriatric Patients:* In a trial of 20 elderly subjects (mean age = 83.9 years) having a mean
411 creatinine clearance of 34.9 mL/min, the mean serum elimination half-life was prolonged to
412 3.5 hours; however, despite the lower elimination of cefuroxime in geriatric patients, dosage
413 adjustment based on age is not necessary [see *Use in Specific Populations (8.5)*].

414 **Drug Interactions**

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

418 **12.4 Microbiology**

419 Mechanism of Action

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

423 Mechanism of Resistance

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

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

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

- 432 • Gram-positive bacteria
- 433 *Staphylococcus aureus* (methicillin-susceptible isolates only)
- 434 *Streptococcus pneumoniae*
- 435 *Streptococcus pyogenes*
- 436 • Gram-negative bacteria
- 437 *Escherichia coli*^a
- 438 *Klebsiella pneumoniae*^a
- 439 *Haemophilus influenzae*
- 440 *Haemophilus parainfluenzae*
- 441 *Moraxella catarrhalis*
- 442 *Neisseria gonorrhoeae*

443 ^a Most extended spectrum β -lactamase (ESBL)-producing and carbapenemase-producing
444 isolates are resistant to cefuroxime axetil.

- 445 • Spirochetes
- 446 *Borrelia burgdorferi*

447 The following in vitro data are available, but their clinical significance is unknown. At least
448 90 percent of the following microorganisms exhibit an in vitro minimum inhibitory concentration
449 (MIC) less than or equal to the susceptible breakpoint for cefuroxime axetil of 1 mcg/mL.

450 However, the efficacy of cefuroxime axetil in treating clinical infections due to these
451 microorganisms has not been established in adequate and well-controlled clinical trials.

- 452 • Gram-positive bacteria
- 453 *Staphylococcus epidermidis* (methicillin-susceptible isolates only)

454 *Staphylococcus saprophyticus* (methicillin-susceptible isolates only)

455 *Streptococcus agalactiae*

456 • Gram-negative bacteria

457 *Morganella morganii*

458 *Proteus inconstans*

459 *Proteus mirabilis*

460 *Providencia rettgeri*

461 • Anaerobic bacteria

462 *Peptococcus niger*

463 Susceptibility Test Methods

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

469 *Dilution Techniques:* Quantitative methods are used to determine antimicrobial MICs. These
470 MICs provide reproducible estimates of the susceptibility of bacteria to antimicrobial
471 compounds. The MICs should be determined using a standardized test method (broth or agar).^{1,2}
472 The MIC values should be interpreted according to criteria provided in Table 10.^{2,3}

473 *Diffusion Techniques:* Quantitative methods that require measurement of zone diameters also
474 provide reproducible estimates of the susceptibility of bacteria to antimicrobial compounds. The
475 zone size provides an estimate of the susceptibility of bacteria to antimicrobial compounds. The
476 zone size should be determined using a standardized test method.⁴ This procedure uses paper
477 disks impregnated with 30 mcg cefuroxime axetil to test the susceptibility of microorganisms to
478 cefuroxime axetil. The disk diffusion interpretive criteria are provided in Table 10.³

479 **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> ^a	≤4	8 - 16	≥32	≥23	15 - 22	≤14
<i>Haemophilus</i> spp. ^{a,b}	≤4	8	≥16	≥20	17 - 19	≤16
<i>Moraxella catarrhalis</i> ^a	≤4	8	≥16	-	-	-
<i>Streptococcus pneumoniae</i>	≤1	2	≥4	-	-	-

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

483 ^b *Haemophilus* spp. includes only isolates of *H. influenzae* and *H. parainfluenzae*.

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

486 Susceptibility of *Streptococcus pyogenes* may be deduced from testing penicillin.³

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

498 **Quality Control:** Standardized susceptibility test procedures require the use of laboratory
499 controls to monitor and ensure the accuracy and precision of supplies and reagents used in the
500 assay, and the techniques of the individual performing the test.^{1,2,4} The QC ranges for MIC and
501 disk diffusion testing using the 30-mcg disk are provided in Table 11.³
502

503 **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

504 ATCC = American Type Culture Collection.

505 **13 NONCLINICAL TOXICOLOGY**

506 **13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility**

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

513 **14 CLINICAL STUDIES**

514 **14.1 Acute Bacterial Maxillary Sinusitis**

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

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

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

	US Subjects ^a		South American Subjects ^b	
	CEFTIN 250 mg Twice Daily (n = 49)	Control ^c (n = 43)	CEFTIN 250 mg Twice Daily (n = 49)	Control ^c (n = 43)
Clinical success (cure + improvement)	65%	53%	77%	74%
Clinical cure	53%	44%	72%	64%
Clinical improvement	12%	9%	5%	10%

530 ^a 95% confidence interval around the success difference [-0.08, +0.32].

531 ^b 95% confidence interval around the success difference [-0.10, +0.16].

532 ^c Control was an antibacterial drug containing a β-lactamase inhibitor.

533 In this trial and in a supporting maxillary puncture trial, 15 evaluable subjects had non-
 534 β-lactamase-producing *Haemophilus influenzae* as the identified pathogen. Of these, 67%
 535 (10/15) had this pathogen eradicated. Eighteen (18) evaluable subjects had *Streptococcus*
 536 *pneumoniae* as the identified pathogen. Of these, 83% (15/18) had this pathogen eradicated.

537 **14.2 Early Lyme Disease**

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

543 A total of 355 adult subjects (181 treated with cefuroxime axetil and 174 treated with
 544 doxycycline) were randomized in the 2 trials, with diagnosis of early Lyme disease confirmed in
 545 79% (281/355). The clinical diagnosis of early Lyme disease in these subjects was validated by
 546 1) blinded expert reading of photographs, when available, of the pretreatment erythema migrans
 547 skin lesion, and 2) serologic confirmation (using enzyme-linked immunosorbent assay [ELISA]
 548 and immunoblot assay [“Western” blot]) of the presence of antibodies specific to *Borrelia*
 549 *burgdorferi*, the etiologic agent of Lyme disease. The efficacy data in Table 14 are specific to
 550 this “validated” patient subset, while the safety data below reflect the entire patient population
 551 for the 2 trials. Clinical data for evaluable subjects in the “validated” patient subset are shown in
 552 Table 13.

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

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

555 ^a 95% confidence interval around the satisfactory difference for Part I (-0.08, +0.05).
 556 ^b 95% confidence interval around the satisfactory difference for Part II (-0.13, +0.07).
 557 ^c n's include subjects assessed as unsatisfactory clinical outcomes (failure + recurrence) in
 558 Part I (CEFTIN - 11 [5 failure, 6 recurrence]; doxycycline - 8 [6 failure, 2 recurrence]).
 559 ^d Satisfactory clinical outcome includes cure + improvement (Part I) and success +
 560 improvement (Part II).

561 CEFTIN and doxycycline were effective in prevention of the development of sequelae of late
 562 Lyme disease.

563 While the incidence of drug-related gastrointestinal adverse reactions was similar in the
 564 2 treatment groups (cefuroxime axetil - 13%; doxycycline - 11%), the incidence of drug-related
 565 diarrhea was higher in the cefuroxime axetil arm versus the doxycycline arm (11% versus 3%,
 566 respectively).

567 **14.3 Secondary Bacterial Infections of Acute Bronchitis**

568 Four randomized, controlled clinical trials were performed comparing 5 days versus 10 days of
 569 CEFTIN for the treatment of subjects with secondary bacterial infections of acute bronchitis.
 570 These trials enrolled a total of 1,253 subjects (Study 1 n = 360; Study 2 n = 177; Study 3
 571 n = 362; Study 4 n = 354). The protocols for Study 1 and Study 2 were identical and compared
 572 CEFTIN 250 mg twice daily for 5 days, CEFTIN 250 mg twice daily for 10 days, and
 573 AUGMENTIN[®] (amoxicillin/clavulanate potassium) 500 mg 3 times daily for 10 days. These
 574 2 trials were conducted simultaneously. Study 3 and Study 4 compared CEFTIN 250 mg twice
 575 daily for 5 days, CEFTIN 250 mg twice daily for 10 days, and CECLOR[®] (cefaclor) 250 mg 3
 576 times daily for 10 days. They were otherwise identical to Study 1 and Study 2 and were
 577 conducted over the following 2 years. Subjects were required to have polymorphonuclear cells
 578 present on the Gram stain of their screening sputum specimen, but isolation of a bacterial
 579 pathogen from the sputum culture was not required for inclusion.

580 Table 14 demonstrates the results of the clinical outcome analysis of the pooled trials Study
581 1/Study 2 and Study 3/Study 4, respectively.

582 **Table 14. Clinical Effectiveness of CEFTIN Tablets 250 mg Twice Daily in Secondary**
583 **Bacterial Infections of Acute Bronchitis: Comparison of 5 versus 10 Days' Treatment**
584 **Duration**

	Study 1 and Study 2 ^a		Study 3 and Study 4 ^b	
	5 Day (n = 127)	10 Day (n = 139)	5 Day (n = 173)	10 Day (n = 192)
Clinical success (cure + improvement)	80%	87%	84%	82%
Clinical cure	61%	70%	73%	72%
Clinical improvement	19%	17%	11%	10%

585 ^a 95% confidence interval around the success difference [-0.164, +0.029].

586 ^b 95% confidence interval around the success difference [-0.061, +0.103].

587 The response rates for subjects who were both clinically and bacteriologically evaluable were
588 consistent with those reported for the clinically evaluable subjects.

589 15 REFERENCES

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604 2015. CLSI document M02-A12, Clinical and Laboratory Standards Institute, 950 West
605 Valley Road, Suite 2500, Wayne, Pennsylvania 19087, USA.

606 16 HOW SUPPLIED/STORAGE AND HANDLING

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

609 20 Tablets/Bottle NDC 0173-0387-00
610 CEFTIN tablets, 500 mg of cefuroxime (as cefuroxime axetil), are white, capsule-shaped,
611 film-coated tablets engraved with "GX EG2" on one side and blank on the other side as follows:

612 20 Tablets/Bottle NDC 0173-0394-00

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

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

618 **125 mg/5 mL:**

619 100-mL Suspension NDC 0173-0740-00

620 **250 mg/5 mL:**

621 50-mL Suspension NDC 0173-0741-10

622 100-mL Suspension NDC 0173-0741-00

623 **Before reconstitution, store dry powder between 2° and 30°C (36° and 86°F).**

624 **After reconstitution, immediately store suspension refrigerated between 2° and 8°C (36°**
625 **and 46°F). DISCARD AFTER 10 DAYS.**

626 **17 PATIENT COUNSELING INFORMATION**

627 Allergic Reactions

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

630 Clostridium difficile-associated Diarrhea

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

636 Phenylketonuria

637 Inform patients and caregivers that CEFTIN for oral suspension contains phenylalanine (a
638 component of aspartame) [*see Warnings and Precautions (5.6)*].

639

640

641 Crushing Tablets

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

644 Oral Suspension

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

647 Drug Resistance

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

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657 GSK group of companies. The makers of these brands are not affiliated with and do not endorse
658 the GSK group of companies or its products.

659



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661 GlaxoSmithKline

662 Research Triangle Park, NC 27709

663

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665 CFT: 4PI