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

---------- ADVERSE REACTIONS ----------

The most common adverse reactions (≥3%) for CEFTIN tablets are diarrhea, nausea/vomiting, Jarisch-Herxheimer reaction, and vaginitis (early Lyme disease). (6.1)

The most common adverse reactions (≥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----------

- Drugs that reduce gastric acidity may lower the bioavailability of CEFTIN. (7.1)
- Coadministration with probenecid increases systemic exposure to CEFTIN and is therefore not recommended. (7.2)

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 3/2021

FULL PRESCRIBING INFORMATION: CONTENTS*

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

1.1 Pharyngitis/Tonsillitis

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

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

Limitations of Use

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

1.2 Acute Bacterial Otitis Media

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

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

1.3 Acute Bacterial Maxillary Sinusitis

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

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

Limitations of Use

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

1.4 Acute Bacterial Exacerbations of Chronic Bronchitis

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

1.5 Uncomplicated Skin and Skin-Structure Infections

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

1.6 Uncomplicated Urinary Tract Infections

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

1.7 Uncomplicated Gonorrhea

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

1.8 Early Lyme Disease (erythema migrans)

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

1.9 Impetigo

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

1.10 Usage

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 susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

2 DOSAGE AND ADMINISTRATION

2.1 Important Administration Instructions

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

2.2 Dosage for CEFTIN Tablets

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

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]
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

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

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

2.3 Dosage for CEFTIN for Oral Suspension

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

Table 2. 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	30 mg/kg	1,000 mg	10
Impetigo	30 mg/kg	1,000 mg	10

[a] Recommended daily dose given twice daily divided in equal doses.

2.4 Preparation and Administration of CEFTIN for Oral Suspension

Prepare a suspension at the time of dispensing as follows:

1. Shake the bottle to loosen the powder.
2. Remove the cap.
3. Add the total amount of cold water for reconstitution (Table 3) and replace the cap.
4. Invert the bottle and vigorously rock the bottle from side to side so that water rises through the powder.
5. Once the sound of the powder against the bottle disappears, turn the bottle upright and vigorously shake it in a diagonal direction for at least one minute.
6. After reconstitution, wait one hour before administering suspension to a patient.

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

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

2.5 Dosage in Patients with Impaired Renal Function

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

Table 4. Dosing in Adults with Renal Impairment

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

3 DOSAGE FORMS AND STRENGTHS

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

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

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

4 CONTRAINDICATIONS

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

5 WARNINGS AND PRECAUTIONS

5.1 Anaphylactic Reactions

Serious and occasionally fatal hypersensitivity (anaphylactic) reactions have been reported in patients on β-lactam antibacterials, including CEFTIN *[see Adverse Reactions (6.2)]*. These reactions are more likely to occur in individuals with a history of β-lactam hypersensitivity and/or a history of sensitivity to multiple allergens. There have been reports of individuals with a

history of penicillin hypersensitivity who have experienced severe reactions when treated with cephalosporins. CEFTIN is contraindicated in patients with a known hypersensitivity to CEFTIN or other β-lactam antibacterial drugs *[see Contraindications (4)]*. Before initiating therapy with CEFTIN, inquire about previous hypersensitivity reactions to penicillins, cephalosporins, or other allergens. If an allergic reaction occurs, discontinue CEFTIN and institute appropriate therapy.

5.2 *Clostridioides difficile*-Associated Diarrhea

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

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

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

5.3 Potential for Microbial Overgrowth

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

5.4 Development of Drug-Resistant Bacteria

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

5.5 Phenylketonuria

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

5.6 Interference with Glucose Tests

A false-positive result for glucose in the urine may occur with copper reduction tests, and a false-negative result for blood/plasma glucose may occur with ferricyanide tests in subjects receiving CEFTIN *[see Drug Interactions (7.3)]*.

6 ADVERSE REACTIONS

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

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

6.1 Clinical Trials Experience

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

Tablets

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

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

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%

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

Immune System Disorders: Hives, swollen tongue.

Metabolism and Nutrition Disorders: Anorexia.

Nervous System Disorders: Headache.

Cardiac Disorders: Chest pain.

Respiratory Disorders: Shortness of breath.

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

Skin and Subcutaneous Tissue Disorders: Rash, itch.

Renal and Urinary Disorders: Dysuria.

Reproductive System and Breast Disorders: Vaginitis, vulvar itch.

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

Investigations: Positive Coombs' test.

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

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

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

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

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

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

Infections and Infestations: Vaginal candidiasis.

Nervous System Disorders: Headache, dizziness, somnolence.

Cardiac Disorders: Tightness/pain in chest, tachycardia.

Gastrointestinal Disorders: Abdominal pain, dyspepsia.

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

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

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

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

Oral Suspension

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

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

Table 7. Adverse Reactions (≥1%) after Multiple-Dose Regimens with CEFTIN for Oral 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%

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

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

Blood and Lymphatic System Disorders: Eosinophilia.

Psychiatric Disorders: Hyperactivity, irritable behavior.

Gastrointestinal Disorders: Abdominal pain, flatulence, ptyalism.

Skin and Subcutaneous Tissue Disorders: Rash.

Musculoskeletal and Connective Tissue Disorders: Joint swelling, arthralgia.

Reproductive System and Breast Disorders: Vaginal irritation.

General Disorders and Administration Site Conditions: Cough, fever.

Investigations: Elevated liver enzymes, positive Coombs' test.

6.2 Postmarketing Experience

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

Blood and Lymphatic System Disorders

Hemolytic anemia, leukopenia, pancytopenia, thrombocytopenia.

Gastrointestinal Disorders

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

Hepatobiliary Disorders

Hepatic impairment including hepatitis and cholestasis, jaundice.

Immune System Disorders

Anaphylaxis, serum sickness-like reaction, acute myocardial ischemia with or without myocardial infarction may occur as part of an allergic reaction.

Investigations

Increased prothrombin time.

Nervous System Disorders

Seizure, encephalopathy.

Renal and Urinary Disorders

Renal dysfunction.

Skin and Subcutaneous Tissue Disorders

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

7 DRUG INTERACTIONS

7.1 Drugs that Reduce Gastric Acidity

Drugs that reduce gastric acidity may result in a lower bioavailability of CEFTIN compared with administration in the fasting state. Administration of drugs that reduce gastric acidity may negate the food effect of increased absorption of CEFTIN when administered in the postprandial state. Administer CEFTIN at least 1 hour before or 2 hours after administration of short-acting antacids. Histamine-2 (H_2) antagonists and proton pump inhibitors should be avoided.

7.2 Probenecid

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

7.3 Drug/Laboratory Test Interactions

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

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Available data from published epidemiologic studies, case series, and case reports over several decades with cephalosporin use, including CEFTIN, in pregnant women have not established drug-associated risks of major birth defects, miscarriage, or adverse maternal or fetal outcomes *(see Data)*.

In studies in pregnant mice and rats administered oral cefuroxime axetil during organogenesis at 14 and 9 times the maximum recommended human dose (MRHD) based on body surface area, respectively, there were no adverse developmental outcomes *(see Data)*.

The estimated background risk of major birth defects and miscarriage for the indicated populations are unknown. All pregnancies have a background risk of birth defects, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Clinical Considerations

Disease-Associated Maternal and/or Embryo/Fetal Risk: Maternal gonorrhea may be associated with preterm birth, low neonatal birth weight, chorioamnionitis, intrauterine growth restriction, small for gestational age, and premature rupture of membranes. Perinatal transmission of gonorrhea to the offspring can result in infant blindness, joint infections, and bloodstream infections.

Data

Human Data: While available studies cannot definitively establish the absence of risk, published data from epidemiologic studies, case series, and case reports over several decades have not

identified an association with cephalosporin use (including CEFTIN) during pregnancy and major birth defects, miscarriage, or other adverse maternal or fetal outcomes. Available studies have methodologic limitations, including small sample size, retrospective data collection, and inconsistent comparator groups.

Animal Data: Studies performed with oral cefuroxime axetil administered to pregnant mice during organogenesis (Gestation Days 7 through 16) at doses up to 3,200 mg/kg/day (14 times the MRHD based on body surface area); and in rats dosed during organogenesis and lactation (Gestation Days 7 through 16 and Gestation Days 17 through Lactation Day 21, respectively) at doses up to 1,000 mg/kg/day (9 times the MRHD based on body surface area) have revealed no adverse developmental outcomes.

8.2 Lactation

Risk Summary

Based on several published case reports describing multiple lactating women who received cefuroxime via intravenous, intramuscular, and oral routes, cefuroxime is present in human milk. The highest maternal milk concentration described occurred in lactating women 8 hours after an intramuscular administration of cefuroxime 750 mg. Allowing for an infant milk consumption of 150 mL/kg/day, the estimated breastfed infant dose would be less than 1% of the adult dose. No data are available on the effects of the drug on the breastfed infant or the effects of the drug on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for cefuroxime and any potential adverse effects on the breastfed infant from cefuroxime or from the underlying maternal condition.

8.4 Pediatric Use

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

8.5 Geriatric Use

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

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

8.6 Renal Impairment

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

10 OVERDOSAGE

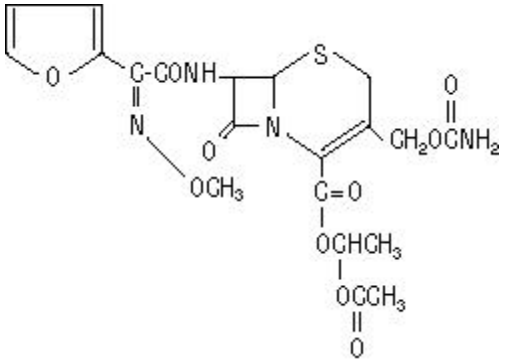
Overdosage of cephalosporins can cause cerebral irritation leading to convulsions or encephalopathy. Serum levels of cefuroxime can be reduced by hemodialysis and peritoneal dialysis.

11 DESCRIPTION

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

The chemical name of cefuroxime axetil (1-(acetyloxy) ethyl ester of cefuroxime) is (*RS*)-1-hydroxyethyl (6*R*,7*R*)-7-[2-(2-furyl)glyoxyl-amido]-3-(hydroxymethyl)-8-oxo-5-thia-1-azabicyclo[4.2.0]-oct-2-ene-2-carboxylate, 7^2-(*Z*)-(*O*-methyl-oxime), 1-acetate 3-carbamate. Its molecular formula is $C_{20}H_{22}N_4O_{10}S$, and it has a molecular weight of 510.48.

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



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

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

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

CEFTIN is an antibacterial drug *[see Microbiology (12.4)]*.

12.3 Pharmacokinetics

Absorption

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

Table 8. Pharmacokinetics of Cefuroxime Administered in the Postprandial State as 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

[a] Mean values of 12 healthy adult volunteers.

[b] Drug administered immediately after a meal.

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

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

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

concentration of the tablets. Therefore, the safety and effectiveness of both the tablet and oral suspension formulations were established in separate clinical trials.

Distribution

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

Metabolism

The axetil moiety is metabolized to acetaldehyde and acetic acid.

Excretion

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

Specific Populations

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

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

Table 9. Pharmacokinetics of Cefuroxime Administered in the Postprandial State as 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

[a] Mean age = 23 months.

[b] Drug administered with milk or milk products.

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

Drug Interaction Studies

Concomitant administration of probenecid with cefuroxime axetil tablets increases the cefuroxime area under the serum concentration versus time curve and maximum serum concentration by 50% and 21%, respectively *[see Drug Interactions (7.2)]*.

12.4 Microbiology

Mechanism of Action

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

Resistance

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

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

Antimicrobial Activity

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

Aerobic Bacteria:

Gram-positive bacteria

- *Staphylococcus aureus* (methicillin-susceptible isolates only)
- *Streptococcus pneumoniae*
- *Streptococcus pyogenes*

Gram-negative bacteria

- *Escherichia coli*[a]
- *Klebsiella pneumoniae*[a]
- *Haemophilus influenzae*
- *Haemophilus parainfluenzae*
- *Moraxella catarrhalis*
- *Neisseria gonorrhoeae*

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

Spirochetes

- *Borrelia burgdorferi*

The following in vitro data are available, but their clinical significance is unknown. At least 90 percent of the following bacteria exhibit an in vitro minimum inhibitory concentration (MIC) less than or equal to the susceptible breakpoint for cefuroxime against isolates of similar genus or organism group. However, the efficacy of cefuroxime axetil in treating clinical infections caused by these bacteria has not been established in adequate and well-controlled clinical trials.

Aerobic Bacteria:

Gram-positive bacteria
- *Staphylococcus epidermidis* (methicillin-susceptible isolates only)
- *Staphylococcus saprophyticus* (methicillin-susceptible isolates only)
- *Streptococcus agalactiae*

Gram-negative bacteria
- *Morganella morganii*
- *Proteus inconstans*
- *Proteus mirabilis*
- *Providencia rettgeri*

Anaerobic Bacteria:
Gram-positive bacteria
- *Peptococcus niger*

Susceptibility Testing

For specific information regarding susceptibility test interpretive criteria and associated test methods and quality control standards recognized by FDA for this drug, please see: https://www.fda.gov/STIC.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Although lifetime studies in animals have not been performed to evaluate carcinogenic potential, no mutagenic activity was found for cefuroxime axetil in a battery of bacterial mutation tests. Positive results were obtained in an in vitro chromosome aberration assay; however, negative results were found in an in vivo micronucleus test at doses up to 1.5 g/kg. Fertility studies in rats (males dosed for 70 days prior to and through mating; females dosed 21 days prior to mating through lactation) at doses up to 1,000 mg/kg/day (9 times the MRHD based on body surface area) have revealed no adverse effects on fertility.

14 CLINICAL STUDIES

14.1 Acute Bacterial Maxillary Sinusitis

One adequate and well-controlled trial was performed in subjects with acute bacterial maxillary sinusitis. In this trial, each subject had a maxillary sinus aspirate collected by sinus puncture

before treatment was initiated for presumptive acute bacterial sinusitis. All subjects had radiographic and clinical evidence of acute maxillary sinusitis. In the trial, the clinical effectiveness of CEFTIN in treating acute maxillary sinusitis was comparable to an oral antimicrobial agent containing a specific β-lactamase inhibitor. However, microbiology data demonstrated CEFTIN to be effective in treating acute bacterial maxillary sinusitis due only to *Streptococcus pneumoniae* or non-β-lactamase–producing *Haemophilus influenzae*. Insufficient numbers of β-lactamase–producing *Haemophilus influenzae* and *Moraxella catarrhalis* isolates were obtained in this trial to adequately evaluate the effectiveness of CEFTIN in treating acute bacterial maxillary sinusitis due to these 2 organisms.

This trial randomized 317 adult subjects, 132 subjects in the U.S. and 185 subjects in South America. Table 10 shows the results of the intent-to-treat analysis.

Table 10. Clinical Effectiveness of CEFTIN Tablets in the Treatment of Acute Bacterial Maxillary Sinusitis

	U.S. 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%

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

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

[c] Control was an antibacterial drug containing a β-lactamase inhibitor.

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

14.2 Early Lyme Disease

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

A total of 355 adult subjects (181 treated with cefuroxime axetil and 174 treated with doxycycline) were randomized in the 2 trials, with diagnosis of early Lyme disease confirmed in 79% (281/355). The clinical diagnosis of early Lyme disease in these subjects was validated by

1) blinded expert reading of photographs, when available, of the pretreatment erythema migrans skin lesion, and 2) serologic confirmation (using enzyme-linked immunosorbent assay [ELISA] and immunoblot assay ["Western" blot]) of the presence of antibodies specific to *Borrelia burgdorferi*, the etiologic agent of Lyme disease. The efficacy data in Table 11 are specific to this "validated" patient subset, while the safety data below reflect the entire patient population for the 2 trials. Clinical data for evaluable subjects in the "validated" patient subset are shown in Table 11.

Table 11. Clinical Effectiveness of CEFTIN Tablets Compared with Doxycycline in the 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%

[a] 95% confidence interval around the satisfactory difference for Part I (-0.08, +0.05).

[b] 95% confidence interval around the satisfactory difference for Part II (-0.13, +0.07).

[c] n's include subjects assessed as unsatisfactory clinical outcomes (failure + recurrence) in Part I (CEFTIN - 11 [5 failure, 6 recurrence]; doxycycline - 8 [6 failure, 2 recurrence]).

[d] Satisfactory clinical outcome includes cure + improvement (Part I) and success + improvement (Part II).

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

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

16 HOW SUPPLIED/STORAGE AND HANDLING

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

20 Tablets/Bottle NDC 0173-0387-00

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

20 Tablets/Bottle NDC 0173-0394-00

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

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

125 mg/5 mL:

100-mL Suspension NDC 0173-0740-00

250 mg/5 mL:

50-mL Suspension NDC 0173-0741-10

100-mL Suspension NDC 0173-0741-00

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

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

17 PATIENT COUNSELING INFORMATION

Allergic Reactions

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

Clostridioides difficile-Associated Diarrhea

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

Phenylketonuria

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

Crushing Tablets

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

Oral Suspension

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

Drug Resistance

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

GlaxoSmithKline

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CFT:XPI