PRODUCT MONOGRAPH

INCLUDING PATIENT MEDICATION INFORMATION

[Pr] CEFTIN

cefuroxime axetil for oral suspension USP
Granules for suspension, 125 mg cefuroxime (supplied as Cefuroxime Axetil) / 5 mL when reconstituted, oral

USP

Antibiotic

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RECENT MAJOR LABEL CHANGES

7 WARNINGS AND PRECAUTIONS, General	06/2024

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Sections or subsections that are not applicable at the time of authorization are not listed.

PART I: HEALTH PROFESSIONAL INFORMATION

1 INDICATIONS

CEFTIN for oral suspension (cefuroxime axetil) is indicated for the treatment of patients with mild to moderately severe infections caused by susceptible strains of the designated organisms in the following diseases:

Upper Respiratory Tract Infections
Pharyngitis and tonsillitis caused by *Streptococcus pyogenes*.
Otitis Media caused by *Streptococcus pneumoniae*, *Streptococcus pyogenes* (group A beta-hemolytic streptococci), *Haemophilus influenzae* (beta-lactamase negative and beta-lactamase positive strains) or *Moraxella catarrhalis*.

Skin Structure Infections
Skin structure infections caused by *Staphylococcus aureus* (methicillin susceptible), *Streptococcus pyogenes* or *Streptococcus agalactiae.*

Susceptibility to cefuroxime axetil will vary with geography and time. Cefuroxime axetil should be used in accordance with local official antibiotic prescribing guidelines and local susceptibility data (see 15 MICROBIOLOGY). Bacteriologic studies to determine the causative organism and its susceptibility to cefuroxime should be performed. Once these results become available antibiotic treatment should be adjusted if required.

To reduce the development of drug-resistant bacteria and maintain the effectiveness of CEFTIN for oral suspension and other antibacterial drugs, CEFTIN for oral suspension should be used only to treat 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.

1.1 Pediatrics

Pediatrics (Infants and Children 3 months to 12 years of age): Based on the data submitted and reviewed by Health Canada, the safety and efficacy of CEFTIN for oral suspension in pediatric patients has been established; therefore, Health Canada has authorized an indication for pediatric use. (See 4 DOSAGE AND ADMINISTRATION).

1.2 Geriatrics

Geriatrics: No data are available to Health Canada regarding CEFTIN for Oral Suspension; therefore, Health Canada has not authorized an indication for geriatric use.

2 CONTRAINDICATIONS

CEFTIN for oral suspension is contraindicated for patients who have shown Type 1 hypersensitivity to cefuroxime, to any of its components, or to any of the cephalosporin group of antibiotics.

4 DOSAGE AND ADMINISTRATION

4.2 Recommended Dose and Dosage Adjustment

The usual duration of treatment for CEFTIN for Oral Suspension is 7 to 10 days. The dose of cefuroxime that is selected to treat an individual infection should take into account:

- The expected pathogens and their likely susceptibility to cefuroxime axetil
- The site of the infection
- The age, weight and renal function of the patient; as shown below.

The duration of therapy should be determined by the type of infection and the response of the patient, and should generally not be longer than recommended.

For β-hemolytic streptococcal infections, therapy should be continued for at least 10 days.

Infants and Children 3 months to 12 Years of Age:
There is no experience in infants under the age of 3 months.

The recommended dosage of CEFTIN for oral suspension for various types of infections is indicated below:

TYPE OF INFECTION	**DOSAGE**
otitis media, skin structure infections	15 mg/kg twice daily Maximum dose 1 g/day
pharyngitis, tonsillitis	10 mg/kg twice daily Maximum dose 500 mg/day

Pharyngitis and Tonsillitis Infections:

Weight (kg)	**Total mg/day**	**doses/day**	**Dosage**	
			multi-dose bottle	
			teaspoon/dose	**mL/dose**
6	125	2	0.5	2.5
13	250	2	1.0	5.0
19	375	2	1.5	7.5
25	500	2	2.0	10.0
>25	500	2	2.0	10.0

Otitis Media and Skin Structure Infections:

Weight (kg)	Total mg/day	doses/day	Dosage	
			multi-dose bottle	
			teaspoon/dose	mL/dose
4	125	2	0.5	2.5
8	250	2	1.0	5.0
13	375	2	1.5	7.5
17	500	2	2.0	10.0
21	625	2	2.5	12.5
25	750	2	3.0	15.0
29	875	2	3.5	17.5
33	1,000	2	4.0	20.0
>33	1,000	2	4.0	20.0

Renal Insufficiency

CEFTIN for oral suspension is primarily excreted by the kidneys. In patients with markedly impaired renal function, it is recommended that the dosage of CEFTIN for oral suspension be reduced to compensate for its slower excretion (see the table below).

Creatinine Clearance	T1/2 (hours)	Recommended Dosage
≥30 mL/min/1.73m^2	1.4 - 2.4	No dose adjustment necessary (standard dose of 62.5 mg to 500 mg given twice daily)
10 - 29 mL/min/1.73m^2	4.6	Standard individual dose given every 24 hours
<10 mL/min/1.73m^2	16.8	Standard individual dose given every 48 hours
During haemodialysis	2 - 4	A single additional standard individual dose should be given at the end of each dialysis

The safety and efficacy of the proposed dosing adjustment has not been established.

4.3 Reconstitution

PHARMACIST: Directions for Reconstituting Suspension in Multi-Dose Bottles
Please note that the time taken to prepare CEFTIN for Oral Suspension before administration of the first dose will take more than one hour. This includes time for the suspension to "settle" in the refrigerator.

Prepare a suspension at time of dispensing as follows:

1. Shake the bottle to loosen the content and make sure all granules are free-flowing. Remove the bottle cap and the heat-seal membrane. If the latter is damaged or not present, do not use.

2. Add the total amount of cold water for reconstitution all at once (see table below) and replace the bottle cap. Allow the bottle to stand to allow the water to fully soak through the granules; this should take about one-minute.

Labelled Volume (mL)	Amount of Water for Reconstitution
70	27
100	37

3. INVERT the bottle and shake well (for at least 15 seconds) as shown until the sound of the granules against the container disappears.

4. Turn the bottle into an upright position and shake well for at least one-minute, until all the granules have blended with the water. Each 5 mL provides 125 mg cefuroxime.

5. Refrigerate immediately at between 2 and 8°C (do not freeze) and let it rest for at least one hour before taking the first dose. The reconstituted suspension should be refrigerated at all times; when refrigerated between 2 and 8°C, the reconstituted suspension can be kept for up to 10 days.

NOTE: SHAKE THE BOTTLE WELL until the suspension can be heard moving in the bottle before each use. Replace cap securely after each opening. If desired, the dose of the reconstituted suspension may be added to one of the following cold beverages immediately after mixing prior to administration: milk (i.e. skim, 2% or homogenized), fruit juice (i.e. apple, orange, or grape) or lemonade.

NOTE: CEFTIN for oral suspension content should NOT be reconstituted in HOT BEVERAGES.

4.4 Administration

For optimal absorption, CEFTIN for oral suspension should be taken with food.

5 OVERDOSAGE

For management of a suspected drug overdose, contact your regional poison control centre.

Other than general supportive treatment, no specific antidote is known. Excessive serum levels of cefuroxime can be reduced by dialysis. For treatment of hypersensitive reactions, (see 7 WARNINGS AND PRECAUTIONS)

6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

Table 1: Route of Administration, Dosage Forms, Strengths and Non-medicinal Ingredients.

Route of Administration	Dosage Form / Strength	Non-medicinal Ingredients
Oral	Oral suspension 125 mg cefuroxime (as cefuroxime axetil) per 5 mL.	Acesulfame potassium, aspartame*, flavor (tutti frutti), polyvinyl pyrrolidone, stearic acid, sucrose (about 3 g/5 mL), and xanthan gum.

*aspartame is a source of phenylalanine and should be avoided in patients with phenylketonuria (see 7 WARNINGS AND PRECAUTIONS, General).

Availability of Dosage Forms

CEFTIN for Oral Suspension is provided as dry, white to pale yellow, tutti frutti flavoured granules. It is supplied in 70 and 100 mL bottles, containing 1.75 g, and 2.5 g cefuroxime (as cefuroxime axetil) respectively. After reconstitution, each teaspoonful (5 mL) contains 125 mg cefuroxime (as cefuroxime axetil).

7 WARNINGS AND PRECAUTIONS

General

Before therapy with CEFTIN for oral suspension is instituted, careful inquiry should be made to determine whether the patient has had previous hypersensitivity reactions to cefuroxime, cephalosporins, penicillin, or other drugs. CEFTIN for oral suspension should be administered with caution to any patient who has demonstrated some form of allergy, particularly to drugs. There is some clinical and laboratory evidence of partial cross-allergenicity of the cephalosporins and penicillin. Special care is indicated in patients who have experienced allergic reaction to penicillins or other beta-lactams. If an allergic reaction to CEFTIN for oral suspension occurs, treatment should be discontinued and standard agents (e.g. epinephrine, antihistamines, corticosteroids) administered as necessary.

There have been reports of hypersensitivity reactions which progressed to Kounis syndrome (acute

allergic coronary arteriospasm that can result in myocardial infarction, see 8.5 Post-Market Adverse Reactions).

CEFTIN for oral suspension contains aspartame, which is a source of phenylalanine and so should be avoided in patients with phenylketonuria.

Severe cutaneous adverse reactions (SCAR) such as acute generalized exanthematous pustulosis (AGEP), drug reaction with eosinophilia and systemic symptoms (DRESS), Stevens-Johnson syndrome (SJS), and toxic epidermal necrolysis (TEN) have been reported in association with beta-lactam treatment. When SCAR is suspected, CEFTIN for oral suspension should be discontinued and appropriate therapy and/or measures should be taken.

As with other antibiotics, use of CEFTIN for oral suspension may result in the overgrowth of *Candida*. Prolonged use may also result in the overgrowth of other non-susceptible organisms (e.g. *enterococci* and *Clostridium difficile*), which may require interruption of treatment. Repeated evaluation of the patient's condition is essential. If superinfection occurs during therapy, appropriate measures should be taken. Should an organism become resistant during antibiotic therapy, CEFTIN for oral suspension should be discontinued and another appropriate antibiotic should be substituted.

Clostridium difficile-Associated Disease

Clostridium difficile-associated disease (CDAD) has been reported with use of many antibacterial agents including CEFTIN for oral suspension (see 8 ADVERSE REACTIONS). CDAD may range in severity from mild diarrhea to fatal colitis. It is important to consider this diagnosis in patients who present with diarrhea, or symptoms of colitis, pseudomembranous colitis, toxic megacolon, or perforation of colon subsequent to the administration of any antibacterial agent. CDAD has been reported to occur over 2 months after the administration of antibacterial agents.

Treatment with antibacterial agents may alter the normal flora of the colon and may permit overgrowth of *Clostridium difficile*. *Clostridium difficile* produces toxins A and B, which contribute to the development of CDAD. CDAD may cause significant morbidity and mortality. CDAD can be refractory to antimicrobial therapy.

If the diagnosis of CDAD is suspected or confirmed, appropriate therapeutic measures should be initiated. Mild cases of CDAD usually respond to discontinuation of antibacterial agents not directed against *Clostridium difficile*. In moderate to severe cases, consideration should be given to management with fluids and electrolytes, protein supplementation, and treatment with an antibacterial agent clinically effective against *Clostridium difficile*. Surgical evaluation should be instituted as clinically indicated, as surgical intervention may be required in certain severe cases.

Driving and Operating Machinery

As this medicine may cause dizziness, patients should be warned to be cautious when driving or operating machinery.

Gastrointestinal

Broad-spectrum antibiotics including CEFTIN for oral suspension should be administered with caution to individuals with a history of gastrointestinal disease, particularly colitis.

Hematologic
CEFTIN for oral suspension SHOULD NOT BE USED IN PATIENTS WITH A HISTORY OF CEPHALOSPORIN-ASSOCIATED HEMOLYTIC ANEMIA SINCE THE RECURRENCE OF HEMOLYSIS IS MUCH MORE SEVERE.

An immune mediated hemolytic anemia has been observed in patients receiving cephalosphorin class antibacterials, including CEFTIN for oral suspension. Severe cases of hemolytic anemia, including fatalities, have been reported in both adults and children. If a patient develops anemia anytime during, or within 2-3 weeks subsequent to the administration of CEFTIN for oral suspension, the diagnosis of a cephalosphorin-associated anemia should be considered and the drug discontinued until the etiology is determined.

Monitoring and Laboratory Tests

Patients may benefit from periodic monitoring for signs and symptoms of hemolytic anemia, including measurement of hematological parameters or drug-induced antibody testing, where appropriate (see 8 ADVERSE REACTIONS).

The sucrose content of CEFTIN for oral suspension (see 6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING) should be taken into account when treating diabetic patients.

Sensitivity/Resistance

Prescribing CEFTIN for oral suspension in the absence of a proven or strongly suspected bacterial infection is unlikely to provide benefit to the patient and risks the development of drug-resistant bacteria.

7.1 Special Populations

7.1.1 Pregnant Women

The safety of CEFTIN for oral suspension in pregnancy has not been established. The use of CEFTIN for oral suspension in pregnant women requires that the likely benefit from the drug be weighed against the possible risk to the mother and fetus. Animal studies following parenteral administration have shown cefuroxime to affect bone calcification in the fetus and to cause maternal toxicity in the rabbit. Reproduction studies that have been performed in mice and rats at oral doses of up to 50 to 160 times the human dose have revealed no evidence of impaired fertility or harm to the fetus due to cefuroxime axetil. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

7.1.2 Breast-feeding

Since cefuroxime is excreted in human milk, consideration should be given to discontinuing nursing temporarily during treatment with CEFTIN for oral suspension.

8 ADVERSE REACTIONS

8.2 Clinical Trial Adverse Reactions

Clinical trials are conducted under very specific conditions. The adverse reaction rates observed in the clinical trials; therefore, may not reflect the rates observed in practice and should not be compared to the rates in the clinical trials of another drug. Adverse reaction information from clinical trials may be useful in identifying and approximating rates of adverse drug reactions in real-world use.

The following adverse reactions have been reported:

Gastrointestinal (approximately 8% of patients): Diarrhea (5.6%), nausea (2.4%), vomiting (2.0%), loose stools (1.3%). Reports of abdominal pain have occurred.

Hepatic (3% of patients): Transient increases of hepatic enzyme levels [ALT, AST, LDH].

Central Nervous System (2.2% of patients): Headache and dizziness.

Hypersensitivity (1.3% of patients): Rashes (0.6%), pruritus (0.3%), urticaria (0.2%), shortness of breath and rare reports of bronchospasm. Hypersensitivity reactions to CEFTIN for oral suspension may occur in patients who report delayed hypersensitivity to penicillins (see 7 WARNINGS AND PRECAUTIONS, General). As with other cephalosporins, there have been rare reports of drug fever.

Hematologic: Increased erythrocyte sedimentation rate, eosinophilia, decreased hemoglobin, Positive Coomb's test and very rarely hemolytic anemia (see 7 WARNINGS AND PRECAUTIONS, Hematologic).

Miscellaneous: The following adverse reactions have been observed to occur, although infrequently, in association with parenteral cefuroxime sodium and may be potential adverse effects of oral cefuroxime axetil: drowsiness, vaginitis and transient increases in serum bilirubin, creatinine, alkaline phosphatase, and urea nitrogen (BUN). In addition, the incidence of diaper rash (1.4%) has been associated with CEFTIN for oral suspension in children.

8.5 Post-Market Adverse Reactions

In addition to adverse events reported during clinical trials, the following events have been identified during clinical practice in patients treated with CEFTIN for Oral Suspension and were reported spontaneously. Data are generally insufficient to allow an estimate of incidence or to establish causation.

Cardiac Disorders: Kounis syndrome.

Hypersensitivity Reactions: The following hypersensitivity reactions have been reported: anaphylaxis, angioedema, pruritus, rash, serum sickness-like reaction, urticaria.

Gastrointestinal: Pseudomembranous colitis (see 7 WARNINGS AND PRECAUTIONS, Gastrointestinal).

Hematologic: Thrombocytopenia, and leucopenia (sometimes profound).

Hepatic: Jaundice (predominantly cholestatic) and hepatitis have been reported very rarely.

Infections and Infestations: *Candida* overgrowth.

Neurologic: Seizure.

Skin: Erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis.

Urologic: Renal dysfunction.

9 DRUG INTERACTIONS

9.4 Drug-Drug Interactions

Drugs which reduce gastric acidity may result in a lower bioavailability of CEFTIN for oral suspension compared with that of the fasting state and tend to cancel the effect of enhanced post-prandial absorption.

In common with other antibiotics, cefuroxime axetil may affect the gut flora, leading to lower estrogen reabsorption and reduced efficacy of combined oral contraceptives**.**

The concomitant administration of aminoglycosides and some cephalosporins has caused nephrotoxicity. There is no evidence that CEFTIN for oral suspension, when administered alone, is nephrotoxic, although transient elevations of BUN and serum creatinine have been observed in clinical studies. However, the effect of administering CEFTIN for oral suspension concomitantly with aminoglycosides is not known.

Studies suggest that the concomitant use of potent diuretics, such as furosemide and ethacrynic acid, may increase the risk of renal toxicity with cephalosporins.

9.7 Drug-Laboratory Test Interactions

A false-positive reaction for glucose in the urine may occur with copper reduction tests (Benedict's or Fehling's solution or with Clinitest Tablets) but not with enzyme-based tests for glycosuria (e.g. Clinistix, Tes-Tape). 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 CEFTIN for oral suspension.

Cefuroxime does not interfere with the assay of serum and urine creatinine by the alkaline picrate method.
Cephalosporins as a class tend to be absorbed onto the surface of red cell membranes and react with antibodies directed against the drug to produce a positive Coombs' test (which can interfere with cross-matching of blood) and very rarely hemolytic anemia (see 7 WARNINGS and PRECAUTIONS, and 8 ADVERSE REACTIONS)

10 CLINICAL PHARMACOLOGY

10.1 Mechanism of Action

Cefuroxime axetil is an orally active prodrug of cefuroxime. The inherent properties of cefuroxime are unaltered after its administration as cefuroxime axetil. Cefuroxime exerts its bactericidal effect by binding to an enzyme or enzymes referred to as penicillin-binding proteins (PBPs) involved in bacterial cell wall synthesis. This binding results in inhibition of bacterial cell wall synthesis and subsequent cell death. Specifically, cefuroxime shows high affinity for PBP 3, a primary target for cefuroxime in gram-negative organisms such as *E. coli.*

10.2 Pharmacodynamics

Animal Pharmacology

The secondary pharmacological effects of cefuroxime axetil have been investigated in mice, rats, and dogs following a single oral dose. Negative controls were administered a placebo suspension while positive controls received mecamylamine HCl (an inhibitor of gastrointestinal propulsion). The results are summarized in Table 2.

Table 2: Secondary pharmacological actions in animals after a single oral dose of cefuroxime axetil

ANIMAL	DOSE (mg/kg)	NO. OF ANIMALS*	PHARMACOLOGICAL ACTIONS	OBSERVATION TIMES	EFFECTS
mice	0.5	10	pupil diameter, body temperature, gross behaviour	0-1h, 24h intervals for 7d	decreased body temperature in females
rat	0.5	10	pupil diameter, body temperature, gross behaviour	0-1h, 24h intervals for 7d	decreased body temperature in females
dog	0.5	2	BP, HR, ECG gross behaviour	2.25, 3, 6, 24h	none
rat	0.5	10	gastrointestinal propulsion	0.75h	none

* Each group consisted of equal numbers of males and females

10.3 Pharmacokinetics

Human

After oral administration, cefuroxime axetil, as CEFTIN for oral suspension, is absorbed from the gastrointestinal tract and rapidly hydrolyzed by nonspecific esterases in the intestinal mucosa and blood to release cefuroxime into the blood stream. Conversion to cefuroxime, the microbiologically active form, occurs rapidly.

As can be seen, cefuroxime axetil had no effects on behaviour or pupil diameter in the mouse or the rat or on gastrointestinal propulsion in the rat. Cefuroxime axetil administered orally to dogs produced no acute effects on blood pressure, heart rate, or the electrocardiogram.

The bioavailability of cefuroxime tablets was investigated in a six-way crossover study with each of 12 male adult volunteers receiving a single intravenous dose of cefuroxime sodium and five oral doses of cefuroxime axetil. Blood samples were collected at specified intervals for 12h and urine for 24h following each dose. The results of this study are presented in Table 3.

Table 3: Pharmacokinetics of cefuroxime axetil administered as CEFTIN Tablets to Adults

DOSE (mg)	ROUTE	FASTED /FED	PEAK SERUM CONCENTRA-TION (µg/mL)	TIME TO PEAK (h)	AREA UNDER SERUM LEVEL-TIME CURVE mg h/L	URINE RECOVERY 0-12 h (mg)	% DOSE RECOVERED IN URINE	% DOSE ABSORBED RELATIVE TO I.V.	HALF-LIFE (h)
500	i.v.	fasted	53.2	0.1	52.8	415	83	100	1.3
500	po	fasted	4.9	2.3	18.9	161	32	36	1.6
125	po	Fed	2.1	2.2	6.7	65	52	51	1.2
250	po	Fed	4.1	2.5	12.9	127	51	49	1.2
500	po	Fed	7.0	3.0	27.4	242	48	52	1.2
1000	po	Fed	13.6	2.5	50.0	434	43	47	1.3

The mean values of pharmacokinetic parameters after 12 volunteers received a single i.v. dose of cefuroxime and 5 oral doses of cefuroxime axetil.

Increasing doses of cefuroxime produced linear increases in peak serum concentrations and AUC.

Bioavailability appears to be independent of dose but is increased by the presence of food. Absolute bioavailability of CEFTIN tablets (500 mg dose) increased from 36% in fasted subjects to 52% after food.

The amount of cefuroxime excreted in the urine over 24h averaged 83% following intravenous dosing and ranged from 43% to 52% following oral dosing when taken after food.

The half-life of cefuroxime following oral administration as CEFTIN to healthy adult volunteers is 1.2 to 1.6 hours.

The bioavailability of cefuroxime suspension was investigated in 36 pediatric patients. The C_{max} and AUC increased proportionately with dose. The results of this study are presented in Table 4.

Table 4: Pharmacokinetics of Cefuroxime axetil Administered as CEFTIN for Oral Suspension in Pediatric Patients

Dose* (cefuroxime equivalent)	N	Age Mean/ Range (months)	Weight Mean/ Range (kg)	C_{max} (µg/ mL)	T_{max} (h)	Area Under Serum Level-Time Curve mg h/L	$T_{1/2}$ (h)	Time Serum Conc. Exceeds 1.0 µg/mL (h)
10 mg/kg	8	18.5 (3-60)	10.3 (5-17)	3.3	3.6	12.4	1.4	4.2
15 mg/kg	12	21.0 (5-72)	10.3 (6-18)	5.1	2.7	22.5	1.9	4.9
20 mg/kg	8	35.0 (4-144)	15.0 (7-47)	7.0	3.1	32.8	1.9	6.6

* Administered with milk or milk products.

In comparative bioavailability studies in healthy adults, CEFTIN for oral suspension was not bioequivalent to CEFTIN tablets. The area under the curve for the suspension averaged 91% of that for the tablet, while the C_{max} for the suspension averaged 71% of the C_{max} of the tablets.

Special Populations and Conditions

Renal insufficiency:

Cefuroxime pharmacokinetics have been investigated in patients with various degrees of renal impairment. Cefuroxime elimination half-life increases with decrease in renal function which serves as the basis for dosage adjustment recommendations in this group of patients (see 4 DOSAGE AND ADMINISTRATION). In patients undergoing haemodialysis, at least 60% of the total amount of cefuroxime present in the body at the start of dialysis will be removed during a 4-hour dialysis period. Therefore, an additional single dose of cefuroxime should be administered following the completion of haemodialysis.

11 STORAGE, STABILITY AND DISPOSAL

SUSPENSION
Store granules between 2°C and 30°C. The reconstituted suspension must be stored immediately between 2°C and 8°C in a refrigerator, and discarded after 10 days.

Keep out of reach and sight of children.

In the absence of compatibility studies cefuroxime axetil must not be mixed with other medicinal products.

12 SPECIAL HANDLING INSTRUCTIONS

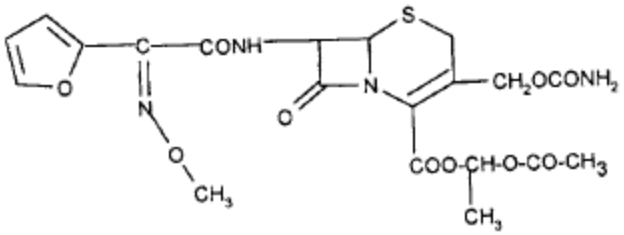
There are no special handling instructions.

PART II: SCIENTIFIC INFORMATION

13 PHARMACEUTICAL INFORMATION

Drug Substance
Proper name: Cefuroxime axetil
Chemical name: (RS)1-Hydroxyethyl(6R,7R)-7[2-(2-furyl)glyoxylamido]-3-(hydroxymethyl)-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylate, 7^2-(Z)-(0-methyl-oxime), 1-acetate 3-carbamate.

Molecular formula and molecular mass: $C_{20}H_{22}N_4O_{10}S$ / 510.5
Structural formula:



Physicochemical properties: Cefuroxime axetil is an amorphous white to cream-coloured powder. It is soluble in dimethyl sulfoxide, dimethylformamide, 1,4-dioxan, chloroform, acetone, glacial acetic acid, ethyl acetate, and methanol. It is soluble with decomposition in 2N sodium hydroxide and slightly soluble in water, diethyl ether, 95% ethanol, and toluene, and insoluble in 2N hydrochloric acid. Cefuroxime axetil decomposes below its melting point.

14 CLINICAL TRIALS

Clinical Trial information was not included in Product Monograph at the time of initial authorization.

15 MICROBIOLOGY

Cefuroxime has been demonstrated to be active against various susceptible strains of the following microorganisms both *in vitro* and in clinical infections (see 1 INDICATIONS).

Aerobic Gram-Positive Microorganisms:
Staphylococcus aureus (methicillin susceptible)
Streptococcus pneumoniae
Streptococcus pyogenes (including group A beta-hemolytic streptococci)
Streptococcus agalactiae

Aerobic Gram-Negative Microorganisms:
Haemophilus influenzae (including beta-lactamase negative, beta-lactamase positive and ampicillin-resistant strains)
Haemophilus parainfluenzae
Klebsiella pneumoniae
Moraxella catarrhalis

In vitro susceptibility data is available for the following microorganisms.

Aerobic Gram-Positive Microorganisms:
Staphylococcus aureus (methicillin susceptible)
Coagulase negative Staphylococcus spp (methicillin susceptible)
Streptococcus agalactiae
Streptococcus pneumoniae (including penicillin-susceptible, -intermediate and –resistant strains)
Streptococci spp.- β-haemolytic
Streptococcus pyogenes

Aerobic Gram-Negative Microorganisms:
Citrobacter freundii
Enterobacteriaceae
Enterobacter spp.
Escherichia coli
Haemophilus influenza (including beta-lactamase negative and positive strains)
Haemophilus parainfluenzae
Klebsiella oxytoca
Klebsiella pneumoniae
Klebsiella spp.
Moraxella catarrhalis
Morganella morganii
Proteus mirabilis
Providencia spp.

Anaerobes
Bacteroides spp.
Clostridium spp.
Fusobacterium nucleatum/necrophorum
Peptostreptococcus micros

Susceptibility Testing:

The results of susceptibility testing, by either disk-diffusion or broth microdilution techniques, should be interpreted according to the criteria established in CLSI M-100 S24 document as shown in Table 5. Quality control (QC) should be performed and evaluated according to CLSI published QC ranges as shown in Table 6.

Table 5: Disk and MIC breakpoints for cefuroxime susceptibility testing

Organism	Zone Diameter Interpretive Criteria* (mm) (30µg disk)			MIC Interpretive Criteria* (µg/mL)		
	Sensitive	**Intermediate**	**Resistant**	**Sensitive**	**Intermediate**	**Resistant**
Hemophilus influenzae	≥20	17-19	≤16	≤4	8	≥16
Enterobacteriaceae	≥23	15-22	≤14	≤4	8-16	≥32
Staphylococcus spp.			Note 1			Note 1
Streptococcus pneumoniae	-	-	-	≤1	2	≥4
Streptococcus pyogenes	Note 2			Note 2		

*Interpretive criteria based on CLSI M100-S24 interpretive criteria

[1]Oxacillin-resistant *S. aureus* and coagulase-negative staphylococci are considered resistant to cefuroxime

[2]Penicillin-susceptible *S. pyogenes* can be considered susceptible to cefuroxime

Table 6: Disk and MIC QC ranges for cefuroxime susceptibility testing

QC Strain	Disk Range* (mm)	MIC Range* (µg/mL)
Escherichia coli ATCC 25922	20-26	2-8
Haemophilus influenzae 49766	28-36	0.25-1
Staphylococcus aureus ATCC 25923	27-35	-
Staphylococcus aureus ATCC 29213	-	0.5-2
Streptococcus pneumoniae ATCC 49619	-	0.25-1

*Disk and MIC QC ranges published from CLSI M100-S24

16 NON-CLINICAL TOXICOLOGY

Acute Toxicity

The experimental details of single-dose toxicity studies are presented in Table 7.

Table 7: Acute Toxicity

ANIMAL	AGE	ROUTE	DOSES (g/kg)	ANIMALS /DOSE*	LENGTH OF OBSERVATION	LD_{50} (g/kg)
mouse	adult	p.o.	0.6	20	3 days	>6
mouse	adult	p.o.	0.6	20	14 days	>6
mouse	adult	p.o.	6	20	14 days	>6
mouse	adult	p.o.	1.5,3	12	14 days	>6
rat	adult	p.o.	0,6	12	3 days	>6
rat	adult	p.o.	0,6	12	14 days	>6
rat	adult	p.o.	6	12	14 days	>6
rat	10 days	p.o.	0,3	20	3 days	>3
rat	10 days	p.o.	0,3	20	14 days	>3
rat	adult	s.c.	1.5,3	12	14 days	>3
dog	8-10 mo.	p.o.	1.5,3	4	14 days	>3

* Each dosage group was composed of equal numbers of males and females

All animals survived the experiments. The median lethal dose of cefuroxime axetil in these animals is therefore, in excess of the test doses administered.

The only symptom of systemic toxicity observed was a temporary reduction in body weight in the juvenile (10-day-old) rats. All other animals remained apparently healthy during the observation period.

Mice and rats were sacrificed following the observation period. Histological examination of major organs and tissues revealed no evidence of systemic toxicity.

Subcutaneous injections in mice and rats caused local swelling due to the accumulation of large volumes of suspension. Small localized subcutaneous accumulations of test compound with slight peripheral tissue reaction were observed at autopsy.

Compacted test material was still present in the stomachs of most mice and rats three days after oral dosing. Inflammatory changes observed in the stomach walls of several animals were considered to be due to the mechanical irritation caused by these masses.

Long Term Toxicity

In subacute and chronic studies in rats receiving high oral doses of cefuroxime axetil (1.0-2.5 g/kg/day), accumulation of drug substance and the formation of concretions in the stomachs of many animals caused high rates of mortality. The concretions consisted of semicrystalline axetil, water, food, polymers and impurities comparable to that in the administered material.

Concretions were not a problem in the dog studies, which all proceeded to completion. Experimental details of subacute and chronic toxicity studies are presented in Table 8.

Table 8: Subacute and Chronic Toxicity

ANIMAL	AGES*	ROUTE	DAILY DOSES (g/kg)	ANIMALS/ DOSE**	INTENDED DURATION OF TREATMENT	RECOVERY
rat	7-9 wk	p.o.	0,0.1,0.4,	12	15 wk	-
rat	7-9 wk	p.o.		12	15 wk	22 days
rat	7-9 wk	p.o.	0.8,1.7,2.5	12	15 wk	-
rat	8-10 wk	p.o.	0,0.1,0.4,1.6	60	28 wk	-
rat	9 wk	p.o.	0,0.15,0.4,1.0	30	90 days	-
rat	7 wk	p.o.		32	28 wk	-
rat	7 wk	p.o.	0,0.1,0.4,1.0	24	28 wk	5 wk
rat	7 wk	p.o.		12	31 wk	-
dog	12-16 wk	p.o.	0,0.1,0.2,0.4,0.8	6	5 wk	-
dog	8 mo	p.o.	0,0.15,0.4,1.0	8	90 days	-
dog	4.5-6 mo	p.o.	0,0.1,0.4,1.6	8	27 wk	-
dog	4.5-6 mo	p.o.	0,0.4	4	27 wk	3 wk

* Ages at commencement of treatment.

** Each dosage group was composed of equal numbers of males and females.

Rat: 5-week study

There were no adverse effects related to treatment in the 0.1 and 0.4 g/kg groups.

By the end of the study, males in the 0.8 and 1.7 g/kg groups exhibited increased clotting times. An increase in serum alkaline phosphatase levels was seen in male rats in the 1.7 g/kg group. Histological changes in the stomach wall, similar to those seen in animals on 2.5 g/kg/day, were observed in males and females in the 1.7 g/kg group, and were considered to be primarily a consequence of the mechanical effects of drug accumulation.

In the high-dose (2.5 g/kg) group, all of the males were killed on day 9 and three of the females were killed or died later during the study. The deaths followed clinical deterioration due to accumulation of drug ester in the stomach. In affected rats there was thrombocytopenia in most cases and a slightly prolonged plasma-activated partial thromboplastin time in one case. Histological examination revealed mechanical damage to the stomach wall, and in one case there was scattered renal tubular eosinophilia and desquamation.

Rat: 90 day study
A number of rats died during the study; macroscopic and microscopic examination confirmed that these deaths were not related to cefuroxime axetil. The general condition of the surviving animals remained satisfactory throughout the study and the treatment did not affect the normal increase in body weight.

There was a slight decrease in total leukocyte counts observed in all dosage groups, resulting from a reduction in the number of neutrophils and lymphocytes and probably due to the protective effect of the test compound against those microbes that may influence leukocyte homeostasis.

A reversible decrease in plasma coagulation activity occurred in males, predominantly in the high-dose (1.0 g/kg) group. This may have been due to a direct action of cefuroxime axetil on the coagulation system or to reduced synthesis of coagulation factors as a result of suppression of Vitamin K-producing organisms in the intestine.

Rat: 28-week study
Rats in the 0.1 and 0.4 g/kg groups showed no significant toxicity and were in good general condition when the study was terminated after 62 to 65 days of treatment. However, the animals given 1.6 g/kg/day suffered from gastrointestinal trauma resulting from the mechanical effects of firm agglomerates of cefuroxime ester. Despite reduction of their dose to 1.0 g/kg/day on Day 7, they continued to deteriorate and either died or were killed after 10 to 14 days treatment.

In a further 28 week study in rats, there were no deaths attributable to any toxic effect of cefuroxime axetil.

Apart from loose faeces, seen mainly during the first six weeks of the study in animals receiving 0.4 and 1.0 g/kg/day, there were no significant effects on the general condition of rats surviving to the end of the study. Salivation, extension of the forearms, and walking on the toes was observed in treated animals at the time of dosing, but were considered to be primarily a response to the dosing procedures rather than a toxic effect of the drug.

A reduction in leukocyte counts was observed in all treatment groups, probably reflecting a protective action of the antibiotic against minor infections. Other laboratory abnormalities observed included lengthened clotting times in males, reduction in AST and ALT, and increases in serum transaminases in a few individual females without histological evidence of hepatic damage.

At the end of the treatment period, 48% of the animals in the high-dose (1.0 g/kg) group had agglomerates of cefuroxime axetil in the stomach at autopsy, with one subject exhibiting an associated inflammation of the stomach wall.

Dog: 5-week study

Apart from a single case of vomiting shortly after dosing, the general condition of the dogs was not adversely affected by the treatment.

Laboratory abnormalities observed included transient decreases in total leukocyte and neutrophil counts, hyponatremia, and increased inorganic phosphorus and triglyceride levels. None of the individual results were sufficiently abnormal to be of clinical significance and there were no histological changes associated with treatment.

Dog: 90-day study
The general condition of the animals remained satisfactory throughout the study with normal increases in body weight attained. Isolated and occasional vomiting was the only apparent adverse effect, but this response can partly be attributed to the oral intubation.

Increases in erythrocyte sedimentation rate and in leukocyte and eosinophil counts were observed in animals with incidental helminthic infections. Females in the 0.4 and 1.0 g/kg groups exhibited increased total serum iron binding capacity. There is a statistically significant decrease in the absolute weights of livers in males and hearts in females in the 0.4 g/kg group, but this is insignificant when related to total body weights.

Dog: 27-week study
The general condition of the animals remained satisfactory throughout the study with the exception of 3 dogs, 2 of which were sacrificed suffering from illnesses unrelated to treatment.

In the high-dose (1.6 g/kg/day) group salivation and vomiting were noted, and in one dog there was a transient reduction in growth rate and a general loss of condition. Laboratory abnormalities included reduced erythrocyte counts, prolonged clotting times, reduction in plasma protein and cholesterol, and an increase in plasma triglyceride. Post mortem examinations revealed no signs of organ toxicity.

Nephrotoxicity Studies

Single Dose Administration

Mouse
Mice received single subcutaneous doses of cefuroxime sodium (10 g/kg) alone or in combination with furosemide (50 mg/kg) or furosemide plus glycerol 5.4 mL/kg. Cefuroxime alone caused no nephrotoxicity; when administered concomitantly with furosemide there was proximal tubular necrosis in 2 out of 9 animals. The combination of furosemide and glycerol caused tubular necrosis in 5 of 8 animals but this was not influenced by the addition of cefuroxime.

Rat
Cefuroxime sodium at doses up to 10 g/kg was administered either alone or in combination with furosemide (100 mg/kg) or furosemide plus glycerol (3.15 mL/kg). Three of 6 animals exhibited proximal tubular necrosis in the inner cortex following administration of 4 g of cefuroxime alone. The incidence and severity of necrosis increased with increasing doses of cefuroxime. The incidence of tubular necrosis also increased when furosemide or furosemide plus glycerol were given concomitantly. Cefuroxime at 1g/kg enhanced the severity of the furosemide-glycerol-induced necrosis in the outer cortex. Treatment with furosemide plus glycerol also lowered the dosage of cefuroxime to 2 g/kg required to produce necrosis of the inner cortex.

Rat: Repeated dose study
Rats received cefuroxime at doses ranging from 1 to 5 g/kg/day subcutaneously for 10 days. There was no histological evidence of tubular necrosis at 5 g/kg, but transient increases in urine volume, protein and enzymes, which peaked at day 2-3 were observed. The body weights of the animals were significantly reduced for the high dose group.

Combination with aminoglycosides
Rats were treated with gentamicin (35 mg/kg) for 10 days. Cefuroxime sodium was given either concomitantly during the 10 days or as a single dose with the ninth dose of gentamicin. Gentamicin-induced tubular necrosis was not potentiated by the administration of single doses of cefuroxime up to 6 g/kg/day. Multiple doses of cefuroxime up to 4 g/kg protected rats against gentamicin-induced nephrotoxicity, but at doses of 6 g/kg/day of cefuroxime, severe tubular necrosis was observed after 4 days of treatment. Similar results were found with amikacin and tobramycin.

Mutagenicity Studies

Several standard assays were done to assess the mutagenic properties of cefuroxime axetil. These included both in vitro (Ames test, fluctuation test, gene conversion assay) and in vivo (micronucleus tests) assays.

In vitro assays
Cefuroxime axetil was subjected to standard Ames tests, fluctuation tests, and gene conversion tests in concentrations of up to 208 µg/plate, 8.3 µg/mL, and 833 µg/mL respectively. The results of these tests were negative. Negative results were also obtained at high concentrations (833 µg/mL) in a modified fluctuation test in which the test strains were rendered resistant to cefuroxime's antibacterial properties. A weak, but statistically significant response was observed at 416 µg/mL, but this was not regarded as biologically significant since no effect was detected at 833 µg/mL.

In vivo micronucleus test
Groups of five male mice received oral doses of cefuroxime axetil equivalent to 1.486, 1.114, 0.743 and 0.372 g/kg cefuroxime. Negative control groups received vehicle only and positive controls were dosed with 100 mg/kg cyclophosphamide. At either 24 or 48h, groups of animals were killed and the bone marrow of both femurs collected. Smears were prepared and examined for micronuclei.

There was no significant increase in the proportion of polychromatic erythrocytes with micronuclei in any of the groups treated with cefuroxime axetil when compared with their negative control at either expression time.

The ratios of mature to immature erythrocytes observed in animals receiving cefuroxime axetil were not significantly different from the negative controls at either expression time.

Tolerance Studies

Cefuroxime axetil, applied as a 50% suspension in soft paraffin/liquid paraffin to intact and abraded guinea pig skin under occlusive dressing for 21 hours, produced negligible irritancy. Cefuroxime axetil was strongly sensitizing when applied to guinea pig skin. Sixteen days after application of sensitizing

doses to 10 animals, challenge with the test material produced a positive erythematous response in 9 animals after 24 hours and in all 10 after 48 hours.

Reproduction and Teratology Studies

Rodents
The reproductive toxicity of oral cefuroxime axetil was investigated in rats and mice as summarized in Table 9.

Table 9: Reproduction and Teratology Studies

ANIMAL	SEX	DOSES (mg/kg/day)	ANIMALS /DOSE	DURATION OF TREATMENT	SIGNIFICANT OBSERVATIONS*
mouse	F	0,150,500,1600	30**	day 7 to day 16 of pregnancy	decreased number of implants (F_0) increased F_1 male: female ratio
rat	F	0.125,250,500	20	day 17 of pregnancy to day 21 *post partum*	delayed pinna detachment (F_1 females)
rat	M F	0,125,250,500 0,125,250,500	10 30**	70 days prior to mating 21 days before mating to day 21 *post partum*	delayed F_1 mating, increased F_2 male: female ratio, delayed primary coat (F_2 females), delayed eye opening (F_2 males), delayed pinna detachment (F_2)
rat	F	0,125,250,500	30***	day 7 to day 16 of pregnancy	decreased number of implants (F_0), decreased number of live F_1 fetuses

* Apparent reproductive toxicity (i.e. other than F_0 organ toxicity) which was dose related and not due to experimental artifacts or to the antimicrobial action of the drug (e.g. suppression of intestinal microflora).
** 20 animals were killed at term; 10 were allowed to litter and complete the treatment.
*** 15 animals were killed at term; 15 were allowed to litter and complete the treatment.

The most common gross abnormality observed in offspring of treated dams was hydronephrosis, seen in comparable numbers at all dose levels including controls. There was no evidence that cefuroxime axetil had adversely affected fertility or peri-/post-natal development or organogenesis in rats or mice.
Rabbit
Rabbits were found to be unsuitable for reproductive toxicity testing of cefuroxime axetil. Six unmated females were treated with daily doses of 0.1 to 0.5 g/kg while 6 mated females received 0.2 g/kg. All but one animal showed a chronic loss of body weight and deterioration in overall conditions (3 animals died). One of the mated animals maintained a viable pregnancy. Two aborted and evidence of earlier

resorption of implants was found in another two.

Post mortem examination of rabbits in both groups revealed liquified intestinal contents and distended, gas-filled caecums in many cases. Changes in intestinal microflora were thought to be the cause of the observed toxicity.

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

[Pr]CEFTIN

cefuroxime axetil for oral suspension USP

Read this carefully before you start taking **CEFTIN for oral suspension** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **CEFTIN for oral suspension**.

What is CEFTIN for oral suspension used for?
CEFTIN for oral suspension is an antibiotic medicine. It is similar to other antibiotic medicines called cephalosporins. Your doctor has prescribed CEFTIN for oral suspension because you have an infection. Your doctor should test the type of bacteria causing your infection and monitor whether the bacteria are sensitive to CEFTIN for oral suspension during your treatment.
Antibacterial drugs like CEFTIN for oral suspension treat only bacterial infections. They do not treat viral infections such as the common cold.

How does CEFTIN for oral suspension work?
CEFTIN for oral suspension contains an antibiotic that reduces infections by:

- Stopping the growth of bacteria.
- Killing bacteria

The infection can be cleared up if you take your medication in the proper way.

What are the ingredients in CEFTIN for oral suspension?
Medicinal ingredients: Cefuroxime (as cefuroxime axetil)
Non-medicinal ingredients: Acesulfame potassium, aspartame, flavour (tutti frutti), polyvinyl pyrrolidone, stearic acid, sucrose (about 3 g / 5 mL), and xanthan gum.

CEFTIN for oral suspension comes in the following dosage form:

Suspension: Each teaspoonful (5 mL) of CEFTIN for oral suspension contains 125 mg of cefuroxime (as cefuroxime axetil).

Do not use CEFTIN for oral suspension if:

You are allergic to cefuroxime, cephalosporin antibiotics or any of the other ingredients in CEFTIN for oral suspension (see **What are the ingredients in CEFTIN for oral suspension?**).

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take CEFTIN for oral suspension. Talk about any health conditions or problems you may have, including if:

- You are allergic to or react badly to penicillins or other antibiotics.
- You have kidney problems.
- You have had gastrointestinal problems, such as colitis.

- You have phenylketonuria. Do not use CEFTIN for oral suspension because it contains aspartame, a source of phenylalanine.
- You are diabetic. CEFTIN for oral suspension contains sugar (about 3 g / 5 mL).
- You are pregnant or planning to become pregnant.
- You are breastfeeding or planning to breastfeed. Cefuroxime is excreted in human breast milk. Discuss breastfeeding with your doctor.

Other warnings that you should know about:

Driving and Operating Machinery:

As this medication may cause dizziness, do not drive or operate machinery if you are feeling dizzy.

Medical Tests:
If you are having a urine test for sugar, tell your healthcare provider that you are taking CEFTIN. False positive reactions may occur when using certain test types. Your healthcare provider may have to use a different type of test.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with CEFTIN for oral suspension:

- Medicines used to reduce the amount of acid in your stomach (e.g. antacids used to treat heartburn).
- Medicines that promote the production of urine (such as furosemide and ethacrynic acid).
- CEFTIN for oral suspension may reduce how well the contraceptive pill works. If you are taking the contraceptive pill while you are being treated with CEFTIN for oral suspension, you also need to use a barrier method of contraception (such as condoms). Ask your doctor for advice.

How to take CEFTIN for oral suspension:

- Although you may feel better early in treatment, CEFTIN for oral suspension should be used exactly as directed.
- Misuse or overuse of CEFTIN for oral suspension could lead to the growth of bacteria that will not be killed by CEFTIN for oral suspension (resistance). This means that CEFTIN for oral suspension may not work for you in the future.
- Do not share your medicine.

Usual dose:

The usual length of treatment is 7 - 10 days, although your doctor may adjust the prescription to suit your treatment. CONTINUE TAKING CEFTIN FOR ORAL SUSPENSION UNTIL FINISHED, EVEN IF YOU BEGIN TO FEEL BETTER.

YOU SHOULD NOT INCREASE OR DECREASE THE PRESCRIBED DOSE UNLESS ADVISED BY YOUR HEALTHCARE PROFESSIONAL.

Take CEFTIN for oral suspension with food. This will help to make the treatment more effective.

The dose depends on the weight of the child. Your doctor or pharmacist will tell you exactly how much of the liquid suspension your child must take.

Bottles: Before removing the cap, you must shake the bottle very well until the medicine can be heard moving in the bottle to make sure you get out the right dose. Replace cap securely after each opening. During treatment, you should use a 5 mL spoon to take the medicine exactly as prescribed, taking care not to overfill the spoon. If desired, the dose may be added to one of the following cold beverages immediately prior to administration: milk (i.e. skim, 2% or homogenized), fruit juice (i.e. apple, orange, or grape) or lemonade.

Do not mix CEFTIN for oral suspension with hot beverages before drinking.

Overdose:
It is important to follow the dosage instructions on the label of your medicine. Taking more than this dose is unlikely to be dangerous unless a large quantity of suspension is taken all at once. In this case, contact your doctor or nearest hospital emergency department immediately.

If you think you, or a person you are caring for, have taken too much CEFTIN for oral suspension, contact a healthcare professional, hospital emergency department, or regional poison control centre immediately, even if there are no symptoms.

Missed Dose:
If you forget to take a dose, take another as soon as possible. Then continue with the normal dose. Do not double doses.

What are possible side effects from using CEFTIN for oral suspension?
These are not all the possible side effects you may have when taking CEFTIN for oral suspension. If you experience any side effects not listed here, tell your healthcare professional.

You may experience diarrhea, nausea, vomiting, loose stools, headache, dizziness and drowsiness.

Other side effects include seizure and kidney problems. CEFTIN for oral suspension may also cause an increase in a type of white blood cell (*eosinophilia*), a decrease in the number of white blood cells (*leukopenia*), a decrease in number of blood platelets (cells that help blood to clot) called thrombocytopenia or an increase in some substances (*enzymes*) produced by the liver. If you are taking a blood test, you should tell your doctor that you are taking CEFTIN for oral suspension, as it may affect your result.

If you feel worse or you have taken all the suspension and do not feel better TELL YOUR DOCTOR AS SOON AS POSSIBLE.

Serious side effects and what to do about them			
Symptom / effect	**Talk to your healthcare professional**		**Stop taking drug and get immediate medical help**
	Only if severe	**In all cases**	
RARE			
Overgrowth of Yeast (*Candida*): fungal infections (such as thrush, diaper rash and inflammation of the vagina). This side effect is more likely to occur with prolonged use.		✓	
Bowel Inflammation (*Clostridium difficile* colitis): severe diarrhea (bloody or watery) with or without fever, abdominal pain, or tenderness.			✓
VERY RARE			
Allergic Reactions: wheezing and tightness of chest, swelling of eyelids, face or lips, skin lumps or hives, or skin rash (red spots).			✓
Erythema Multiforme (severe skin reaction): skin rash which may blister and looks like small targets (central dark spots surrounded by a paler area with a dark ring around the edge).			✓
Breaking down of red blood cells (hemolytic anemia): pale skin, weakness, tiredness, shortness of breath, yellowing of your skin and/or the whites of your eyes, fever.			✓
Liver problems with symptoms such as abdominal pain, vomiting, nausea, and yellowing of the whites of the eyes or skin.		✓	
UNKNOWN			
Severe Cutaneous Adverse Reactions (SCAR) (severe skin reactions that may also affect other organs)**:** • Skin peeling, scaling, or blistering (with or without pus) which may also affect your eyes, mouth,			✓

Serious side effects and what to do about them			
Symptom / effect	**Talk to your healthcare professional**		**Stop taking drug and get immediate medical help**
	Only if severe	**In all cases**	
nose or genitals, itching, severe rash, bumps under the skin, skin pain, skin color changes (redness, yellowing, purplish). • Swelling and redness of eyes or face. • Flu-like feeling, fever, chills, body aches, swollen glands, cough. • Shortness of breath, chest pain, or discomfort.			
Kounis syndrome: a mixture of symptoms and signs of an allergic reaction and heart attack or unstable angina, with chest pain, shortness of breath, faintness, nausea, vomiting, syncope, pruritus, urticaria, sudden, heavy sweating, unusual paleness, palpitations, hypotension, slow heartbeat.			✓

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

- Store reconstituted CEFTIN for oral suspension in the refrigerator at 2°C to 8°C (do not freeze) and let it rest for at least one hour before taking the first dose. The reconstituted suspension should be refrigerated at all times and can be stored for up to 10 days.
- After 10 days of refrigerated storage, the suspension should be discarded.
- Keep out of reach and sight of children.

If you want more information about CEFTIN for oral suspension:

- Talk to your healthcare professional.
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website: https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html; the manufacturer's website www.sandoz.ca, or by calling 1-800-361-3062.

This leaflet was prepared by Sandoz Canada Inc.

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