CEFALEXIN

CEFALIN®

100 mg/mL Powder for Suspension (Oral Drops)
125 mg/5 mL Powder for Suspension
250 mg/5 mL Powder for Suspension
ANTIBACTERIAL

FORMULATIONS

Each mL reconstituted suspension (oral drops) contains:
Cefalexin (as monohydrate).....100 mg

Each 5 mL reconstituted suspension contains:
Cefalexin (as monohydrate).....125 mg or 250 mg

PRODUCT DESCRIPTIONS

Cefalexin (Cefalin®) 100 mg/mL Powder for Suspension (Oral Drops) and 250 mg/5 mL Powder for Suspension are off-white to cream powder for reconstitution into pink, tutti-frutti flavored suspensions.

Cefalexin (Cefalin®) 125 mg/5 mL Powder for Suspension is a yellow powder for reconstitution into yellow, cherry-tutti-frutti flavored suspension.

PHARMACODYNAMICS

Cefalexin is a semi-synthetic, first generation cephalosporin which exerts its bactericidal activity by interfering with the bacterial cell wall synthesis. It binds to specific penicillin-binding proteins responsible for the synthesis of peptidoglycan, a heteropolymeric structure that gives the cell wall its mechanical stability. The final stage of peptidoglycan synthesis involves completion of the cross-linking of the terminal glycine residue of the pentaglycine bridge to the fourth residue of the pentapeptide. The transpeptidase enzyme that catalyzes this step is inhibited by cephalosporins. As a result the bacterial cell wall is weakened, the cell swells and then ruptures.

ANTIMICROBIAL SPECTRUM OF ACTIVITY

Cefalexin is active *in vitro* and in clinical infections against most strains of the following microorganisms:

Aerobic Gram-positive	Aerobic Gram-negative
Staphylococcus aureus (including penicillinase-producing strains) *Staphylococcus epidermidis* (penicillin-susceptible strains) *Streptococcus pneumoniae* (penicillin-susceptible strains) *Streptococcus pyogenes*	*Escherichia coli* *Haemophilus influenzae* *Klebsiella pneumoniae* *Moraxella catarrhalis* *Proteus mirabilis*

Cefalexin is inactive against methicillin-resistant staphylococci and most strains of enterococci (e.g., *Enterococcus faecalis*), *Enterobacter* spp., *Morganella morganii*, and *Proteus vulgaris*. It has no activity against *Pseudomonas spp.* or *Acinetobacter calcoaceticus*. Penicillin-resistant *Streptococcus pneumoniae* is usually cross-resistant to beta-lactam antibiotics.

It is suggested to carry out susceptibility tests.

PHARMACOKINETICS

Cefalexin is acid stable and is rapidly and completely absorbed from the gastrointestinal (GI) tract. Absorption of cefalexin is delayed in young children and may be decreased up to 50% in neonates. Peak serum concentrations of the drug have been reported to occur within 3 hours in infants younger than 6 months old, within 2 hours in children 9 to 12 months old, and within 1 hour in older children.

Cefalexin readily diffuses into tissues, including bone, joints and the pericardial as well as pleural cavities. It reaches therapeutic levels in the blood, urine, bile, synovial fluid, pus, tonsillar tissue, amniotic fluid, cord blood, and fetal blood. Cefalexin does not enter the cerebrospinal fluid (CSF) in significant quantities. The drug crosses the placenta and small quantities are found in breast milk.

The serum half-life ($t_{1/2}$) of cefalexin is about 5 hours in neonates and 2.5 hours in children 3 to 12 months old.

Cefalexin is not metabolized in the body. It is excreted unchanged in the urine by both glomerular filtration and tubular secretion.

INDICATIONS

For the treatment of the following infections caused by susceptible microorganisms:

- Skin and skin structure infections
- Bone and joint infections
- Genitourinary tract infections, including acute prostatitis
- Respiratory tract infections including acute and chronic bronchitis and infected bronchiectasis
- Ear, nose and throat infections including otitis media, mastoiditis, sinusitis, follicular tonsillitis, and pharyngitis
- Dental infections

Note: Penicillin is the usual drug of choice in the treatment and prevention of streptococcal infections, including the prophylaxis of rheumatic fever. Cefalexin is generally effective in the eradication of streptococci from the nasopharynx; however, substantial data establishing the efficacy of cefalexin in the subsequent prevention of rheumatic fever are not available at present.

DOSAGE AND ADMINISTRATION

Cefalexin is administered orally.

Usual Pediatric Dose: 25 to 50 mg/kg body weight per day to be given in equally divided doses every 6 hours

- For severe infections, the dosage may be doubled (Maximum dose: 4 g per day).
- For streptococcal pharyngitis (in patients>1 year old), skin and skin structure infections, and mild, uncomplicated urinary tract infections, the total daily dose may be divided and administered every 12 hours.
- For otitis media, the dose may be increased to 75 to 100 mg/kg body weight per day to be given in equally divided doses every 6 hours.
- Children receiving intermittent dialysis should be given an additional 8 mg per kg of cefalexin after each dialysis.

Age Group	Recommended Cefalexin Oral Dose (based on 50 mg/kg body weight per day)				
	100 mg/mL Drops	125 mg/5 mL Suspension		250 mg/5 mL Suspension	
	Every 6 hours	Every 6 hours	Every 12 hours	Every 6 hours	Every 12 hours
Birth to 3 months	0.5 mL	-	-	-	-
4 to 6 months	0.75 to 1 mL	-	-	-	-
7 to 12 months	1 mL	-	-	-	-
1 to 2 years		5 mL (1 teaspoonful)	10 mL (2 teaspoonsful)	2.5 mL (1/2 teaspoonful)	5 mL (1 teaspoonful)
3 to 6 years		5 to 10 mL (1 to 2 teaspoonsful)	10 to 20 mL (2 to 4 teaspoonsful)	2.5 to 5 mL (1/2 to 1 teaspoonful)	5 to 10 mL (1 to 2 teaspoonsful)
7 to 12 years		-	-	5 to 10 mL (1 to 2 teaspoonsful)	10 to 20 mL (2 to 4 teaspoonsful)
	Or, as prescribed by a physician.				

Usual Duration of Treatment:

- **For mild to moderate infections:** 5 to 7 days
- **For cystitis:** 7 to 14 days
- **For ß-hemolytic streptococcal infections:** At least 10 days

Or, as prescribed by a physician.

Directions for Reconstitution:

Cefalexin Dosage Format and Pack Size	Volume of Distilled Water to be Added	Directions
100 mg/mL powder for suspension (oral drops), 10 mL	7 mL	Tap the bottle several times to loosen the powder before reconstitution. Add the required amount of distilled water in two portions, replace the bottle cap and shake vigorously after each addition until all contents are evenly suspended. Keep bottle tightly closed. Shake well before use.
125 mg/5 mL or 250 mg/5 mL powder for suspension, 60 mL	40 mL	
Store for not more than 7 days at 25°C to 30°C or not more than 14 days under refrigeration (2°C to 8°C). Protect from light.		

CONTRAINDICATION

Known hypersensitivity to cephalosporins, penicillins, or any component of the product.

WARNINGS AND PRECAUTIONS

- **Careful inquiry should be made prior to cefalexin therapy to determine whether the patient has had previous hypersensitivity reactions to cefalexin, cephalosporins, penicillins, or other drugs. Use with caution in penicillin-sensitive patients since cross-sensitivity among ß-lactam antibiotics has been clearly documented and may occur in up to 10% of patients with a history of allergy to penicillin. In case of an allergic reaction to cefalexin, the drug should be discontinued.**
- **Serious acute hypersensitivity reactions may require immediate treatment with epinephrine and other emergency measures, including oxygen, intravenous fluids, corticosteroids, pressor amines, and airway management, as clinically indicated.**
- *Clostridium difficile*-associated diarrhea (CDAD) and colitis have been reported with the use of nearly all antibacterial agents, including cefalexin, and may range in severity from mild to life-threatening. It is important to consider this diagnosis in patients who present with diarrhea after administration of antibacterial agents.
- Cephalosporins, including cefalexin, have been associated with the development of seizures, particularly in patients with renal impairment, in whom dosage of the drug was not reduced. If seizures due to cefalexin develop, the drug should be discontinued and treatment with an anticonvulsant be given as clinically indicated.
- Cephalosporins may be associated with a fall in prothrombin activity. Patients who are at risk are those with renal or hepatic impairment or poor nutritional state, as well as patients receiving a protracted course of antimicrobial therapy, and patients previously stabilized on anticoagulant therapy. Prothrombin time should be monitored in patients at risk and exogenous Vitamin K administered as indicated.
- A false-positive Coombs' test has been reported during treatment with other cephalosporin antibiotics; therefore, it should be recognized that a positive Coombs' test may be due to the drug, e.g., Coombs' testing of newborns whose mothers have received cephalosporins before parturition or in hematologic studies or in transfusion cross-matching procedures when antiglobulin tests are performed.
- Use with caution in patients with renal impairment. Careful clinical and laboratory studies should be made since safe dosage may be lower than that usually recommended.
- Indicated surgical procedures (e.g., incision and drainage of abscesses) should be performed in conjunction with antibiotic therapy.
- As with any potent drug, periodic assessment of organ system functions, including renal, hepatic, hematopoietic, is recommended during prolonged therapy.
- Prescribing cefalexin 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 antibiotic resistance.
- As with other antibacterial drugs, long term or repeated use may result in overgrowth of non-susceptible organisms, including fungi.

INTERACTIONS WITH OTHER MEDICAMENTS

No potentially hazardous interactions have been reported. However, it may share the interaction potential of other cephalosporins as with the following:

- **Alcohol:** Disulfiram-like reactions have occurred when alcohol was ingested within 48 to 72 hours after administration of ß-lactam antibiotics that contain *N*-methylthiotetrazole side chain. The reactions appear to result from accumulation of acetaldehyde and do not occur if alcohol is ingested prior to the first dose of antibiotic. Ingestion of alcohol during and for 24 to 72 hours after administration of some cephalosporins should be avoided.
- **Probenecid:** Concomitant administration of oral probenecid competitively inhibits tubular secretion resulting in higher and more prolonged serum concentrations of most cephalosporins.
- **Estrogens or Progestins:** Some cephalosporins (e.g., ceftazidime) may affect gut flora, leading to lower estrogen reabsorption and reduced efficacy of oral contraceptives.
- **Metformin:** When single 500 mg doses of cefalexin and metformin were given to 12 healthy subjects, plasma metformin C_{max} and AUC increased by an average of 34% and 24%, respectively, and metformin's renal clearance decreased by an average of 14%. Information on the interaction of cefalexin and metformin after multiple dose administration is unavailable. Careful patient monitoring and metformin dose adjustment is recommended during concomitant therapy.
- **Nephrotoxic Drugs:** Concurrent use of nephrotoxic agents such as aminoglycosides, colistin, polymyxin B, or vancomycin may increase the risk of nephrotoxicity with some cephalosporins and probably should be avoided, if possible.
- **Diuretics:** Concurrent treatment with high doses of cephalosporins and potent diuretics (e.g., furosemide) may adversely affect renal function.
- **Other Anti-infective Agents:** *In vitro* studies indicate that the antibacterial activity of cephalosporins against some organisms may be additive or synergistic with aminoglycosides and penicillins. Although some *in vitro* studies showed additive or synergistic antibacterial activity between chloramphenicol and a cephalosporin, there is more recent *in vitro* evidence of antagonism between cephalosporins and chloramphenicol against a variety of Gram-negative and Gram-positive bacteria, particularly when chloramphenicol was added to the medium before the ß-lactam. In addition, at least one case of *in vivo* antagonism has been reported in an infant with *Salmonella enteritidis* meningitis. Therefore, it is recommended that combined therapy with chloramphenicol and a cephalosporin be avoided, particularly when bactericidal activity is considered important.

Interference with Laboratory Tests:

- Cefalexin capsules may cause false-positive glucose reaction in urine with Benedict's and Fehling's solutions and Clinitest® tablets.
- A false-positive direct Coombs' test has been reported during treatment with other cephalosporin antibiotics; therefore it should be recognized that a positive Coombs' test may be due to the drug.
- Cefalexin can interfere with the alkaline picrate assay for creatinine, giving a falsely high reading, although the degree of elevation is unlikely to be of clinical importance.
- The quantitative determination of urinary protein excretion using strong acids is misleading during cefalexin therapy as precipitation of cefalexin in the urine may occur.

STATEMENT ON USAGE FOR HIGH RISK GROUPS

PREGNANCY AND LACTATION

Pregnancy Category B. There are no adequate and well-controlled studies in pregnant women. Although laboratory and clinical studies have shown no evidence of teratogenicity, caution should be exercised when prescribing cefalexin to pregnant patients.

The excretion of cefalexin in human milk increased up to 4 hours after a 500 mg dose; the drug reached a maximum level of 4 mcg/mL, then decreased gradually, and had disappeared 8 hours after administration. Cefalexin should be used with caution during breastfeeding.

CHILDREN

The safety and effectiveness of cefalexin in the pediatric population have been established and reported in various clinical trials.

RENAL IMPAIRMENT

In patients with impaired renal function, decreases in doses and/or frequency of administration of cefalexin may be required and should be based on the degree of renal impairment, severity of infection, susceptibility of the causative organism, and serum concentrations of cefalexin.

UNDESIRABLE EFFECTS

Body as a whole: Nuchal swelling, superinfection, fatigue, tiredness, fever

Cardiovascular: Cardiac arrhythmia, vasodilatation

CNS: Dizziness, nausea, headache, agitation, confusion, hallucination

Dermatologic/Hypersensitivity Reactions: Anaphylaxis, angioedema, eosinophilia, erythema multiforme, fever, genital and anal pruritus, intertrigo, pruritus, rash (maculopapular erythematous, or morbilliform), serum sickness-like reactions, Stevens-Johnson syndrome, toxic epidermal necrolysis, urticaria

Endocrine-Metabolic: Elevated cholesterol, anorexia

Gastrointestinal: Abdominal cramp/pain, CDAD and colitis, diarrhea, dyspepsia, gastritis, gastroenteritis, glossitis/stomatitis, vomiting

Hematologic: Decreased hemoglobin and/or hematocrit, hemolytic anemia, reversible leukopenia; neutropenia, decreased platelets; positive direct and indirect antiglobulin (Coombs') test results; thrombocytopenia; eosinophilia

Hepatic: Transient increases in serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), and alkaline phosphatase concentrations; increased serum bilirubin; transient hepatitis, cholestatic jaundice, cholestatic icterus

Musculoskeletal: Arthralgia, myalgia, arthritis, joint disorder, back pain

Nervous System: Agitation, confusion, diplopia, dizziness, fatigue, headache, hallucinations, insomnia, malaise, paresthesia, somnolence, tremor, toxic paranoid reactions (rarely in patients with renal impairment). Vertigo, tinnitus, hearing loss and behavioral changes in young children have been reported with cefalexin use.

Renal and Genitourinary: Transient increases in blood urea nitrogen (BUN) and serum creatinine concentrations; dysuria, reversible interstitial nephritis; nephrotoxicity, leukorrhea, pruritus vulvae, vaginal discharge, vulvo-vaginitis, genital and anal pruritus, genital candidiasis

Respiratory: Dyspnea

The following AEs have also been reported for cephalosporin-class antibiotics:

Body as a whole: Hot flushes

Cardiovascular: Chest pain

CNS: Anxiety, nightmares, hyperactivity, nervousness, weakness, hypertonia. Cephalosporins, in general, have been implicated in triggering seizures, particularly in patients with renal impairment when the dosage was not reduced.

Dermatologic/Hypersensitivity Reactions: Hypersensitivity reactions including chills, joint pain or inflammation, edema, facial edema, erythema, shock, hypotension, exfoliative dermatitis

Endocrine and Metabolic: Increased or decreased serum glucose concentration

Hematologic: Agranulocytosis, aplastic anemia, pancytopenia, thrombocythemia, prolonged prothrombin time, leukocytosis, granulocytosis, monocytosis, lymphocytopenia, basophilia, anemia, epistaxis or hemorrhage

Hepatic: Transient increases in serum γ-glutamyl transferase concentrations; increased serum concentrations of lactate dehydrogenase (LDH); decreased serum albumin and/or total protein; hepatic dysfunction, including cholestasis

Gastrointestinal: Epigastric pain, decreased appetite, flatulence, candidiasis, decreased salivation, tenesmus, heartburn

Renal and Genitourinary: Renal dysfunction, toxic nephropathy, menstrual irregularities

Respiratory: Pleural effusion, pulmonary infiltrate, respiratory distress, cough, rhinitis

Special Senses: Taste alteration, alteration in color perception

OVERDOSE AND TREATMENT

Clinical features of cefalexin overdose may include nausea, vomiting, epigastric distress, diarrhea, and hematuria.

Unless 5 to 10 times the normal cefalexin dose has been ingested, GI decontamination should not be necessary.

It is important to protect the patient's airway and support ventilation and perfusion during overdose. Meticulously monitor and maintain, within acceptable limits, the patient's vital signs, blood gases, serum electrolytes, etc. Absorption of drugs from the GI tract may be decreased by giving activated charcoal, which, in many cases, is more effective than emesis or lavage; consider charcoal instead of or in addition to gastric emptying. Repeated doses of charcoal over time may hasten elimination of some drugs that have been absorbed. Safeguard the patient's airway when employing gastric emptying or charcoal.

Forced diuresis, peritoneal dialysis, hemodialysis, or charcoal hemoperfusion have not been established as beneficial for cefalexin overdose; however, it would be extremely unlikely that one of these procedures would be indicated.

There have been reports of hematuria, without renal impairment, in children accidentally ingesting more than 3.5 g of cefalexin in a day. Treatment has been supportive fluids and no sequelae have been reported.

STORAGE CONDITIONS

Store in a dry place at temperatures not exceeding 30°C. Protect from light.
Keep the products out of sight and reach of children.

CAUTION

Foods, Drugs, Devices, and Cosmetics Act prohibits dispensing without prescription.

AVAILABILITY

Cefalexin (Cefalin®) 100 mg/mL Suspension (Oral Drops)
- in amber bottle of 10 mL and 5 mL (Physician's sample)

Cefalexin (Cefalin®) 125 mg/5 mL Suspension
- in amber bottle of 60 mL and 10 mL (Physician's sample)

Cefalexin (Cefalin®) 250 mg/5 mL Suspension
- in amber bottle of 60 mL and 10 mL (Physician's sample)

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Trusted Quality Healthcare