# CECLOR®
## CEFACLOR
## FOR ORAL SUSPENSION

### DESCRIPTION

Cefaclor is a semisynthetic cephalosporin antibiotic for oral administration. It is chemically designated as 3-chloro-7-D-(2-phenylglycinamido)-3-cephem-4-carboxylic acid monohydrate.

After mixing, each 5 mL of cefaclor for oral suspension will contain cefaclor monohydrate equivalent to 125 mg (0.34 mmol), 187.5 mg (0.51 mmol), 250 mg (0. 68 mmol), or 375 mg ( 1.0 mmol) cefaclor.

### CLINICAL PHARMACOLOGY

Cefaclor is well absorbed after oral administration to fasting subjects. Total absorption is the same whether the drug is given with or without food; however, when it is taken with food; the peak concentration achieved is 50% to 75% of that observed when the drug is administered to fasting subjects and generally appears from three fourths to 1 hour later. Following administration of 250-mg, 500-mg, and 1-g doses to fasting subjects, average peak serum levels of approximately 7, 13, and 23 mg/Lrespectively were obtained within 30 to 60 minutes. Approximately 60% to 85% of the drug is excreted unchanged in the urine within 8 hours, the greater portion being excreted within the first 2 hours. During this 8-hour period, peak urine concentrations following the 250-mg, 500-mg, and 1-g doses were approximately 600, 900, and 1,900 mg/L respectively. The serum half-life in normal subjects is approximately 1 hour (range 0.6 to 0.9). In patients withreduced renal function, the serum half-life of cefaclor is slightly prolonged. In those with complete absence of renal function, the plasma half-life of the intact molecule is 2.3 to 2 .8 hours. Excretion pathways in patients with markedly impaired renal function have not been determined.

Hemodialysis shortens the hal f-life by 25% to 30%.

*Microbiology*-- In vitro tests demonstrate that the bactericidal action of the cephalosporins results from their inhibition of cell-wall synthesis. While in vitro studies have demonstrated the susceptibility of most strains of the following organisms to cefaclor, clinical efficacy for infections other than those included in the Indications and Usage section is unknown.

Aerobes, Gram-positive

*Staphylococci*, including coagulase-positive, coagulase-negative, and penicillinase-producing strains (when tested by in vitro methods), exhibit cross-resistance between cefaclor and methicillin

*Streptococcus pneumoniae*

*Streptococcus pyogenes*

Aerobes Gram-negative

*Citrobacter diversus*

*Escherichia coli*

*Haemophilus influenzae*, including β-lactamase-producing, ampicillin-resistant strains

*Klebsiella spp*

*Moraxella (Branhamella) catarrhalis*

*Neisseria gonorrhoeae*

*Proteus mirabilis*

Anaerobes

*Bacteroides spp* (excluding *Bacteroides fragilis*)

*Peptococcus niger*

*Peptostreptococcus spp*

*Propionibacteria acnes*

*Note:* Methicillin-resistant staphylococci and most strains of enterococci (*Enterococcus faecalis* [formerly *Streptococcus faecalis*] and *Enterococcus faecium* (formerly *Streptococcus faecium*)] are resistant to cefaclor and other cephalosporins.

Cefaclor is not active against most strains of *Enterobacter* spp, *Serratia* spp, *Morganella morganii, Proteus vulgaris*, and *Providencia rettgeri*. It has no activity against *Pseudomonas* spp or *Acinetobacter* spp.

*Disk Susceptibility Tests* —

Diffusion techniques: Quantitative methods that require measurement of zone diameters give the most precise estimates of antibiotic susceptibility of bacteria to antimicrobial agents. One such standard procedure[1] has been recommended for use with disks to test susceptibility of organisms to cefaclor, using the 30 µg cefaclor disk. Interpretation involves the correlation of the diameters obtained in the disk test with the minimum inhibitory concentration (MIC) for cefaclor.

Reports from the laboratory giving results of the standard single-disk susceptibility test with a 30 µg cefaclor disk should be interpreted according to the following criteria:

| Zone Diameter (mm) | Interpretation |
|---|---|
| ≥18 | (S) Susceptible |
| 15-17 | (I) Intermediate |
| ≤14 | (R) Resistant |

When Testing* H. influenzae

| Zone Diameter (mm) | Interpretation |
|---|---|
| ≥20 | (S) Susceptible |
| 17-19 | (I) Intermediate |
| ≤16 | (R)Resistant |

* Disk susceptibilitytests performed using Haemophilus Test Medium (HTM)

Although the spectrum of activity of cefaclor is qualitatively similar to that of cephalothin and of the other first-generation cephalosporins, its activity against *H. influenzae* is considerably greater than that of the first generation cephalosporins.

For this reason, a disk containing 30 µg of cefaclor may be used to determine the susceptibility of *H. influenzae* using the method described by NCCLS. In the testing of *H. influenzae* (on Mueller-Hinton agar supplemented with hemoglobin and a commercial VX supplement) or other organisms, zone diameter interpretive criteria, are identical to those used for the cephalothin disk: ≥18 mm, susceptible; 15-17 mm, moderately susceptible (intermediate for *Haemophilus*); and ≤14 mm, resistant.

A report of "Susceptible" indicates that the pathogen is likely to be inhibited by generally achievable blood levels. A report of "Intermediate" suggests that the organism would be susceptible if high dosage is used or if the infection is confined to tissue and fluids in which high antibiotic levels are obtained. A report of "Resistant" indicates that achievable concentration of the antibiotic are unlikely to be inhibitory and other therapy should be selected.

Standardized procedures require the use of laboratory control organisms. The 30 µg cefaclor disk should give the following zone diameters:

| Organism | Zone Diameter (mm) |
|---|---|
| *E. coli* ATCC 25922 | 23-27 |
| *S. aureus* ATCC 25923 | 27-31 |
| *H. influenzae* ATCC 49766* | 25-31 |

* Disk susceptibility tests performed using Haemophilus Test Medium (HTM)

Dilution techniques: Use a standardized dilution method[2] (broth, agar, microdilution) or equivalent with cefaclor powder. The MIC values obtained should be interpreted according to the following criteria:

| MIC (µg/mL) | Interpretation |
|---|---|
| ≤8 | Susceptible |
| 16 | Intermediate |
| ≥32 | Resistant |

As with standard diffusion techniques, dilution methods require the use of laboratory control organisms. Standard cefaclor powder should provide the following MIC values:

| Organism | MIC (µg/mL) |
|---|---|
| *S. aureus* ATCC 29213 | 1-4 |
| *E. coli* ATCC 25922 | 1-4 |
| *E. faecalis* ATCC 29212 | >32.0 |
| *H. influenzae* ATCC 49766* | 1-4 |

* Broth microdilution tests performed using Haemophilus Test Medium (HTM)

### INDICATIONS AND USAGE

Cefaclor is indicated in the treatment of the following infections when caused by susceptible strains of the designated microorganisms:

Otitis media caused by *S. pneumoniae, H. influenzae, staphylococci, S. pyogenes* (group A β-hemolytic streptococci), and *M. catarrhalis*

Lower respiratory tract infections, including pneumonia, caused by *S. pneumoniae, H. influenzae, S. pyogenes* (group A β-hemolytic streptococci), and *M. catarrhalis*.

Upper respiratory tract infections, including pharyngitis and tonsillitis, caused by *S. pyogenes* (group A β-hemolytic streptococci), and *M. catarrhalis*.

Note: Penicillin is the usual drug of choice in the treatment and prevention of streptococcal infections, including the prophylaxis of rheumatic fever. Amoxicillin has been recommended by the American Heart Association as the standard regimen for the prophylaxis of bacterial endocarditis for dental, oral, and upper respiratory tract procedures, with penicillin V a rational and acceptable alternative in the prophylaxis against a-hemolytic streptococcal bacteremia in this setting. Cefaclor is generally effective in the eradication of streptococci from the nasopharynx; however, substantial data establishing the efficacy of cefaclor in the subsequent prevention of either rheumatic fever or bacterial endocarditis are not available at present.

Urinary tract infections, including pyelonephritis and cystitis, caused by *E. coli, P. mirabilis, Klebsiella* spp, and coagulase-negative staphylococci.

Note -- Cefaclor has been found to be effective in both acute and chronic urinary tract infections.

Skin and skin structure infections caused by *staphylococcus aureus* and *S. pyogenes* (group A β-hemolytic streptococci)

Sinusitis

Gonococcal urethritis

Appropriate culture and susceptibility studies should be performed to determine susceptibility of the causative organism to cefaclor.

### CONTRAINDICATION

Cefaclor is contraindicated in patients with known allergy to the cephalosporin group of antibiotics.

### WARNINGS

BEFORE THERAPY WITH CEFACLOR IS INSTITUTED, CAREFUL INQUIRY SHOULD BE MADE TO DETERMINE WHETHER THE PATIENT HAS HAD PREVIOUS HYPERSENSITIVITY REACTIONS TO CEFACLOR, CEPHALOSPORINS, PENICILLINS, OR OTHER DRUGS. IF THIS PRODUCT IS TO BE GIVEN TO PENICILLIN-SENSITIVE PATIENTS, CAUTION SHOULD BE EXERCISED BECAUSE CROSS-HYPERSENSITIVITY, INCLUDING ANAPHYLAXIS, AMONG β-LACTAM ANTIBIOTICS HAS BEEN CLEARLY DOCUMENTED.

If an allergic reaction to cefaclor occurs, the drug should be discontinued, and, if necessary, the patient should be treated with appropriate agents, eg, pressor amines, antihistamines,or corticosteroids.

Antibiotics, including cefaclor, should be administered cautiously to any patient who has demonstrated some form of allergy, particularly to drugs.

Pseudomembranous colitis has been reported with virtually all broad-spectrum antibiotics (including macrolides, semisynthetic penicillins, and cephalosporins); therefore, it is important to consider its diagnosis in patients who develop diarrhea in association with the use of antibiotics. Such colitis may range in severity from mild to life threatening. Mild cases of pseudomembranous colitis usually respond to drug discontinuance alone .In moderate to severe cases, appropriate measures should be taken.

### PRECAUTIONS

*General*- Prolonged use of cefaclor may result in the overgrowth of nonsusceptible organisms .Careful observation of the patient is essential. If superinfection occurs during therapy, appropriate measures should be taken.

Positive direct Coombs' tests have been reported during treatment with the cephalosporin antibiotics. It should be recognized that a positive Coombs' test may be due to the drug, eg, in hematologic studies or in transfusion cross-matching procedures when antiglobulin tests are performed on the minor side or in Coombs' testing of newborns whose mothers have received cephalosporin antibiotics before parturition.

Cefaclor should be administered with caution in the presence of markedly impaired renal function. Since the half-life of cefaclor in anuria is 2.3 to 2.8 hours, dosage adjustments for patients with moderate or severe renal impairment are usually not required. Clinical experience with cefaclor under such conditions is limited; therefore, careful clinical observation and laboratory studies should be made.

Antibiotics, including cephalosporins, should be prescribed with caution in individuals with a history of gastrointestinal disease, particularly clotitis.

*Drug/Laboratory Test Interactions* -- Patients receiving cefaclor may show a false-positive reaction for glucose in the urine with tests that use Benedict's and Fehling's solutions and also with Clinitest® tablets but not with Tes-Tape® (Glucose Enzymatic Test Strip, USP, Lilly).

There have been rare reports of increased anticoagulant effect when cefaclor and oral anticoagulants were administered concomitantly (see Adverse Reactions).

As with other β-lactam antibiotics, the renal excretion of cefaclor is inhibited by probenecid.

*Carcinogenesis, Mutagenesis, Impairment of Fertility*-- Studies have not been performed to determine potential for carcinogenicity or mutagenicity. Reproduction studies have revealed no evidence of impaired fertility.

*Usage in pregnancy*— Reproduction studies have been performed in mice and rats at doses up to 12 times the human dose and in ferrets given 3 times the maximum human dose and have revealed no evidence of impaired fertility or harm to the fetus due to cefaclor. 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.

*Labor and Delivery*-- The effect of cefaclor on labor and delivery is unknown.

*Nursing Mothers*-- Small amounts of cefaclor have been detected in mother's milk following administration of single 500- mg doses. Average levels were 0.18, 0.20, 0.21, and 0.16 mg/L at 2, 3, 4 and 5 hours respectively. Trace amounts were detected at 1 hour. The effect on nursing infants is not known. Caution should be exercised when cefaclor is administered to a nursing woman.

*Pediatric Use*-- Safety and effectiveness of this product for use in infants less than 1 month of age have not been established.

## ADVERSE REACTIONS

Adverse effects considered to be related to therapy with cefaclor are listed below:

*Hypersensitivity* reactions have been reported in about 1.5% of patients and include morbilliform eruptions (1 in 100). Pruritus, urticaria, and positive Coombs' tests each occur in less than 1 in 200 patients.

Cases of **serum –sickness-like** reactions have been reported with the use of cefaclor. These are characterized by findings of erythema multiforme, rashes, and other skin manifestations accompanied by arthritis/arthralgia, with or without fever, and differ from classic serum sickness in that there is infrequently associated lymphadenopathy and proteinuria, no circulating immune complexes, and no evidence to date of sequelae of the reaction. Occasionally, solitary symptoms may occur, but do not represent a **serum-sickness-like** reaction. While further investigation is ongoing, **serum-sickness-like** reactions appear to be due to hypersensitivity and more often occur during or following a second (or subsequent) course of therapy with cefaclor. Such reactions have been reported more frequently in children than in adults with an overall occurrence ranging from 1 in 200 (0.5%) in one focused trial to 2 in 8,346 (0.024%) in overall clinical trials (with an incidence in children in clinical trials of 0.055%) to 1 in 38,000 (0.003%) in spontaneous event reports. Signs and symptoms usually occur a few days after initiation of therapy and subside within a few days after cessation of therapy; occasionally these reactions have resulted in hospitalization, usually of short duration (median hospitalization = 2 to 3 days, based on postmarketing surveillance studies). In those requiring hospitalization, the symptoms have ranged from mild to severe at the time of admission with more of the severe reactions occurring in children. Antihistamines and glucocorticoids appear to enhance resolution of the signs and symptoms. No serious sequelae have been reported.

More severe hypersensitivity reactions, including Stevens-Johnson syndrome, toxic epidermal necrolysis, and anaphylaxis have been reported rarely. Anaphylactoid events may be manifested by solitary symptoms including angioedema, asthenia, edema (including face and limbs), dyspnea, paresthesias, syncope, or vasodilation. Anaphylaxis may be more common in patients with a history of penicillin allergy. Rarely, hypersensitivity symptoms may persist for several months.

*Gastrointestinal symptoms* occur in about 2.5% of patients and include diarrhea (1 in 70). Symptoms of pseudomembranous colitis may appear either during or after antibiotic treatment. Nausea and vomiting have been reported rarely. As with some penicillins and some other cephalosporins, transient hepatitis and cholestatic jaundice have been reported rarely.

*Other effects* considered related to therapy included eosinophilia (1 in 50 patients), genital pruritus, moniliasis or vaginitis and, rarely, thrombocytopenia or reversible interstitialnephritis.

*Causal Relationship Uncertain*--

*CNS*-- Rarely, reversible hyperactivity, agitation, nervousness, insomnia, confusion, hypertonia, dizziness, hallucinations, and somnolence have been reported.

Transitory abnormalities in clinical laboratory test results have been reported. Although they were of uncertain etiology, they are listed below to serve as altering information for the physician.

*Hepatic*— Slight elevations of AST (SGOT), ALT (SGPT), or alkaline phosphatase values (1 in 40).

*Hematopoietic*-- As has also been reported with other β-lactam antibiotics, transient lymphocytosis, leukopenia, and, rarely, hemolytic anemia, aplastic anemia, agranulocytosis, and reversible neutropenia of possible clinical significance.

There have been rare reports of increased prothrombin time with or without clinical bleeding in patients receiving cefaclor and Coumadin concomitantly.

*Renal* — Slight elevations in BUN or serum creatinine (less than 1 in 500) or abnormal urinalysis (less than 1 in 200).

Several cephalosporins have been implicated in triggering seizures, particularly in patients with renal impairment when the dosage was not reduced. If seizures associated with drug therapy occur, the drug should be discontinued.

Anticonvulsant therapy can be given if clinically indicated.

## OVERDOSAGE

*Signs and Symptoms*-- The toxic symptoms following an overdose of cefaclor may include nausea, vomiting, epigastric distress, and diarrhea. The severity of the epigastric distress and diarrhea are dose related. If other symptoms are present, it is probable that they are secondary to an underlying disease state, an allergic reaction, or the effects of other intoxication.

*Treatment*-- In managing overdosage, consider the possibility of multiple drug overdoses, interaction among drugs, and unusual drug kinetics in your patient.

Unless 5 times the normal dose of cefaclor has been ingested, gastrointestinal decontamination will not be necessary.

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

Forced diuresis, peritoneal dialysis, hemodialysis, or charcoal hemoperfusion have not been established as beneficial for an overdose of cefaclor.

## DOSAGE AND ADMINISTRATION

Cefaclor is administered orally.

*Adults*-- The usual adult dosage is 250 mg every 8 hours. For bronchitis and pneumonia, the dosage is 250 mg administered 3 times daily. A dosage of 250 administered 3 times daily for 10 days is recommended for sinusitis. For more severe infections (such as pneumonia) or those caused by less susceptible organisms, doses may be doubled. Doses of 4 g/day have been administered safely to normal subjects for 28 days, but the total daily dosage should not exceed this amount.

For the treatment of acute gonococcal urethritis in males and females, a single dose of 3 g combined with probenecid, 1 g, is given.

*Children*-- The usual recommended daily dosage for children is 20 mg/kg/day in divided doses every 8 hours. For bronchitis and pneumonia, the dosage is 20 mg/kg/day in divided doses administered 3 times daily.

In more serious infections, otitis media, and infections caused by less susceptible organisms, 40 mg/kg/day in divided doses are recommended, with a maximum dosage of 1 g/day.

Cefaclor Suspension

| | | |
|---|---|---|
| **20 mg/kg/day** | | |
| Child's weight | 125 mg/5 mL | |
| 9 Kg | 1/2 tsp t.i.d. | |
| 18 Kg | 1 tsp t.i.d. | 1/2 tsp t.i.d. |
| **40 mg/kg/day** | | |
| 9 Kg | 1 tsp t.i.d. | 1/2 tsp t.i.d. |
| 18 Kg | | 1 tsp t.i.d. |

*B.I.D. Treatment Option*— For the treatment of otitis media and pharyngitis, the total daily dosage may be divided and administered every 12 hours.

Cefaclor Suspension

| | | |
|---|---|---|
| **20 mg/kg/day (Pharyngitis)** | | |
| Child's weight | 187.5 mg/5 mL | |
| 9 Kg | 1/2 tsp b.i.d. | |
| 18 Kg | 1 tsp b.i.d. | 1/2 tsp b.i.d. |
| **40 mg/kg/day (Otitis Media)** | | |
| 9 Kg | 1 tsp b.i.d. | 1/2 tsp b.i.d. |
| 18 Kg | | 1 tsp b.i.d. |

Cefaclor may be administered in the presence of impaired renal function. Under such a condition, the dosage usually is unchanged (see Precautions).

In the treatment of β-hemolytic streptococcal infections, a therapeutics dosage of cefaclor should be administered for at least 10 days.

*Store at controlled room temperature, 59° to 86 ° F (15° to 30° C).*

*After mixing the oral suspension, store in refrigerator. Keep tightly closed and shake well before using. The mixture may be kept for 14 days without significant loss of potency. Discard unused portion after 14 days.*

**Presentation**

Ceclor® is available as Oral suspension of 125mg/5ml & 250mg/5ml in bottles of 60ml.


1. National Committee for Clinical Laboratory Standards. Performance standards for antimicrobial disk susceptibility tests- 5th ed., Approved Standard NCCLS Document M2-A5, Vol 13, No 24, NCCLS, Villanova, PA, 1993.

2. National Committee for Clinical Laboratory Standards. Methods for dilution antimicrobial susceptibility tests for bacteria that grow aerobically-3rd ed., Approved Standard NCCLS Document M7-A3, Vol 13, No 25, NCCLS, Villanova, PA, 1993.


**This is a medicament**

- A medicament is a product which affects your health, and its consumption contrary to instructions is dangerous for you.
- Follow strictly the doctor's prescription, the method of use and the instructions of the pharmacist who sold the medicament.
- The doctor and the pharmacist are experts in medicine, its benefits and risks.
- Do not by yourself interrupt the period of treatment prescribed.
- Do not repeat the same prescription without consulting your doctor.

KEEP MEDICAMENT OUT OF REACH OF CHILDREN

**Do not use after expiry date**.