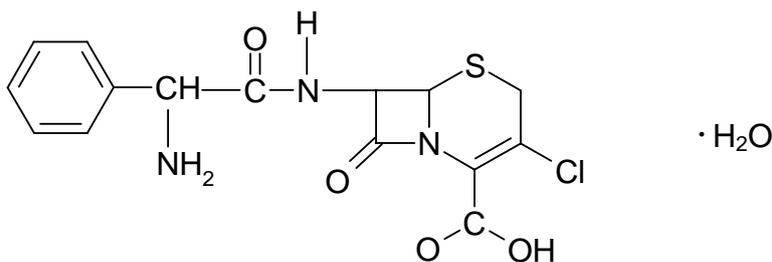


PRODUCT INFORMATION

CECLOR® (cefaclor monohydrate)

NAME OF THE DRUG

CECLOR (cefaclor monohydrate)



DESCRIPTION

CECLOR (cefaclor monohydrate) is a semisynthetic cephalosporin antibiotic for oral administration. The active ingredient is chemically designated as 3-chloro-7-D-(2-phenylglycinamido)-3-cephem-4-carboxylic acid monohydrate.

Cefaclor monohydrate is a white to off white crystalline powder, slightly soluble in water, but is insoluble in alcohol and chloroform.

CECLOR powder for oral liquid in bottles contains the active cefaclor monohydrate equivalent to 125 mg or 250 mg of cefaclor per 5 mL upon reconstitution. They also contain sucrose, erythrosine, methylcellulose, sodium lauryl sulfate, strawberry flavour 52312 AP0551, xanthan gum, dimethicone 350 and starch-tapioca.

PHARMACOLOGY

Clinical Pharmacology

CECLOR is well absorbed after oral administration, whether taken with food or while fasting; 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 45 minutes to 1 hour later. The presence of food in the gastrointestinal tract does not alter the total amount of cefaclor absorbed. Following administration of 250 mg,

500 mg, and 1 g doses to fasting subjects average peak plasma levels of antibacterial activity (expressed as µg/mL of cefaclor) of 7, 13 and 23 µg/mL, respectively, were obtained at 30 to 60 minutes. The reduced peak serum levels resulting from the administration of cefaclor with food should be considered with reference to the sensitivity of the infecting organism, severity of illness, the dose being administered and the variability in the peak plasma levels which occur with cefaclor.

The plasma half-life in healthy subjects is independent of dosage form and averages 40-60 minutes. In elderly subjects (over age 65) with normal serum creatinine values, a higher peak plasma concentration and AUC are effects resulting from mildly diminished renal function and are not expected to have clinical significance. Therefore, dosage changes are not necessary in elderly subjects with normal renal function. There is no evidence of metabolism of cefaclor in humans.

Microbiology

In vitro tests demonstrate that the bactericidal action of cephalosporins results from inhibition of cell-wall synthesis. Cefaclor is stable in the presence of bacterial β-lactamases; consequently, β-lactamase-producing organisms resistant to penicillins and some cephalosporins may be susceptible to cefaclor. Cefaclor has been shown to be active against most strains of the following organisms both in vitro and in clinical infections:

Staphylococci, including coagulase-positive and penicillinase-producing strains
(but not methicillin-resistant strains of *Staph. aureus*).

Streptococcus pyogenes (group A beta-haemolytic streptococci).

Streptococcus (Diplococcus) pneumoniae

Escherichia coli

Proteus mirabilis

Klebsiella sp

Haemophilus influenzae

Neisseria gonorrhoeae (penicillinase-producing and non-penicillinase producing strains).

Moraxella (branhamella) catarrhalis

NOTE: *Pseudomonas* species, *Acinetobacter calcoaceticus*, enterococci, *Enterobacter*, indole-positive *Proteus*, and *Serratia* species are resistant to cefaclor. Methicillin resistant strains are also resistant to cefaclor.

Susceptibility Testing --

Dilution or diffusion techniques - either quantitative (MIC) or breakpoint, should be used following a regularly updated, recognised and standardised method (e.g. NCCLS). Standardised susceptibility test procedures require the use of laboratory control microorganisms to control the technical aspects of the laboratory procedures.

A report of "Susceptible" indicates that the pathogen is likely to be inhibited if the antimicrobial compound in the blood reaches the concentrations usually achievable. A report of "Intermediate" indicates that the result should be considered equivocal, and if the microorganism is not fully susceptible to alternative, clinically feasible drugs, the test should be repeated. This category implies possible clinical applicability in body sites where the drug is physiologically concentrated or in situations where high dosage of drug can be used. This category also provides a buffer zone, which prevents small-uncontrolled technical factors from causing major discrepancies in interpretation. A report of "Resistant" indicates that the pathogen is not likely to be inhibited if the antimicrobial compound in the blood reaches the concentrations usually achievable; other therapy should be selected.

Note: The prevalence of resistance may vary geographically for selected species and local information on resistance is desirable, particularly when treating severe infections.

INDICATIONS

CECLOR is indicated for the treatment of the following types of infections caused by or likely to be caused by susceptible organisms:

Lower respiratory infections, including pneumonia, bronchitis and exacerbations of chronic bronchitis.

Upper respiratory infections, including pharyngitis, tonsillitis and otitis media.

Skin and skin structure infections.

Urinary tract infections, including pyelonephritis and cystitis.

NOTE:

1. Penicillin is the usual drug of choice in the treatment and prevention of streptococcal infections, including the prophylaxis of rheumatic fever. CECLOR appears to be as effective as phenoxymethyl penicillin in the eradication of streptococci from the nasopharynx; however, substantial data establishing the efficacy of cefaclor in the subsequent prevention of rheumatic fever are not available at present.

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

CONTRAINDICATIONS

CECLOR is contraindicated in patients with known allergy to the cephalosporin group of antibiotics or who have previously experienced a major allergy to penicillin (*see* PRECAUTIONS).

CECLOR is also contraindicated in infants under the age of one month as safety and efficacy of this product has not been established in prematures and infants under one month of age.

PRECAUTIONS

In penicillin-sensitive patients, cephalosporin antibiotics should be administered cautiously. There is clinical and laboratory evidence of partial cross-allergenicity of the penicillins and the cephalosporins and there are instances in which patients have had reactions, including anaphylaxis, to both drug classes. Serious and occasionally fatal hypersensitivity (anaphylactic/anaphylactoid) reactions have been reported in patients on penicillin/ cephalosporin therapy. Although anaphylaxis is more frequent following parenteral therapy, it has occurred in patients on oral penicillins/ cephalosporins. These reactions are more likely to occur in individuals with a history of penicillin hypersensitivity and/or a history of sensitivity to multiple allergens. There have been reports of individuals with a history of penicillin/cephalosporin hypersensitivity who have experienced severe reactions when treated with a penicillin/cephalosporin.

Past history of a severe allergic reaction to penicillin/cephalosporin is a contraindication to the use of CECLOR. Before initiating therapy with any cephalosporin, careful inquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins, or other allergens. If an allergic reaction occurs, CECLOR should be discontinued and the appropriate therapy instituted. Serious anaphylactoid reactions require immediate emergency treatment with adrenaline. Oxygen, intravenous steroids and airway management, including intubation, should also be administered as indicated.

Broad-spectrum antibiotics should be prescribed with caution in individuals with a history of gastrointestinal disease, particularly colitis.

Antibiotic associated pseudomembranous colitis has been reported with many antibiotics including cefaclor. A toxin produced with *Clostridium difficile* appears to be the primary cause. The severity of the colitis may range from mild to life threatening. It is important to consider this diagnosis in patients who develop diarrhoea or colitis in association with antibiotic use (this may occur up to several weeks after cessation of antibiotic therapy). Mild cases usually respond to drug discontinuation alone. However, in moderate to severe cases appropriate therapy with a suitable oral antibacterial agent effective against *C. difficile* should be considered. Fluids, electrolytes and protein replacement should be provided when indicated. Drugs which delay peristalsis, e.g. opiates and diphenoxylate with atropine (Lomotil) may prolong and/or worsen the condition and should not be used.

As with antibiotic therapy in general, administration of CECLOR should be continued for a minimum of 48 to 72 hours after the patient becomes asymptomatic or after evidence of bacterial eradication has been obtained. A minimum of ten days of treatment is recommended in infections caused by group A beta-haemolytic streptococci in order to guard against the risk of rheumatic fever or glomerulonephritis.

Prolonged use of CECLOR may result in the overgrowth of non-susceptible organisms. Careful observation of the patient is essential. If superinfection occurs during therapy, appropriate measures should be taken.

CECLOR 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.

CECLOR should be used with caution in patients with liver disease, as documented clinical experience in this group of patients is lacking.

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

Laboratory Test Interactions -- Administration of CECLOR may result in a false-positive reaction for glucose in the urine. This phenomenon has been seen in patients taking cephalosporin antibiotics when the test is performed using Benedict's and Fehling's solutions and also with Clinitest[®] tablets but not with Tes-Tape[®] (Glucose Enzymatic Test Strip, USP).

Positive direct Coombs tests have been reported during treatment with CECLOR. In haematologic studies or in transfusion cross-matching procedures when anti-globulin tests are performed on the minor side, or in Coombs testing of newborns whose mothers have received cephalosporin antibiotics before parturition, it should be recognised that a positive Coombs test may be due to the drug.

Use in Pregnancy -- Category B1 --

The oral administration of high dose cefaclor (500 mg/kg) in pregnant rats and mice has resulted in a slight increase of minor skeletal malformations. Safety of this product for use during pregnancy has not been established. Cefaclor should not be used in women of child bearing potential unless, in the judgement of the treating clinician, its use is considered essential to the welfare of the patient and the expected benefits outweigh potential risks.

Use in Lactation -- Small amounts of cefaclor have been detected in mother's milk following administration of single 500 mg doses of CECLOR. Average levels were 0.18, 0.20, 0.21 and 0.16 µg/mL 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 CECLOR is administered to a nursing woman.

Use in Children -- Safety and effectiveness of this product for use in infants less than one month of age have not been established. **Serum sickness-like reactions including arthritis and arthralgia have been reported more frequently in children than in adults.**

ADVERSE REACTIONS

Gastrointestinal -- The most frequent side effect has been diarrhoea.

Nausea and vomiting have been reported rarely. Colitis, including rare instances of pseudomembranous colitis, has been reported in conjunction with therapy with CECLOR. (see PRECAUTIONS)

Hepatic -- Transient hepatitis and cholestatic jaundice have been reported rarely.

Hypersensitivity -- Allergic reactions, such as urticaria and morbilliform eruptions, have been observed, as have pruritus and positive Coombs' tests. These reactions usually subsided upon discontinuation of the drug. Angioedema and fever have been reported rarely.

Cases of serum-sickness-like reactions have been reported with the use of cefaclor. These have been reported more frequently in children than in adults with an overall occurrence ranging from 0.5% (1 in 200) in one trial, to 0.024% (2 in 8,346) in overall clinical trials (with an incidence in children in clinical trials of 0.055%). The worldwide reporting rate for serum-sickness-like reactions in adults is very rare (<0.01%). **Serum-sickness-like reactions are characterised 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.** 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. 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 hospitalisation usually of short duration (median hospitalisation = 2 to 3 days, based on postmarketing surveillance studies). In those requiring hospitalisation, 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 and toxic epidermal necrolysis have been reported rarely. Anaphylaxis may be more common in patients with a history of penicillin allergy. The worldwide reporting rate for anaphylaxis in the total population is very rare (<0.01%).

Blood -- Eosinophilia, transient lymphocytosis, leukopenia, and rarely, thrombocytopenia, thrombocytosis, haemolytic anaemia, aplastic anaemia, 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 warfarin concomitantly.

Kidney -- reversible interstitial nephritis.

Superinfection -- Genital pruritis, moniliasis or vaginitis.

Central Nervous System -- Rare: reversible hyperactivity, nervousness, insomnia, confusion, hypertonia, dizziness, hallucinations, headache or somnolence have been reported.

Other -- Transitory abnormalities in clinical laboratory test results have been reported, but their clinical significance is uncertain. These include slight elevations in AST, ALT, or alkaline phosphatase values; transient fluctuations in leukocyte count, predominantly lymphocytosis in infants and young children; and slight elevations in serum urea or serum creatinine or abnormalities of urinalysis (haematuria; pyuria).

DOSAGE AND ADMINISTRATION

CECLOR is administered orally.

Directions for reconstitution of CECLOR powder for oral liquid bottle

125 mg/5 mL - Add 60 mL of water in two portions to the dry mixture in the bottle. Shake well after each addition.

250 mg/5 mL - Add 45 mL of water in two portions to the dry mixture in the bottle. Shake well after each addition.

Adults-The usual adult dosage is 250 mg every 8 to 12 hours. For bronchitis and pneumonia, the dosage is 250 mg administered 3 times daily. For more severe infections or those caused by less susceptible organisms, doses may be doubled (500 mg 8 hourly). Doses of 2 g/day should not be exceeded.

For skin and skin structure infections the dosage is 250 mg 2-3 times a day.

Children-The usual recommended daily dosage for children with mild to moderate infections is 20 mg/kg/day in divided doses every 8 hours (maximum 1 g/day).

For streptococcal pharyngitis/tonsillitis and impetigo, 12 hourly administration appears equally effective.

In more serious infections, otitis media, and infections caused by less susceptible organisms, the recommended dosage is 40 mg/kg/day in divided doses every 8 to 12 hours (maximum 2 g/day). For otitis media, 12 hourly administration appears equally effective.

CECLOR 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 beta-haemolytic streptococcal infections, a therapeutic dosage of CECLOR should be administered for at least 10 days.

OVERDOSAGE

Signs and Symptoms -- The toxic symptoms following an overdose of CECLOR may include nausea, vomiting, epigastric distress and diarrhoea. The severity of the epigastric distress and the diarrhoea 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.

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, 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, haemodialysis, or charcoal haemoperfusion have not been established as beneficial for an overdose of cefaclor.

Contact the Poisons Information Centre on 131126 for management of overdose.

STORAGE

Store below 25 degrees Celsius and protect from light. Upon reconstitution, the suspension must be stored in a refrigerator between 2 and 8 degrees Celsius. Discard unused portion 14 days after mixing.

PRESENTATION

CECLOR powder for oral liquid is available in two strengths in bottles.

125 mg/5 mL: A pink free flowing dry powder. After constitution a red coloured suspension with a characteristic strawberry odour containing 125 mg cefaclor per 5 mL.

250 mg/5 mL: A pink free flowing dry powder. After constitution a red coloured suspension with a characteristic strawberry odour containing 250 mg cefaclor per 5 mL.

POISON SCHEDULE

S4

SPONSOR

Aspen Pharmacare Australia Pty Ltd
34-36 Chandos St
St Leonards NSW 2065

DATE OF TGA APPROVAL

Approved by the Therapeutic Goods Administration: 14 June 1996

Date of editorial amendment: 19 October 2009