Cefacloril

Cefaclor

It overcame other Cephalosporins because:

- Its activity combined with pharmacokinetic superiority provides blood levels in excess of the minimum densities required for vulnerable microorganisms and the treatment of serious infections.
- It has certified efficiency
- It has good tolerance and flexibility in administration
- It is available in capsules and suspension with the same therapeutic results
- The oral suspension has a strawberry taste

Dosage 20-40mg/mg/kg/24h (3 equal doses)
Maximum daily dose in children: 1gr

Body weight (kg)	20mg/kg dose ml / 24h	40mg/kg dose ml / 24h
4.5	0.9	1.8
6	1.2	2.4
7.5	1.5	3.0
9	1.8	3.6
10.5	2.1	4.2
12	2.4	4.8
15	3.0	6.0
18	3.6	7.2
21	4.2	8.4
24	4.8	9.6

Cefacloril

Cefaclor

- Broad spectrum antibiotic
- More resistant to many lactamases
- Active against haemophilus and hospital strains

With strawberry taste

Name of the medicinal product:	Cefacloril
Active ingredient:	Cefaclor (as Cefaclor Monohydrate)
Pharmaceutical form:	• Caps, 500mg/cap • Gra. Or. Sus., 500mg/5ml
Packaging:	• Box containing 12 capsules • Box containing 1 bottle with small granules for the preparation of 60 ml oral suspension.
Therapeutic indications:	Otitis media, Acute bronchitis and acute exacerbations of chronic bronchitis, Pharyngitis and tonsillitis, Pneumonia, Uncomplicated infections of the genitourinary system, Skin and soft tissue infections, Rhinosinusitis
Method of administration:	For oral use, with or without food.
Posology:	Adults: 250mg every 8 hours Children: 20-40mg/kg/day in 3 equal doses
Marketing Authorization Holder:	ADELCO S.A.

Under prescription only medicine

For more information please refer to the Summary of Product Characteristics

Help to the safety of the products.
Fill the **«YELLOW CARD».**
REPORT:
- ALL adverse reactions for ALL drugs

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Cefacloril

Cefaclor

Second-generation Cephalosporin
Effective against a variety of Gram+ and Gram- microorganisms

With strawberry taste

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT: CEFACLORIL
2. QUALITATIVE AND QUANTITATIVE COMPOSITION: Capsules
Active ingredient: Cefaclor monohydrate corresponding to 500mg Cefaclor / Granules for Oral Suspension
Active ingredient: Cefaclor monohydrate corresponding to 500mg/5ml Cefaclor
3. PHARMACEUTICAL FORM
a) Capsules / b) Granules for Oral Suspension
4. CLINICAL PARTICULARS
4.1. Therapeutic indications
CEFACLORIL is indicated for the treatment of the following infections due to susceptible micro-organisms:
Otitis media caused by S. pneumoniae, H. influenzae, Staphylococci (excluding strains resistant to methicillin), S.pyogenes (Group A β-hemolytic streptococci) and M.catarrhalis.
Acute bronchitis and acute exacerbations of chronic bronchitis caused by S.pneumoniae, H. influenzae (including β-lactamase-producing strains), H. parainfluenzae, M.catarrhalis (including β-lactamase-producing strains), S.aureus where their susceptibility has been confirmed in-vitro. **Pharyngitis and tonsillitis** caused by S.pyogenes (Group A β-hemolytic streptococci).
(NOTE: Penicillin is usually the medicine of choice for the treatment and prevention of streptococcus infections, including the prophylaxis of rheumatic fever. Cefaclor is generally effective on the eradication of streptococci from the oropharynx.
Yet, there is no sufficient information for its effectiveness in the prophylaxis of rheumatic fever.)
Pneumonia caused by S.pneumoniae (in low-severity cases), H.influenzae (including β-lactamase-producing strains) and M.catarrhalis (including β-lactamase-producing strains). **Uncomplicated infections of the genitourinary system** including pyelonephritis and cystitis (with concurrent anaerobic coverage), caused by E.coli, P.mirabilis, Klebsiella spp. **Skin and soft tissue infections** caused by Staphylococcus aureus (including β-lactamase-producing strains) and S. pyogenes (Group A β-hemolytic streptococci). Staphylococci resistant to penicillin are also resistant to cefaclor. **Rhinosinusitis** caused by sensitive H.influenzae strains (including β-lactamase-producing strains), S.pyogenes (Group A β-hemolytic streptococci), S.pneumoniae, M.catarrhalis and S. Aureus (including β-lactamase-producing strains). Staphylococci resistant to penicillin are also resistant to cefaclor. In chronic conditions, the addition of another antimicrobial agent, effective on anaerobic organisms, is usually required. In order to identify the pathogen microorganism causing the infection as well as its susceptibility to cefaclor, the appropriate bacteriological tests should be performed. Therapeutic treatment can start in anticipation of the results of these tests. According to the findings, the antimicrobial treatment is adjusted.
4.2. Dosage: Cefaclor is orally administered, with or without food.
Adults: The usual adult dosage is 250mg every eight hours. For more severe infections or those caused by less susceptible organisms, doses may be doubled. Doses of 4g per day have been administered safely to normal subjects for 28 days, but the total daily dosage should not exceed this amount. ***Children aged over one (1) month: The usual recommended dosage for children is 20-40 mg/kg/day, divided in three (3) equal doses.***
For bronchitis and pneumonia, the dosage is 20 mg/kg/day in divided doses administered 3 times daily. The usual dosage for severe infections (such as pneumonia), otitis media or infections caused by less-susceptible micro-organisms, is 40 mg/kg/day, in three (3) divided doses. The maximum recommended dosage in children is 1 g/day. Examples of dosage calculation are given below.
1. Dosage for Suspension CEFACLORIL (for 20 mg/kg/day dose)

FORM OF CEFACLORIL SUSPENSION

Child's Body Weight	125mg/5ml	250mg/5ml	375mg/5ml*
9kg	½ teaspoon/8 hours	_	_
18kg	1 teaspoon/8 hours	½ teaspoon/8 hours	½ teaspoon/8 hours*

2. Dosage for Suspension CEFACLORIL (for 40 mg/kg/day dose)

FORM OF CEFACLORIL SUSPENSION

Child's Body Weight	125mg/5ml	250mg/5ml	375mg/5ml*
9kg	1 teaspoon/8 hours	½ teaspoon/8 hours	½ teaspoon/12 hours*
18kg	_	1 teaspoon/8 hours	1 teaspoon/12 hours*

Notice: 1 teaspoon corresponds to 5ml
***In the treatment of otitis media and pharyngitis, total daily dose may be divided and administered every 12 hours.**
CEFACLORIL may be administered to patients with moderate to severe renal failure to whom the recommended dosage usually remains unchanged (see also section 4.4 Special precautions and warnings during use)
In the treatment of beta-haemolytic streptococcal infections, therapy should be continued for at least 10 days.
4.3. Contraindications: Its administration is contraindicated in patients with known hypersensitivity to cefaclor and other cephalosporins as well as in patients with a history of anaphylactic reaction to penicillins.
4.4 Special precautions and warnings during use: Before instituting therapy with cefaclor, every effort should be made to determine whether the patient has had previous hypersensitivity reactions to cephalosporins, penicillins or other drugs. CEFACLORIL should be given cautiously to penicillin-sensitive patients because cross-hypersensitivity (including anaphylaxis) among beta-lactam antibiotics has been clearly documented. **If an allergic reaction to cefaclor occurs, the drug should be discontinued and the patient treated with antihistamine or corticosteroid agents.** In severe cases of acute hypersensitivity, the administration of adrenaline may be required and measures of emergency treatment should be taken. Abitibiotics, including cefaclor, should be cautiously administered to patients who have ever had any form of allergy, especially to drugs. Pseudomembranous colitis has been reported with virtually all broad-spectrum antibiotics (including macrolides, semi-synthetic penicillins and cephalosporins). It is important, therefore, to consider its diagnosis in patients who develop diarrhoea in association with the use of antibiotics. Such colitis may range in severity from mild to life-threatening. Mild cases usually respond to drug discontinuance alone. In moderate to severe cases, appropriate measures should be taken. The safety and efficacy of the drug in infants aged less than one (1) month have not been established. CEFACLORIL should be administered with caution in the presence of markedly impaired renal function. Since the half-life of cefaclor in anuric patients is 2.3 to 2.8 hours (compared to 0.6-0.9 hours in normal subjects), dosage adjustments for patients with moderate or severe renal impairment are not usually required. Clinical experience with cefaclor under such conditions is limited; therefore, careful clinical observation and laboratory studies should be made during treatment. Prolonged use of antibiotics may result in the overgrowth of non-susceptible organisms. Close monitoring of the patient is important. If superinfection occurs during therapy, appropriate measures should be taken. CEFACLORIL Granules for oral Suspension contains Sucrose. Patients with with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction: There have been rare reports of increased prothrombin time, with or without clinical bleeding, in patients receiving cefaclor and warfarin concomitantly. It is recommended that in such patients, regular monitoring of prothrombin time should be considered, with adjustment of dosage if necessary. The renal excretion of cefaclor is inhibited by probenecid. When cefaclor is administered with tetracyclines or chloramphenicol, it has a competitive effect. If there is an absolute indication for concurrent administration, the two antimicrobial products should be administered at a different time through another route. Cefaclor administration may result in a false-positive urine glucose test reaction. This has been observed in patients receiving cephalosporins when the test is performed with Benedict and Fehling solutions as well as with Clintest tablets, but not with the Tes-Tape strip (Glucose Enzymatic Test Strip, USP, Lilly).
4.6. Fertility, pregnancy and lactation: **Pregnancy:** Reproduction studies on mice and rats have been conducted, with doses up to 12 fold the maximum dose administered to humans and other laboratory animals (ferrets) to which 3 fold the maximum human dose was administered. In these studies disturbance of fertility or foetus abnormalities related to cefaclor, have not been observed. Nevertheless, there are no adequate and well controlled studies on pregnant women. Since reproduction studies on laboratory animals are not always indicative of the effect on the human organism, cefaclor should be administered during pregnancy only if it is absolutely necessary. Cefaclor has not been studied for administration during labour. Treatment should be given only if it is absolutely necessary. **Lactation:** There are no studies for cefaclor administration in lactating mothers. Small quantities of cefaclor have been traced in human milk after administration of simple doses of 500mg. Mean levels observed were 0.18, 0.20, 0.21 and 0.16 mg/L on the 2nd, 3rd, 4th and 5th hour respectively. Minor amounts were traced on the 1st hour. The effect of the drug on breast-feeding infants is unknown. Therefore, caution is required when cefaclor is administered to a lactating mother.
4.7 Effects on ability to drive and use machines: CEFACLORIL is safe and not expected to affect the ability to drive or operate machinery.
4.8. Undesirable effects: The following undesirable effects have been reported in patients receiving cefaclor.
Hypersensitivity reactions: They have been reported to 1.5% of patients and included skin rashes. Pruritus, urticaria and positive direct Coombs' test appear in less than 0.5% of patients. Rarely, more severe hypersisitivity reactions have been reported such as Stevens-Johnson syndrome, toxic epidermal necrolysis, and anaphylactic reactions (angioedema. dyspnoea etc). Serum sickness-like reactions with findings of multiforme erythema, rashes and other skin rections accompanied by arthritis (arthtalgia with or without fever) have been particularly rarely reported (0.024-0.5%), more frequently in children than in adults.
Gastro-intestinal: They appear in 2.5% of patients including diarrhea (one case in 70 patients). Also, nausea, vomiting and epigastric distress have been reported. Rarely, pseudomembranous colitis may occur during or after therapy with the antibiotic. As also with the administration of penicillins and other cephalosporins, transient hepatitis and cholestatic jaundice have been rarely reported. Superinfections by resistant micro-organisms may appear. Other undesirable effects that have rarely been reported in patients treated with cefaclor: Eosinophilia, thrombocytopenia, reversible interstitial nephritis, genital pruritus, and vaginitis. The following undesirable effects have been reported in patients treated with cefaclor without a clear causative relationship: **Blood and lymphatic system:** transient lymphocytosis, leucopenia and rarely haemolytic anaemia, agranulocytosis and reversible neutropenia have been reported. There have also been rare reports of increased prothrombin time, with or without bleeding, in patients receiving cefaclor and warfarin concomitantly. Hypothrombinemia may be observed due to reduced vitamin K production owed to the disruption of the intestinal flora.
Renal: transient elevations in blood urea or serum creatinine (less than 1 in 500 patients) or abnormal urinalysis (less than 1 in 200 patients). In patients receiving beta-lactam antibiotics renal impairment and nephrotoxicity may appear. Several beta-lactam antibiotics have been implicated for causing convulsions, especially in patients with renal impairment, when the dose was not reduced. When convulsions occur, drug administration should be discontinued. If there is a clinical indication, antiepileptic treatment can be administered.
Reporting of suspected adverse reactions: Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Greek *National Organization for Medicines:* 284 Mesogeion Av., GR-15562 Xolargos, Athens, Greece / Tel: + 30 21 32040380/337, Fax: + 30 21 06549585, Website: http://www.eof.gr
4.9. Overdose, management and antidotes
Symptoms: toxic overdose symptoms may include: nausea, vomiting, epigastric distress and diarrhea. The severity of epigastric distress and diarrhea is dose-dependent. When other symptoms are present these may be secondary and owed to an underlying disease, allergic reaction or other poisoning.
Management: all possibilities of multiple drug overdoses, drug interactions and unusual pharmacokinetics for the specific patient should be considered. Protect the patient's airways and support airflow and the maintenannce of the route of intravenous drug administration. Vital signs of the patient, blood gases and serum electrolytes should be carefully monitored and maintained within the acceptable levels. Gastrointestinal drug absorption may be reduced with the administration of active charcoal, which in many cases is more effective than provocation of vomiting or lavage. Prefer active charcoal instead of/or in combination with emptying the stomach. The repeated administration of charcoal may (after a time point) accelerate the excretion of certain drugs already absorbed.
Protect the patient's airway when emptying the stomach or administering charcoal.
The beneficial effect of therapeutic enuresis, haemodialysis or haemoperfusion with charcoal in cases of cefaclor overdose, has not been established.
5. PHARMACOLOGICAL PROPERTIES
5.1. Pharmacodynamic properties
ATC code: J01DC04/ Cefaclor is an antibiotic that belongs to the group of semi-synthetic second-generation cephalosporins and is destined for oral administration. In vitro tests have shown that the bactericidal action of cefaclor is owed to the inhibition of the bacterial cellular wall synthesis. In vitro tests have shown the susceptibility of most of the below microorganisms to cefaclor.
Aerobic Gram-positive microorganisms: Staphylococci (including coagulase-negative strains or strains producing penicillinase in vitro and presenting cross-resistance between cefaclor and methicillin)/ Streptococcus pneumoniae: Streptococcus pyogenes
Aerobic Gram-negative microorganisms: Citrobacter diversus/ Escherichia coli / Klebsiella spp.
Haemophilus influenzae (including β-lactamase-producing strains resistant to ampicillin) / Moraxella (Branhamella) catarrhalis / Neisseria gonorrhoeae / Proteus mirabilis.
Anaerobic microorganisms: Bacteroides spp (except Bacteroides fragilis)/ Peptococcus niger/ Peptostreptococcus spp. Propionibacteria acnes NOTICE: Resistance to cefaclor and other cephalosporins present: Methicillin-resistant staphylococci, all strains of enterococci (Streptococcus faecalis και Streptococcus faecium), Enterobacter spp, Serratia spp, Morganella morganii, Proteus vulgaris, (positive to indole), Providencia rettgeri, Pseudomonas spp, and Acinetobacter spp.
Sensitivity test: **a) Perfusion techniques:** Antibiotic sensitivity is measured with qualitative methods in which the zones diameter is measured. This procedure is specified by the National Committee for Clinical Laboratory Standards (NCCLS).
This disk method is recommended for the control of sensitivity cefaclor.
The result is based on the correlation of diameters accomplished in the disk test with the slightest inhibitory cconcentrations (MIC) for cefaclor. Laboratory reports which provide results in compliance with the standard sensitivity test of a single disk (standard single-disk susceptibility test), with disk containing 30μg cefaclor, should be interpreted with the following criteria:

Zone diameter (mm)	Interpretation
≥18	(S) Sensitive
15-17	(MS) Moderately sensitive
≤14	(R) Resistant

The term "sensitive" means that the action of the pathogen microorganism is inhibited by the generally achieved blood concentration of the antibiotic. The term "moderately sensitive" is indicative of the fact that the inhibiting concentrations of the antibiotic can be achieved with the administration of high doses or when the infection is limited in tissues and body fluids (e.g. urine), where high concentrations of the antibiotic are achieved. The term "resistant" is indicative of the fact that the achieved concentrations of the antibiotic are impossible to be inhibiting and that other treatment needs to be adopted.
The standardized procedures require the use of microorganisms for laboratory testing. The disk of 30mg cefaclor should give the following zone diameters

Organism	Zone diameter (mm)
E. coli ATCC 25922	23-27
S. aureus ATCC 25923	27-31

β) Dilution techniques
For the determination of MIC of cefaclor, the recommended dilution methods from NCCLS2 in agar or broth, can be used. The results of the MIC test must be interpreted according to the following criteria:

MIC (μg/mL)	Interpretation
≥18	(S) Sensitive
16	(MS) Moderately sensitive
≤32	(R) Resistant

As in the standardized perfusion methods, dilution procedures require the use of organisms for laboratory testing. Standard cefaclor powder should give the following MIC values:

Organism	MIC range (μg/mL)
E. coli ATCC 25922	1-4
S. aureus ATCC 29213	1-4

5.2. Pharmacokinetic properties: Cefaclor is well absorbed after oral administration. 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 50-75% of that observed when the drug is administered to fasting subjects and generally appears from to one hour later. Following administration of 250mg, 500mg and 1G doses to fasting subjects, average peak serum levels of approximately 7, 13 and 23 mcg/L respectively were obtained within 30 - 60 minutes. Approximately 60 - 85% of the drug is excreted unchanged in the urine within eight hours, the greater portion being excreted within the first two hours. During the eight hour period, peak urine concentrations following the 250mg, 500mg and 1G doses were approximately 600, 900 and 1,900 mcg/L respectively. The serum half-life in normal subjects is approximately 1 hour. In patients with reduced 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 - 2.8 hours. Excretion pathways in patients with markedly impaired renal function have not been determined. Haemodialysis shortens the half- life by 25 - 30%.
5.3. Preclinical safety data: No animal studies have been conducted to assess the carcinogenicity or mutagenicity potential after the administration of cefaclor. Reproduction studies have not revealed fertility effects.
6. PHARMACEUTICAL PARTICULARS
6.1. List of excipients: Capsules: Lactose monohydrate / Pregelatinised starch/ Magnesium stearate
Composition of empty capsule No 0
White (body 60%) – Dark green (cap 40%) / Indigocarmine – FD & C Blue 2, E 132 / Quinoline yellow E 104, CI 47005
Titanium dioxide E 171, CI 77891 / Water / Gelatin
Granules for oral suspension: Sodium lauryl sulfate (purified)/ Emulsion silicone 30%
Erythrosine E 127 CI 45430/ Methylcellulose 15/ Xanthan gum/ Pregelatinised maize starch/ Strawberry (vioryl) / Sucrose
6.2. Incompatibilities
Cefaclor is not possible to present any physical or chemical incompatibility with other substances.
6.3. Shelf life
Capsules: 24 months / **Granules for oral suspension:** 24 months
After reconstitution, the suspension should be stored in a refrigerator (2-8°C) and be used within 14 days.
6.4. Special precautions for disposal and other handling:
Capsules/ Keep at temperature below 25°C.
Granules for oral suspension: Keep at temperature below 25oC. After reconstitution, the suspension should be stored in a refrigerator (2-8°C) and be used within 14 days.
6.5. Nature and contents of container
Capsules 500 mg: Carton box containing 12 capsules in 3 blisters (of 4 capsules each).
Granules for oral suspension 500 mg / 5 ml:
Carton box containing a 60 ml bottle with small granules (powder) for reconstitution to 60 ml.
6.6. Instructions for use
Capsules: No particular instructions are necessary. **Granules for oral suspension:** Fill gradually with water, up to the mark with the bow. Shake well and refill again with water up to the mark. Shake well again and do the same before every use.
7. MARKETING AUTHORIZATION HOLDER: ADELCO – CHROMATOURGIA ATHINON E. COLOCOTRONIS BROS S.A., 37 PIREOS STR., 183 46 MOSCHATO, ATHENS-GREECE, TEL.(0030) 210 4819 311- 4, FAX: (0030) 210 4816790
8. MARKETING AUTHORIZATION NUMBER
Capsules: 79720/15/10-05-2016
Granules for oral suspension: 112547/14/05-05-2015
9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
Capsules and Granules for oral suspension:
Date of first M.A.: 17-06-1991
Date of last renewal: 06-02-2007
9. DATE OF LAST REVISION OF THE TEXT: 19/07/2016