SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Cefaclor 500mg Capsules

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains 524.48 mg of cefaclor monohydrate, equivalent to

500 mg of cefaclor.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Hard gelatine capsule

Size 0. Body: opaque, light grey. Cap: opaque, violet, containing white to slightly yellow powder.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Cefaclor is indicated for the treatment of the following infections due to susceptible micro-organisms:

- Respiratory tract infections, including pneumonia, bronchitis, exacerbations of chronic bronchitis, pharyngitis and tonsillitis, and as part of the management of sinusitis.
- Otitis media.
- Skin and soft tissue infections.
- Urinary tract infections, including pyelonephritis and cystitis.

- Cefaclor has been found to be effective in both acute and chronic urinary tract infections.
- Cefaclor is generally effective in the eradication of streptococci from the nasopharynx, but data establishing efficacy in the subsequent prevention of either rheumatic fever or bacterial endocarditis are not available.

4.2 Posology and method of administration

Posology

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.

Total daily dosage should not exceed 4g.

Cefaclor 500mg Capsules may be administered in the presence of impaired renal function. Under such conditions, dosage is usually unchanged.

(see section 4.4).

Patients Undergoing Haemodialysis: Haemodialysis shortens serum half-life by 25-30%. In patients undergoing regular haemodialysis, a loading dose of 250mg -1g administered prior to dialysis and a therapeutic dose of 250-500mg every six to eight hours maintained during interdialytic periods is recommended.

Elderly: As for adults.

Paediatric population: The usual recommended daily dosage for children is 20mg/kg/day in divided doses, every eight hours, as indicated. For bronchitis and pneumonia, the dosage is 20mg/kg/day in divided doses, administered 3 times daily. For otitis media and pharyngitis the total daily dosage may be divided and administered every 12 hours. Safety and efficacy have not been established for use in infants aged less than one month.

Method of administration

Oral administration.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1
- Hypersensitivity to cephalosporins

4.4 Special warnings and precautions for use

Warnings

Before instituting therapy with cefaclor, every effort should be made to determine whether the patient has had previous hypersensitivity reactions to cefaclor, cephalosporins, penicillins or other drugs. Cefaclor 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 the appropriate agents.

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.

Precautions

Cefaclor 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.

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

Prolonged use of cefaclor may result in the overgrowth of non-susceptible organisms. If superinfection occurs during therapy, appropriate measures should be taken.

Positive direct Coombs' tests have been reported during treatment with the cephalosporin antibiotics. In haematological 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.

A false-positive reaction for glucose in the urine may occur with Benedict's or Fehling's solutions or with copper sulphate test tablets.

4.5 Interaction with other medicinal products and other forms of interaction

Warfarin

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.

Probenecid

The renal excretion of cefaclor is inhibited by probenecid.

4.6 Fertility, Pregnancy and lactation

Pregnancy

Animal studies have shown no evidence of impaired fertility or teratogenicity. However, since there are no adequate or well-controlled studies in pregnant women, caution should be exercised when prescribing for the pregnant patient.

Breast-feeding

Small amounts of cefaclor have been detected in breast milk following administration of single 500mg doses. Average levels of about 0.2 micrograms/ml or less were detected up to 5 hours later. Trace amounts were detected at one hour. As the effect on nursing infants is not known, caution should be exercised when cefaclor is administered to a nursing woman

4.7 Effects on ability to drive and use machines

Cefaclor does not affect the ability to drive or operate machinery.

4.8 Undesirable effects

Gastro-intestinal: The most frequent side-effect has been diarrhoea. It is rarely severe enough to warrant cessation of therapy. Colitis, including rare instances of pseudomembranous colitis, has been reported. Nausea and vomiting have also occurred.

Hypersensitivity: Allergic reactions such as morbilliform eruptions, pruritus and urticaria have been observed. These reactions usually subside upon discontinuation of therapy. Serum sickness-like reactions (erythema multiforme minor, rashes or other skin manifestations accompanied by arthritis/arthralgia, with or without fever) have been reported.

Lymphadenopathy and proteinuria are infrequent; there are no circulating immune complexes and no evidence of sequelae. Occasionally, solitary symptoms may occur, but do not represent a serum sickness-like reaction. Serum sickness-like reactions are apparently due to hypersensitivity and have usually occurred 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 usually subside within a few days of cessation of therapy. Antihistamines and corticosteroids appear to enhance resolution of the syndrome. No serious sequelae have been reported.

There are rare reports of erythema multiforme major (Stevens-Johnson syndrome), toxic epidermal necrolysis, and anaphylaxis. Anaphylaxis may be more common in patients with a history of penicillin allergy. Anaphylactoid events may present as solitary symptoms, including angioedema, asthenia, oedema (including face and limbs), dyspnoea, paraesthesia, syncope, or vasodilatation.

Rarely, hypersensitivity symptoms may persist for several months.

Haematological: Eosinophilia, positive Coombs' tests and, rarely, thrombocytopenia. Transient lymphocytosis, leucopenia and, rarely, haemolytic anaemia, aplastic anaemia, agranulocytosis and reversible neutropenia of possible clinical significance. See section 4.5

Hepatic: Transient hepatitis and cholestatic jaundice have been reported rarely, slight elevations in AST, ALT or alkaline phosphatase values.

Renal*:* Reversible interstitial nephritis has occurred rarely, also slight elevations in blood urea or serum creatinine or abnormal urinalysis.

Central nervous system: Reversible hyperactivity, agitation, nervousness, insomnia, confusion, hypertonia, dizziness, hallucinations and somnolence have been reported rarely.

Miscellaneous: Genital pruritus, vaginitis and vaginal moniliasis.

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 Yellow Card Scheme at: www.mhra.gov.uk/yellowcard.

4.9 Overdose

The symptoms of cefaclor overdose are non-specific and are generally nausea, vomiting, diarrhoea and gastric upsets.

Treatment for cefaclor overdose is mainly supportive. If a large amount has been ingested (around five times the normal daily dose) then gastric lavage will be necessary.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Second generation cephalosporins antibiotics

ATC classification: J01DC04

Mode of action: The reported mode of action is predominantly by the inhibition of cell wall synthesis in susceptible bacteria. This is mainly achieved by inhibiting the trans-peptidation reaction, the final stage of the cell wall synthesis process, thus preventing the complete formation of peptidoglycan cross-links. Other earlier stages in this synthesis process may also be inhibited and there may be some induction of bacterial lysis

Mechanism of resistance: (1) Permeability – failure of cephalosporins to reach receptor sites, (2) Destroyed by beta-lactamase, (3) Alteration of PBPs

Breakpoints:

Species-related breakpoints

Species	Species-related breakpoints (S≤/R>)
Staphylococcus	See notes F and G

Streptococcus A, B, C, G	See note H
H. influenzae	0.5/0.5
M. catarrhalis	0.5/0.5

F. Susceptibility of staphylococci to cephalosporins is inferred from the methicillin susceptibility

G. For cefachlor, high dose therapy is required for the treatment of staphylococcal infections.

H. The susceptibility of streptococcus groups A, B, C and G can be inferred from their susceptibility to benzylpenicillin

Susceptibility Table

The prevalence of acquired resistance may vary geographically and with time for selected species and local information on resistance is desirable, particularly when treating severe infections. As necessary, expert advice should be sought when the local prevalence of resistance is such that the utility of the agent in at least some types of infections is questionable.

Commonly susceptible species

Gram-positive aerobes

Staphylocci (coagulase positive, coagulase negative and penicillin producing strains)

Alpha and beta-haemolytic *streptococci*

Streptococcus pneumoniae

Streptococcus pyogenes (group A beta-haemolytic streptococcoi)

Gram negative aerobes

Escericha coli

Haemophilus influenzae

Klebsiella species

Moraxella catarrhalis

Proteus mirabilis

Species for which acquired resistance may be a problem

Inherently resistant organisms

Enterococci

Methicillin resistant *staphylococci*

5.2 Pharmacokinetic properties

Absorption

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 50-75% of that observed when the drug is administered to fasting subjects and generally appears from ¾ to one hour later.

Linearity

Following administration of 250mg, 500mg and 1g doses to fasting subjects, average peak serum levels of approximately 7, 13 and 23 mg/l, respectively, were obtained within 30-60 minutes.

Biotransformation and Elimination

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 mg/l, respectively.

The serum half-life in normal subjects is 0.6-0.9 hours. 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

There are no preclinical data of relevance to the prescriber which are additional to that already included in other sections of the SPC.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Pregelatinised starch

Dimethicone 350

Magnesium stearate

Capsule Shell Components:

Cap:

Gelatin

Titanium dioxide (E171)

Patent Blue V

Erythrosine (E127)

Body:

Gelatin

Titanium Dioxide (E171)

Black Ferric Oxide (E172)

6.2 Incompatibilities

Not applicable

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Do not store above 25°C. Store in a dry place.

Keep the capsules in the original container in order to protect from light.

6.5 Nature and contents of container

PVC blister backed by hard tempered aluminium foil containing 3, 15, 21, 50 or 100 capsules.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements for disposal.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Clydesdale Pharma Ltd
Unit 3-4 Campbell Court
Campbell Road
Tadley
RG26 5EG
United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL 51718/0004

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