SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Ceporex Capsules 250mg

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Cefalexin BP 250mg per capsule.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Capsule.

Size '2' hard gelatin capsules having a caramel coloured body and grey coloured cap,
printed 'CEPOREX on body and 250 on cap' in white.

4.1 Therapeutic indications

Ceporex is a semisynthetic cephalosporin antibiotic for oral administration.

Cefalexin is indicated in the treatment of the following infections due to susceptible micro-organisms:.

Respiratory tract infections
Otitis media
Skin and soft tissue infections
Bone and joint infections
Genito-urinary tract infections, including acute pro statitis
Dental infections

4.2 Posology and method of administration

Posology

Adults

The adult dosage ranges from 1-4g daily in divided doses; most infections will respond to a dosage of 500 mg every 8 hours. For skin and soft tissue infections, streptococcal pharyngitis and mild,

uncomplicated urinary tract infections, the usual dosage is 250 mg every 6 hours, or 500 mg every 12 hours.

For more severe infections or those caused by less susceptible organisms, larger doses may be needed. If daily doses of cefalexin greater than 4g are required, parenteral cephalosporins, in appropriate doses, should be considered.

The elderly and patients with impaired renal function

As for adults. Reduce dosage if renal function is markedly impaired (see section 4.4).

Paediatric population

The usual recommended daily dosage for children is 25-50 mg/kg (10-20 mg/lb) in divided doses. For skin and soft tissue infections, streptococcal pharyngitis and mild, uncomplicated urinary tract infections, the total daily dose may be divided and administered every 12 hours. For most infections the following schedule is suggested:

Children under 5 years:	125 mg every 8 hours.
Children 5 years and over:	250 mg every 8 hours.

In severe infections, the dosage may be doubled. In the therapy of otitis media, clinical studies have shown that a dosage of 75 to 100 mg/kg/day in 4 divided doses is required.

In the treatment of beta-haemolytic streptococcal infections, a therapeutic dose should be administered for at least 10 days

Method of administration

For oral use.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1. Cefalexin is contra-indicated in patients with known allergy to the cephalosporin group of antibiotics.

4.4 Special warnings and precautions for use

Warnings

Before instituting therapy with cefalexin, every effort should be made to determine whether the patient has had previous hypersensitivity reactions to the cephalosporins, penicillins or other drugs. Cefalexin 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 cefalexin 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, semisynthetic 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
Reports of neurotoxicity have been identified in association with cephalosporin treatment. Symptoms may include encephalopathy, myoclonus and seizures. Elderly patients, patients with severe renal impairment or central nervous system disorders are particularly at risk. Cefalexin should be administered with caution in the presence of markedly impaired renal function. Since the half-life of cefalexin 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 cefalexin under such conditions is limited; therefore, careful clinical observation and laboratory studies should be made. If cefalexin associated neurotoxicity is suspected, discontinuation of cefalexin should be considered.

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

Prolonged use of cefalexin 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 antiglobulin 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 solution, or with copper sulphate test tablets.

4.5 Interaction with other medicinal products and other forms of interaction

As with other beta-lactam drugs, renal excretion of cephalexin is inhibited by probenecid.

In a single study of 12 healthy subjects given single 500 mg doses of cefalexin and metformin, plasma metformin Cmax and AUC increased by an average of 34% and 24%, respectively, and metformin renal clearance decreased by an average of 14%. No side-effects were reported in the 12 healthy subjects in this study. No information is available about the interaction of cefalexin and metformin following multiple dose administration. The clinical significance of this study is unclear, particularly as no cases of "lactic acidosis" have been reported in association with concomitant metformin and cefalexin treatment.

Hypokalaemia has been described in patient taking cytotoxic drugs for leukaemia when they were given gentamicin and cefalexin.

4.6 Fertility, Pregnancy and lactation

Pregnancy

Although laboratory and clinical studies have shown no evidence of teratogenicity, caution should be exercised when prescribing for the pregnant patient.

Breast-feeding

The excretion of cefalexin in human breast milk increased up to 4 hours following a 500mg dose. The drug reached a maximum level of4 micrograms/ml, then decreased gradually and had disappeared 8 hours after administration. Caution should be exercised when cefalexin is administered to a nursing woman, since the neonate is presented with the risk of candidiasis and CNS toxicity due to immaturity of the blood-brain barrier. There is a theoretical possibility of later sensitisation.

4.3 Effects on ability to drive and use machines

Not relevant.

4.8 Undesirable effects

Gastro-intestinal: The most frequent side-effect has been diarrhoea. It was very 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 have been observed in the form of rash, urticaria, angioedema, and rarely erythema multiforme, Stevens-Johnson syndrome and toxic epidermal necrolysis. These reactions usually subsided upon discontinuation of the therapy.

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 cefalexin. 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, paraesthesias, 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 'Interactions with other Medicaments and other forms of Interaction'.

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. There have been reports of neurological sequelae including tremor, myoclonia, convulsions,

encephalopathy with drugs belonging to the class of cephalosporins. Most cases occurred in patients with renal impairment who received doses that exceeded the recommended dose and resolved following discontinuation of treatment.

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 Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

Symptoms of oral overdose may include nausea, vomiting, epigastric distress, diarrhoea and haematuria.

In the event of severe overdosage,general supportive care is recommended, including close clinical and laboratory monitoring of haematological, renal and hepatic functions and coagulation status until the patient is stable. Forced diuresis, peritoneal dialysis, haemodialysis, or charcoal haemoperfusion have not been established as beneficial for an overdose of cefalexin. It would be extremely unlikely that one of these procedures would be indicated.

Unless 5 to 10 times the normal total daily dose has been ingested, gastro- intestinal decontamination should not be necessary.

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

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antibacterials for systemic use, first-generation cephalosporins, ATC code: J01DB01

In vitro tests demonstrate that cephalosporins are bactericidal because of their inhibition of cell-wall synthesis.

Cefalexin is active against the following organisms in vitro:

Beta-haemolytic streptococci

Staphylococci, including coagulase-positive, coagulase-negative and

penicillinaseproducing strains.

Streptococcus pneumoniae

Escherichia coli

Proteus mirabilis

Klebsiella species

Haemophilus influenzae

Branhamella catarrhalis

Most strains of enterococci (*Streptococcus faecalis*) and a few strains of *staphylococci*
are resistant to cefalexin. It is not active against most strains of *Enterobacter species*,
Morganella morganii and *Pr. vulgaris*. It has no activity against *Pseudomonas* or
Herellea species or *Acinetobacter calcoaeticus*. Penicillin-resistant *Streptococcus*
pneumoniae is usually cross-resistant to beta-lactam antibiotics. When tested by
in-vitro methods, staphylococci exhibit cross-resistance between cefalexin and
methicillin-type antibiotics.

5.2 Pharmacokinetic properties

Absorption
Human pharmacology - cefalexin is acid stable and may be given without regard to meals.

It is rapidly absorbed after oral administration. Following doses of 250 mg, 500 mg and 1g, average peak serum levels of approximately 9, 18 and 32 mg/L respectively were obtained at 1 hour. Measurable levels were present 6 hours after administration.

Cefalexin is almost completely absorbed from the gastro-intestinal tract, and 75-100% is rapidly excreted in active form in the urine. Absorption is slightly reduced if the drug is administered with food.

The half-life is approximately 60 minutes in patients with normal renal function. Haemodialysis and peritoneal dialysis will remove cefalexin from the blood.

Distribution
Peak blood levels are achieved one hour after administration, and therapeutic levels are maintained for 6-8 hours. Approximately 80% of the active drug is excreted in the urine within 6 hours. No accumulation is seen with dosages above the therapeutic maximum of 4 g/day.
The half-life may be increased in neonates due to their renal

immaturity, but there is no accumulation when given at up to 50 mg/kg/day.

Elimination
Cefalexin is excreted in the urine by glomerular filtration and tubular secretion. Studies showed that over 90% of the drug was excreted unchanged in the urine within 8 hours. During this period peak urine concentrations following the 250 mg, 500 mg and 1 g doses were approximately 1000, 2200 and 5000 mg/L respectively.

5.3 Preclinical safety data

The daily oral administration of cefalexin to rats in doses of 250 or 500mg/kg prior to and during pregnancy, or to rats and mice during the period of organogenesis only, had no adverse effect on fertility, foetal viability, foetal weight, or litter size.

Cefalexin showed no enhanced toxicity in weanling and newborn rats as compared with adult animals.

The oral LD50 of cefalexin in rats is 5,000mg/kg.

SUMMARY OF PRODUCT CHARACTERISTICS

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Magnesium stearate

Capsule Shell
Constituents:
Gelatin
Titanium dioxide (E171)
Red iron oxide (E172) Yellow iron oxide (E172) Black iron oxide (E172)

Shellac E 904
Titanium

dioxide E171
Dehydrated Alcohol
E 1510
Isopropyl Alcohol
Butyl Alcohol
Propylene Glycol
E1520
Sodium hydroxide
E524
Povidone E1201

6.2 Incompatibilities

No incompatibilities have been reported.

6.3 Shelf life

36 months

6.4 Special precautions for storage

The product is stored at a temperature not exceeding 30°C, protected from light.

6.5 Nature and contents of container

1) Tubular glass vial with polyethylene snap-plug closure.

2) Tamper evident polypropylene container with low density polyethylene lid. One or more cartridges of activated charcoal according to pack size are included.

3) Capsules are sealed into individual pockets in an aluminium/ polyethylene/ foil laminate (30 and 38 micrometres respectively).

4) Capsules are sealed into individual pockets in an aluminium foil blister with an aluminium lid (43 and 20 micrometres respectively).

5) Capsules are sealed into individual pockets in PVC-Aluminium
foil blister packs.

All container presentations contain 20, 28, 100 or 500 tablets.

6.6 Special precautions for disposal

None stated.

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

7. MARKETING AUTHORISATION HOLDER

Crescent Pharma Limited
Key House, Sarum Hill,
Basingstoke, RG21 8SR,
United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL 20416/0650

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

30 August 2004

10 DATE OF REVISION OF THE TEXT

17/03/2025