SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Cefalexin 500 mg Capsules, HARD

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

500 mg Cefalexin (as monohydrate)

For a full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Capsules, hard
Size 0 grey/orange capsule containing white powder printed CHX 500.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Cefalexin is a semi synthetic 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 prostatitis; dental infections.

Cefalexin is active against the following organisms in vitro: beta-haemolytic streptococci; staphylococci, including coagulase-positive, coagulase-negative and penicillinase-producing 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, Colstridium difficule, and the following species: legionella, campylobacter, pseudomonas or Herellea species. When tested by

in vitro methods, staphylococci exhibit cross-resistance between cefalexin and methicillin-type antibiotics.

4.2 Posology and method of administration

Adults
The adult dosage ranges from 1-4g daily in divided doses; most infections will respond to a dosage of 500mg every 8 hours. For skin and soft tissue infections, streptococcal pharyngitis and mild, uncomplicated urinary tract infections, the usual dosage is 250mg every 6 hours or 500mg 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.

Elderly and patients with impaired renal function
As for adults although dosage should be reduced to a daily maximum of 500mg if renal function is severely impaired (glomerular filtration rate < 10ml/min).
Paediatric population
The usual recommended daily dosage for children is 25-50mg/kg (10-20mg/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:	125mg every 8 hours.
Children 5 years and over:	250mg 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 75-100mg/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
Oral

4.3 Contraindications

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

Cefalexin is contraindicated in patients with known allergy to the cephalosporins group of antibiotics or any of the excipients listed in Section 6.1.

Cefalexin should be given cautiously to patients who have shown hypersensitivity to other drugs. Cephalosporins should be given with caution to penicillin-sensitive

patients, as there is some evidence of partial cross-allergenicity between the penicillins and the cephalosporins. Patients have had severe reactions (including anaphylaxis) to both drugs.

Cefalexin is contraindicated in patients with porphyria.

4.4 Special warnings and precautions for use

Cefalexin should be given cautiously to patients who have shown hypersensitivity to other drugs. Cephalosporins should be given with caution to penicillin-sensitive patients, as there is some evidence of partial cross-allergenicity between the penicillins and the cephalosporins. Patients have had severe reactions (including anaphylaxis) to both drugs.

If an allergic reaction to cefalexin occurs the drug should be discontinued and the patient treated with the appropriate agents. Prolonged use of cefalexin 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.

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 of pseudomembranous colitis usually respond to drug discontinuance alone. In moderate to severe cases, appropriate measures should be taken.

Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Cefalexin should be administered with caution in the presence of markedly impaired renal function. Careful clinical and laboratory studies should be made because safe dosage may be lower than that usually recommended.

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 solutions or with copper sulphate test tablets.

Acute generalized exanthematous pustulosis (AGEP) has been reported in association with cefalexin treatment. At the time of prescription patients should be advised of the signs and symptoms and monitored closely for skin reactions. If signs and symptoms suggestive of these reactions appear, cefalexin should be withdrawn immediately and an alternative treatment considered. Most of these reactions occurred most likely in the first week during treatment.

4.5 Interaction with other medicinal products and other forms of interaction

Probenecid causes reduced excretion of cefalexin, leading to increased plasma concentration. Cephalosporins have an increased risk of nephrotoxicity in the presence of amphotericin, loop diuretics, aminoglycosides, capreomycin or vancomycin.

In a single study of 12 healthy subjects given single 500mg 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 patients 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 of 4 micrograms/ml then decreased gradually and had disappeared 8 hours after administration. Caution should be exercised when cefalexin is administered to a nursing woman, possible effects to the infant include modification of bowel flora.

4.7 Effects on ability to drive and use machines

Cefalexin has no or negligible influence on the ability to drive and use machines. Not applicable

4.8 Undesirable effects

Infections and infestations: vaginitis, genital moniliasis

Blood and lymphatic system disorders: - eosinophilia, neutropenia, thrombocytopenia haemolytic anaemia and positive Coombs' test have been reported.

Psychiatric disorders: agitation, confusion, hallucinations, nervousness, sleep disturbances, restlessness

Nervous system disorders: dizziness, headache, hyperactivity, hypertonia

Hepatobiliary disorders; As with some penicillins and some other cephalosporins, transient hepatitis and cholestatic jaundice have been reported rarely. Slight elevations of AST and ALT have been reported.

Musculoskeletal and connective tissue disorders: arthralgia, arthritis, joint disorder

Renal and urinary disorders: reversible interstitial nephritis

Reproductive system and breast disorders: vaginal discharge

General disorders and administration site conditions: fatigue, fever

Gastrointestinal disorders: Nausea and vomiting have been reported rarely. Dyspepsia, and abdominal pain have also occurred. Diarrhoea has been reported most frequently. It is rarely severe enough to warrant cessation of therapy. Colitis, including rare instances of symptoms of pseudomembranous colitis, has been reported either during or after antibiotic treatment.

Hypersensitivity: Allergies have been observed in the form of rash, urticaria and angioedema, and rarely erythema multiforme, Stevens-Johnson syndrome and toxic epidermal necrolysis. These reactions usually subside upon discontinuation of the drug. Anaphylaxis has also been reported. Other reactions have included genital and anal pruritus.

Skin and subcutaneous tissue disorders:
Not known – Acute generalised exanthematous pustulosis (AGEP)

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorization 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

Symptoms of overdosage may include nausea, vomiting, epigastric distress, diarrhoea and haematuria.
Treatment of overdosage - serum levels can be considerably reduced by haemodialysis or peritoneal dialysis.

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 - 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 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: ATC code: J01DB01 First generation cephalosporins

Cefalexin is bactericidal and has antimicrobial activity similar to that of cephaloridine or cephalothin against both gram-positive and gram-negative organisms.

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 penicillinase producing strains.

Streptococcus pneumonia

Escherichia coli

Proteus mirabilis

Klebsiella species

Haemophilus influenza

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

Cefalexin is acid stable and may be given without regard to meals. Cefalexin is rapidly absorbed from the gastro-intestinal tract and produces peak plasma concentrations about 1 hour after administration. Following doses of 250mg, 500mg and 1g, average peak serum levels of approximately 9, 18 and 32mg/L respectively, were obtained at 1 hour.

Measurable levels were present 6 hours after administration. 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 250mg, 500mg and 1g doses were approximately 1000, 2200 and 5000mg/L respectively.

Cefalexin is almost completely absorbed from the gastro-intestinal tract, and 75-100% is rapidly excreted in active form in the urine. If cefalexin is taken with food there is delayed and slightly reduced absorption and there may be delayed elimination from the plasma. The half-life is approximately 60 minutes in patients with normal renal function. The biological half-life has been reported to range from 0.6 to at least 1.2 hours and this increase’s with reduced renal function. About 10 to 15% of a dose is bound to plasma proteins. Haemodialysis and peritoneal dialysis will remove cefalexin from the blood.

Peak blood levels are achieved one hour after administration, and therapeutic levels are maintained for 6-8 hours. About 80% or more of a dose is excreted unchanged in the urine in the first 6 hours by glomerular filtration and tubular secretion; urinary

concentrations greater than 1mg per ml have been achieved after a dose of 500mg. Probenecid delays urinary excretion and has been reported to increase biliary excretion. Cefalexin is widely distributed in the body but does not enter the cerebrospinal fluid in significant quantities unless the meninges are inflamed. It diffuses across the placenta and small quantities are found in the milk of nursing mothers. Therapeutically effective concentrations may be found in the bile.

No accumulation is seen with dosages above the therapeutic maximum of 4g/day.

The half-life may be increased in neonates due to their renal immaturity, but there is no accumulation when given at up to 50mg/kg/day

5.3 Preclinical safety data

There are no preclinical data of relevance to the prescriber, which are additional to those already in other sections of the SmPC.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose
Magnesium stearate

Capsule shell
Black iron oxide (E172)
Titanium dioxide (E171)
Erythrosin (E127)
Quinoline yellow (E104)
Gelatin

6.2 Incompatibilities

None known.

6.3 Shelf life

36 months.

6.4 Special precautions for storage

Do not store above 25°C.
Keep the container tightly closed (for bottles).
Store in the original package (for blisters).

6.5 Nature and contents of container

Each container consists of a polypropylene tubular container with an open end equipped to accept a polyethylene closure, with a tamper-evident tear strip, or PVC/aluminium blisters, or PVDC coated PVC/ Aluminium blisters (60g/m^2 PVDC on 250µm PVC/20µm Al) of an appropriate size to accommodate 7, 14, 20, 21, 28, 30, 50, 56, 60, 100, or 500 capsules. Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special instructions

7 MARKETING AUTHORISATION HOLDER

Kent Pharmaceuticals Limited, Connect 38, 1, Dover Place, Ashford, Kent, United Kingdom. TN23 1FB

8 MARKETING AUTHORISATION NUMBER(S)

PL 08215/0170

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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