SmPC FOR CEPHALEXIN CAPSULES 500MG

1. Name of the medicinal product

Cephalexin 500mg Capsules

2. Qualitative and quantitative composition

Each capsule contains Cephalexin monohydrate equivalent to 500mg Cephalexin (anhydrous)

3. Pharmaceutical form -Capsules, hard, Size 0 white/purple

4. Clinical particulars

4.1 Therapeutic indications

Cephalexin is a semi synthetic cephalosporin antibiotic for oral administration.

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

Respiratory tract infections.

media.

Skin and soft tissue infections.

Bone and joint infections.

infections, including acute prostatitis.

Dental infections

It is active against the following organisms in vitro: β -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 cephalexin. Cephalexin is inactive against most strains of enterobacter, morganella morganii, 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 cephalexin and methicillin-type antibiotics.

4.2 Posology and method of administration

Posology

Adults

The adult dosage ranges from 1-4 g 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 cephalexin 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 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
For oral use.
4.3 Contraindications
Hypersensitivity to the active substance or to any of the excipients listed in section 6.1. Cephalexin is contraindicated in patients with known allergy to the cephalosporins group of antibiotics or to any of the excipients listed in section 6.1.
Cephalexin 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.
Cephalexin is contraindicated in patients with acute porphyria.
4.4 Special warnings and precautions for use
Before instituting therapy with cephalexin, every effort should be made to determine whether the patient has had previous hypersensitivity reactions to the cephalosporins, penicillins or s.
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 of pseudomembranous colitis usually respond to drug discontinuance alone. In moderate to severe cases, appropriate measures should be taken.
If an allergic reaction to cephalexin occurs the drug should be discontinued and the patient treated with the appropriate agents.
Prolonged use of cephalexin 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.
Cephalexin 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. If dialysis is required for renal failure, the daily dose of cephalexin should not exceed 500mg.
Concurrent administration with certain other drug substances, such as aminoglycosides, other cephalosporins, or furosemide, (frusemide) and similar potent diuretics, may increase the risk of nephrotoxicity.
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 cephalexin 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, cephalexin should be withdrawn immediately and an alternative treatment considered. Most of these reactions occurred most likely in the first week during treatment.
Cephalexin capsule contains lactose

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

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. Probenecid causes reduced excretion of cephalexin leading to increased plasma concentrations. Cephalosporins may 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 cephalexin 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 cephalexin 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 cephalexin treatment.

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

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.

Breastfeeding

The excretion of cephalexin 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 cephalexin is administered to a nursing mother, 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.

4.7 Effects on ability to drive and use machines

Not relevant.

4.8 Undesirable effects

Gastro-intestinal: Symptoms of pseudomembranous colitis may appear either during or after antibiotic treatment. Nausea and vomiting have been reported rarely. The most frequent side-effect has been diarrhoea. It was very rarely severe enough to warrant cessation of therapy. Dyspepsia and abdominal pain have also occurred. As with some penicillins and some other cephalosporins, transient hepatitis and cholestatic jaundice have been reported rarely.

Hypersensitivity: Allergic reactions have been observed in the form of rash, urticaria, angiooedema, rarely erythema multiforme, Stevens-Johnson syndrome and toxic epidermal necrolysis. These reactions usually subside upon discontinuation of the drug, although in some cases supportive therapy may be necessary. Anaphylaxis has also been reported.

Haemic and Lymphatic System: Eosinophilia, neutropenia, thrombocytopenia, haemolytic anaemia and positive Coombs' test have been reported.

Hepatic; 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.

Skin and subcutaneous tissue disorders:

Acute generalised exanthematous pustulosis (AGEP) has been reported with unknown frequency.

Other: These have included genital and anal pruritus, genital moniliasis, vaginitis and vaginal discharge, dizziness, fatigue, headache, agitation, confusion, hallucinations, fever, arthralgia, arthritis and joint disorder, acute generalised exanthematous pustulosis (AGEP), hyperactivity, nervousness, sleep

disturbances and hypertonia. Reversible interstitial nephritis has been reported rarely Slight elevations in AST and ALT have been observed rarely.
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: 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 cephalexin. 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 cephalexin in a day. Treatment has been supportive (fluids) and no sequelae have been reported.
5. Pharmacological properties
5.1 Pharmacodynamic properties
Pharmacotherapeutic group: Antibacterials for systemic use, first generation cephalsporins, ATC code: J01DB01
Cephalexin 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.
Cephalexin 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 cephalexin. 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 cephalexin and methicillin type antibiotics
5.2 Pharmacokinetic properties
Absorption
Human pharmacology - Cephalexin is acid stable and may be given without regard to meals.

It is rapidly absorbed after oral administration 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 32 mg/L respectively were obtained at 1 hour. Measurable levels were present 6 hours after administration.
Cephalexin is almost completely absorbed from the gastro-intestinal tract, and 75-100% is rapidly excreted in active form in the urine. If cephalexin 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. Haemodialysis and peritoneal dialysis will remove cephalexin from the blood.
The biological half-life has been reported to range from 0.6 to at least 1.2 hours and this increases with reduced renal function. About 10 to 15% of a dose is bound to plasma proteins.
Distribution
Peak blood levels are achieved one hour after administration, and therapeutic levels are maintained for 6-8 hours. About 80% of the active drug is excreted in the urine within 6 hours. 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.
Elimination
Cephalexin 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.
5.3 Preclinical safety data
The daily oral administration of cephalexin 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.
Cephalexin showed no enhanced toxicity in weaning and newborn rats as compared with adult animals.
6. Pharmaceutical particulars
6.1 List of excipients-mag stearate, talcum powder
6.2 Incompatibilities
None known
6.3 Shelf life-36 months.
6.4 Special precautions for storage
NMT 30°C
6.6 Special precautions for disposal and other handling
No special instructions
7. Marketing authorisation holder
MIRAFLASH NIGERIA LIMITED (pharmaceuticals)
Ogun State, Nigeria.

8. Marketing authorisation number(s)

E-mail: miraflashnigerialtd@yahoo.com Tel: 08052006942