1.17.1 Summary Product Characteristics (SPC):

1. Name of the medicinal product SANCEPH - 500 CAP

Cephalexin Capsules USP 500mg

2. Qualitative and quantitative composition

Each hard gelatin capsule contains: Cephalexin monohydrate USP equivalent to anhydrous Cephalexin 500mg

Remarks:

* The above quantity is based on 98.0% w/w assay and 6.0% w/w water content of Cephalexin onohydrate.

** Quantity to be adjusted to the final dose weight of 575.00 mg per capsule, based on actual assay and % w/w water content of Cephalexin Monohydrate.

3. . Pharmaceutical form

Hard Gelatin Capsule

Description: Green/White coloured hard gelatin capsules of size „0" containing white to off white granular powder.

4. Clinical particulars

Therapeutic indications alexin 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

Genitourinary tract infections , including acute prostatitis

Dental infections

Posology and method of administration

Route of administration: Oral.

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 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.

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.

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 cephalosporin group of antibiotics.

4.4 Special warnings and special 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 other drugs. Cephalexin should be given cautiously to penicillin-sensitive patients. There is some clinical and laboratory evidence of partial cross-allergenicity of the penicillins and cephalosporins. Patients have had severe reactions (including anaphylaxis) to both drugs.

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 generalised 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.

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 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.

Breast-feeding

The excretion of Cephalexin in human breast milk increased up to 4 hours following a 500 mg 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 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.

4.7 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, angioedema, and rarely erythema multiforme, Stevens-Johnson syndrome and toxic epidermal necrolysis. These reactions usually subsided 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 and haemolytic anaemia 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 candidiasis, vaginitis and vaginal discharge, dizziness, fatigue, headache, agitation, confusion, hallucinations, arthralgia, arthritis and joint disorder. Reversible interstitial nephritis has been reported rarely. Slight elevations in
AST and ALT have been reported.

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 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 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 cephalosporins, ATC code: J01DB01.

In vitro tests demonstrate that cephalosporins are bactericidal because of their inhibition of cellwall 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 betalactam 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. 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.

Cephalexin 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 Cephalexin 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

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 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 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 weanling and newborn rats as compared with adult animals.

The oral LD_{50} of Cephalexin in rats is 5,000mg/kg.

6. Pharmaceutical particulars 6.1

List of excipients

Lactose anhydrous, Croscarmellose sodium, Magnesium stearate and Hard gelatin capsule.

6.2 Incompatibilities

Not applicable

6.3 Shelf life

36 Months

6.4 Special precautions for storage

Store at temperature below 30° C. Protect from light.

Keep out of reach of children.

6.5 Nature and contents of container

10 capsules in a Blister. 10 such Alu/Pvc blisters are packed with package insert in a carton (10×10"s).

6.6 Special precautions for disposal and other handling

No special requirements

7. Marketing authorisation holder and Manufacturing Site addresses

Sance Laboratories Private Limited,

VI/51B, P.B. No: 2, Kozhuvanal - 686573,

Pala, Kottayam District, Kerala, India.

Ph: 0091-4822- 267799

Fax: 0091-4822-269406

Email: info@sancepharma.com

Web site:www.sancepharma.com

8. Marketing authorisation number(s)

9. Date of first authorisation/renewal of the authorisation

10. Date of Revision of the text