SUMMARY OF PRODUCT CHARACTERISTIC

1. Name of the medicinal product

SALEXIN 250 DRY SYRUP - Cefalexin Oral Suspension BP

2. Qualitative and quantitative composition

Each 5 ml reconstituted Suspension contains:

Cefalexin Monohydrate BP	
Eq. to Anhydrous Cefalexin	250 mg
Excipients	q.s.

For the full list of excipients, see section 6.1.

3. Pharmaceutical form

Dry powder for oral suspension

White to off white coloured, flavoured powder which on constitution forms Orange coloured suspension.

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 infections, including acute prostatitis

Dental infections.

4.2 Posology and method of administration

Posology

Adults

The adult dosage 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 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) (see section 4.4).

Paediatric population

The usual recommended daily dosage for children is 25-50 mg/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 is suggested:

Children under 5 years:	125mg 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 75-100 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

For instructions on reconstitution of the medicinal product before administration, see section 6.6.

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 or to 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 acute porphyria.

4.4 Special warnings and precautions for use

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. 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 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.

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. If dialysis is required for renal failure, the daily dose of cefalexin 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 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 new-borns 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.

Cefalexin contains sorbitol:

Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrose-isomaltase insufficiency should not take this medicine.

Cefalexin contains sodium:

This medicinal product contains 6.50mg sodium per 5ml, equivalent to 0.33% of the WHO recommended maximum daily intake of 2g sodium for an adult.

Cefalexin contains sodium benzoate:

This medicine contains 4.82 mg sodium benzoate in each 5 ml cefalexin oral suspension.

Sodium Benzoate may increase jaundice (yellowing of the skin and eyes) in newborn babies (up to 4 weeks old).

4.5 Interaction with other medicinal products and other forms of interaction

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

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 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 cefalexin 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 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.

4.7 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 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' tests have been reported.

Skin and subcutaneous tissue disorders:

Not known – 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, fever, arthralgia, arthritis and joint disorder and acute generalised exanthematous pustulosis (AGEP). Hyperactivity, nervousness, sleep disturbances and hypertonia have also been reported. Reversible interstitial nephritis has been reported rarely and toxic epidermal necrolysis have been observed rarely. Slight elevations of AST and ALT have been observed.

4.9 Overdose

Symptoms of overdosage 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 – 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: 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 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.* It has no activity against *Pseudomonas* or *Herellea species* or *Acinetobacter calcoaceticus*. Penicillin-resistant *Strptococcus pneumonia* 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

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 increases 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.

Distribution

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 1 mg per ml have been achieved after a dose of 500 mg. 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.

Elimination

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 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

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 LD_{50} of cefalexin in rats is 5,000 mg/kg.

6. Pharmaceutical particulars

6.1 List of excipients

Sodium Benzoate

Disodium Edetate

Citric Acid (Anhydrous)

Sodium Citrate

Flavour Orange Powder

Colloidal Anhydrous Silica

Carmellose Sodium

Aspartame

Sugar Pharma grade**

Colour Sunset Yellow

Croscarmellose sodium

6.2 Incompatibilities

Not applicable

6.3 Shelf life

Dry Powder: 2 years

6.4 Special precautions for storage

Store in cool, dry place Below 30 °C. Protect from light.
The re-constituted suspension mixture should be stored in refrigerator (2°C to 8°C)

6.5 Nature and contents of container

Cefalexin Oral Suspension BP (SALEXIN -250 Dry Syrup) is to be packed in 100 ml ring marked Amber Glass Bottle with 25 mm cap & 10 ml measuring cup. Such 1 Bottle is further packed in Printed carton with Package insert

6.6 Special precautions for disposal and other handling

To the Pharmacist:

To prepare, add 87 ml of potable water and shake until powder is dissolved.

The reconstituted solution may be further diluted with sorbitol solution BP, syrup BP or purified water if required.

A pale yellow, free flowing granular powder, which readily disperses in water to give a yellow suspension with an odour of orange.

7. Marketing authorisation holder

SAKAR Healthcare Limited

Block No. 10-13, Sarkhej-Bavla Highway,

Changodar, Ahmedabad – 382213, Gujarat, India

8. Marketing authorisation number(s)

04575/4984/NMR/2017

9. Date of first authorisation/renewal of the authorisation

31/07/2019

10. Date of revision of the text

July 2023