Summary Product Characteristics (SPC)

1. Name of the medicinal product

Cephaxim 250

2. Qualitative and quantitative composition

Each capsule contains as the active ingredient, Cefalexin monohydrate equivalent to 250 mg of Cefalexin base.

For the full list of excipients, see section 6.1.

3. Pharmaceutical form

Hard Gelatin Capsule
White coloured powder filled in size “2” hard gelatin capsule having a Blue coloured cap and Red coloured body.

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 susceptiblemicro-organisms:

- Exacerbation of chronic bronchitis
- Mild to moderate community-acquired pneumonia
- Uncomplicated upper and lower urinary tract infections
- Skin and soft tissue infections

4.2 Posology and method of administration

Adults

Cefalexin is administered orally.
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 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.

Patients with impaired renal function: Reduce dosage if renal function is markedly impaired.

Elderly patients:
The recommended dose for adults should be used in elderly patients except those with impaired renal function.

Children:
The recommended daily dosage for children is 25-50mg/kg body weight divided in 3 doses. In severe infections the dosage may be doubled.
In the treatment of beta-haemolytic streptococcal infections, a therapeutic dose should be administered for at least 10 days.

4.3 Contraindications

Cefalexin is contra-indicated in patients with known allergy to the cephalosporin group of antibiotics or to any of the excipients.

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 medicinal products. 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 medicinal products.

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. 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 super infection occurs during therapy, appropriate measures should be taken.

Cefalexin should not be used in infections in which Haemophilus influenzae is, or is likely to be, implicated.

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.
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 recognized 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.

Cefalexin capsules contain colouring agents, sunset yellow (E110), quinoline yellow (E104) and patent blue V (E131) which may cause allergic reactions.

Acute generalised 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.

This medicinal product contains less than 1 mmol sodium (23 mg) per capsule, that is to

say essentially 'sodium-free'.

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. Concurrent administration with certain other drug substances, such as aminoglycosides, other cephalosporins, or furosemide, and similar potent diuretics, may increase the risk of nephrotoxicity.

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 “lacticacidosis” have been reported in association with concomitant metformin and cefalexin treatment.

4.6 Fertility, pregnancy and lactation

Pregnancy: There are no adequate and well controlled studies in pregnant women. Although animal studies have shown no evidence of teratogenicity, caution should be exercised when prescribing cefalexin during pregnancy.

Lactation: Cefalexin is excreted in human milk. Caution should be exercised when cefalexin is administered to a nursing woman.

4.7 Effects on ability to drive and use machines

There are no known effects of cephalexin on a patient's ability to drive or use machinery. However, when driving vehicles or operating machines it should be taken into account that occasionally dizziness or confusion may occur.

4.8 Undesirable effects

Adverse events that have been reported in cefalexin trials are categorized below, according tosystem organ class and frequency.
Frequencies are defined as:
Very common (1/10); common (1/100<1/10); uncommon (1/1,000, <1/100);rare (1/10,000, <1/1,000);
very rare (<1/10,000),
not known (cannot be estimated from the available data) Undesirable effects for cefalexin occur at a frequency of 3-6%.Investigations:
Uncommon: Increase in ASAT and ALAT (reversible)
Frequency not known: Positive direct Coombs test. False positive reaction to glucose in the urine
Blood and lymphatic system disorders:
Uncommon: Eosinophilia
Rare: neutropenia, thrombocytopenia, haemolytic anaemia

Nervous system disorders:
Rare: Dizziness, headache

Gastrointestinal disorders:
Common: Diarrhoea, nausea
Rare: Abdominal pain, vomiting, dyspepsia, pseudomembranous colitis.

Renal and urinary disorders:
Rare: Reversible interstitial nephritis
Skin and subcutaneous tissue disorders:
Uncommon: Rash, urticaria, pruritus
Rare: Stevens-Johnson syndrome, erythema multiforme, toxic epidermal necrolysis (Lyell's syndrome), anaphylaxis
Frequency not known: Acute generalised exanthematous pustulosis (AGEP)

Musculoskeletal and connective tissue disorders:
Frequency not known: Arthralgia, arthritis
Infections and infestations
Rare: Genital and anal pruritus, vaginitis Frequency not known: Vaginal candidiasis

General disorders and administration site conditions
Rare: Tiredness
Frequency not known: FeverImmune System Disorders Rare: Anaphylactic reaction
Hepatobiliary Disorders
Rare: Hepatitis, cholestatic icterus

Psychiatric Disorders
Frequency not known: Hallucinations, agitation, confusion

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. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: First generation cephalosporinATC code: J01DB01

Mode of Action

Cefalexin is an antibacterial agent of the cephalosporin class. Like other cephalosporins cefalexin exerts antibacterial activity by binding to and inhibiting the action of penicillin-binding proteins involved in the synthesis of bacterial cell walls. This leads to bacterial cell lysis and cell death.

Mechanisms of resistance

Bacterial resistance to cefalexin may be due to one or more of the following mechanisms:

- Hydrolysis by extended-spectrum beta-lactamases and/or by chromosomally-encoded (AmpC) enzymes that may be induced or de-repressed in certain aerobic gram-negative bacterial species.
- Reduced affinity of pencillin-binding proteins.
- Reduced permeability of the outer membrane of certain gram-negative organisms restricting access to penicillin-binding proteins
- Drug efflux pumps

More than one of these mechanisms of resistance may co-exist in a single bacterial cell. Depending on the mechanism(s) present, bacteria may express cross-resistance to several or all other beta-lactams and/ or antibacterial medicinal products of other classes.

Breakpoints

Minimum inhibitory concentration (MIC) breakpoints established by the British Society of Antimicrobial Chemotherapy for beta-haemolytic Streptococci and Streptococcus pneumoniae are: susceptible ≤ 2mg /l, resistant ≥2.5mg/l.

Susceptibility

The prevalence of resistance may vary geographically and over time for selected species and local information on resistance is desirable, particularly when treating severe infections. As necessary, expert advice should be sought when the local prevalence of resistance is such that the utility of the agent in at least some types of infections is questionable.

Commonly susceptible species

Aerobes, Gram positive:

Staphylococcus aureus (methicillin susceptible)

Streptococcus agalactiae Streptococcus pneumoniae Streptococcus pyogenes Aerobes, Gram negative:

*Escherichia coli Moraxella catarrhalis*Anaerobes:

Peptostreptococcus species

Species for which acquired resistance may be a problem

Gram-negative aerobes:

Citrobacter species Enterobacter species *Morganella morganii*. Inherently resistant species Gram-negative aerobes:

Haemophilus influenzae

5.2 Pharmacokinetic properties:

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 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 medicinal product was excreted unchanged in the urine within 8 hours. During thisperiod, peak urine concentrations following the 250mg, 500mg, and 1g doses were approximately 1,000, 2,200, and 5,000mg/l, respectively.

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.

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 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

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.

6. Pharmaceutical particulars

6.1 List of excipients

Microcrystalline Cellulose
Magnesium Stearate

EHG capsule shell (Gelatin, Purified Water, Brillient Blue, Erythrosine, Titanium Di oxide and Red Iron Oxide)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life:

36 months

6.4 Special precautions for storage

Do not store above 30°c, store in original container

6.5 Nature and contents of container

10 capsules packed in Alu-PVC blister and such 10 blisters are packed in a printed carton along with pack insert.

6.6 Special precautions for disposal

No special requirements. Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. Marketing authorization holder

Sameeksha Pharmaceutical Private Limited

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Pune-411040, (Maharashtra), INDIA

Manufacturer

Medreich Limited
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INDIA.

8. Marketing authorisation number (s)

TAN 21 HM 0470

9. Date of first authorisation/renewal of the authorization

Date of first authorization: November 26, 2021
Date of latest renewal: N/A

10. Date of revision of the text

April, 2022

Distribution category: Prescription Only Medicine (POM)