

Summary of Product Characteristics

1.0 Name of the Medicinal Product

THEOFLEX-125 Oral Suspension

2.0 Qualitative and Quantitative Composition

Each 5 ml of reconstituted suspension contains:

Cefalexin Monohydrate BP eq. to Anhydrous Cefalexin 125 mg

For a full list of excipients, see section 6.1.

3.0 Pharmaceutical Form

Dry powder for oral suspension

Off white colored granular powder forming light orange colored suspension after reconstitution.

4.0 Clinical Particulars

4.1 Therapeutic Indications

Cefalexin is indicated in the treatment of the following infections: Respiratory tract infections; otitis media; skin and soft tissue infections; bone and joint infections; genito-urinary infections, including acute prostatitis and dental infections.

Cefalexin is active against the following organisms in vitro: α -haemolytic streptococci; staphylococci, including coagulase-positive, coagulase-negative and penicillinase-producing strains; *Streptococcus pneumoniae*; *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. Cefalexin is inactive against most strains of enterobacter, *morganella morganii*, pr. *Vulgaris*, *colstridium difficile*, 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

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.

More severe infections, or those caused by less susceptible organisms may need larger doses.

If daily doses greater than 4g are required other 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).

Children

The recommended daily dosage for children is 25-50 mg/kg (10-20mg/lb) in divided doses.

For skin, 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 α -haemolytic streptococcal infections, a therapeutic dose should be administered for at least 10 days.

Route of administration

Oral

4.3 Contraindications

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

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.

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, 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.

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 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.

Patients with rare hereditary problems of fructose intolerance should not take this medicine.

4.5 Interaction with other Medicinal Products and other Forms of Interaction

Probenecid causes reduced excretion of cefalexin leading to increased plasma concentration. 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 cefalexin and metformin, plasma metformin C_{max} 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 cephalixin.

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 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

Not Applicable.

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.

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.

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 observed.

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. 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.

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 National Regulatory Authority.

4.9 Overdose

Symptoms of overdosage may include nausea, vomiting, epigastric distress 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, gastrointestinal 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.

5.0 Pharmacological Properties**5.1 Pharmacodynamic Properties**

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 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 *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 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.

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.

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.

6.0 Pharmaceutical Particulars

6.1 List of Excipients

- Sucrose
- Xanthan Gum
- Sodium Benzoate
- Aspartame
- Colloidal anhydrous silica
- Flavour Orange
- Sunset Yellow FCF Supra

6.2 Incompatibilities

Not applicable

6.3 Shelf Life

24 months.

6.4 Special Precautions for Storage

Store below 30°C. Protect from light & moisture.

6.5 Nature and Contents of Container

Off white colored granular powder forming light orange colored suspension after reconstitution.

Powder for oral suspension is supplied in 100 ml HDPE bottle packed in a unit carton along with package insert.

6.6 Special Precautions for Disposal and other Handling

To the pharmacist:

To prepare, 89 ml of portable 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. Off- white colored granular powder forming light orange colored suspension after reconstitution.

7.0 Marketing Authorization Holder

H2024/CTD10746/20923

8.0 Marketing Authorization Number(s)

H2024/CTD10746/20923

9.0 Date of First Authorization/Renewal of the Authorisation

2024 September 16

10.0 Date of revision of the text

2024 September 16