SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF MEDICINAL PRODUCT

GENLEX-250
Cephalexin Capsules USP 250 mg

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each hard gelatin capsule contains:
Cephalexin Monohydrate USP
Eq. to Anhydrous Cephalexin 250 mg

Excipients q.s.
Approved colours used in empty capsule shells

3. PHARMACEUTICAL FORM

Capsules

Description: A white to almost white granular powder filled in blue/blue size "2" hard gelatin capsule.

4. CLINICAL PARTICULARS

1. Therapeutic Indications

Cephalexin is a semisynthetic cephalosporin antibiotic for oral administration.
Cephalexin 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 tract infections, including acute pro statitis
- Dental infections Syphilis

4.2 Posology and Method of Administration

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.

The elderly and patients with impaired renal function:

As for adults. Reduce dosage if renal function is markedly impaired.

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-hemolytic streptococcal infections, a therapeutic dose should be administered for at least 10 days.

Method of administration
For oral use

4.3 Contra-indications
Cephalexin is contraindicated in patients with known allergy to the cephalosporin group of antibiotics or to any of the excipients.

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, 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.

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.

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.

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 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 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.

4.7 Effects on Ability to Drive and Use Machines

No studies on the effects on the ability to drive and use machines have been performed.

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.

Other: These have included genital and anal pruritus, genital candidiasis, vaginitis and vaginal discharge, dizziness, fatigue, headache, agitation, confusion, hallucinations, arthralgia, arthritis, joint disorder and acute generalized exanthematous pustulosis (AGEP). Reversible interstitial nephritis has been reported rarely. Slight elevations in AST and ALT have been reported.

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 to **TMDA.**

9. Overdose

Symptoms of oral overdose may include nausea, vomiting, epigastric distress, diarrhoea and haematuria.

In the event of severe over dosage, 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

Pharmacological Classification: Antibacterial for systemic use, first-generation cephalosporins,

ATC Code: J01DB01

In-vitro tests demonstrate that the 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.

Escherichia coli

Proteus mirabilis

Klebsiella species

Haemophilus influenzae

Branhamella catarrhaliseptococcus pneumoniae

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 calcoaceticus. Penicillinresistant Steptococcus pneumonia 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. Following doses of 250 mg, 500 mg and 1 g, 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 1g 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 500 mg/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 LD50 of Cephalexin in rats is 5,000 mg/kg.

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

Magnesium Stearate USP
Purified Talc USP
Sodium Lauryl Sulphate USP
Colloidal Silicon Dioxide USP
Sodium Starch Glycolate USP
E.H.G Capsule Size “2” IH

Excipients of EHG Capsules:

CAP	BODY
Gelatin	Gelatin
Purified Water	Purified Water
Brilliant Blue	Brilliant Blue
Titanium di oxide	Titanium di oxide

6.2 Incompatibilities

Not Applicable

6.3 Shelf Life

36 Months

6.4 Special Precautions for Storage

Do not store above 30^0C. Protect from light.

6.5 Nature and Contents of Container

10×10 Alu/PVC Blister Pack.

6.6 Special precautions for disposal and other handling

No special requirements.

7. MARKETING AUTHORISATION HOLDER

Generics & Specialities Ltd

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Upanga Dar es salaam

Tanzania

E-Mail: genericstz@cats-net.com

8. MARKETING AUTHORISATION NUMBER

TAN 22 HM 0434

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

07th October, 2022

10. DATE OF REVISION OF THE TEXT