Summary of Product Characteristics

1. Name of the Medicinal Product

Genlex 125mg/5ml Dry Syrup
(Cephalexin For Oral Suspension USP 125 mg/5mL)

2. Qualitative and Quantitative Composition

Each 5mL (after reconstitution) contains:
Cephalexin Monohydrate USP
Eq. to Anhydrous Cephalexin 125 mg
Excipients q.s.
Colour: Approved colour used

Excipients of Safety concern:
Sodium Benzoate USP 130mg
Sunset Yellow 0.80mg
Sugar (Pharma grade) USP 20729mg

3. Pharmaceutical Form

Dry powder for suspension for oral administration.

Description: White to off white granular powder filled in bottle, after reconstitution light orange color suspension produced.

4. Clinical Particulars

4.1 Therapeutic Indications

Cephalexin is a semi synthetic cephalosporin antibiotic for oral administration.

Cephalexin 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

Dental infections.

Cephalexin is active against the following organisms in vitro: β-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 Cephalexin. Cephalexin is inactive against most strains of enterobacter, morganella morganii, pr. Vulgaris, colstridium difficule, and the following species: legionella, campylobacter, pseudomonas or herellea species. When tested by in vitro methods, staphylococci exhibit cross-resistance between Cephalexin and methicillin-type antibiotics.

4.2 Posology and Method of Administration

Posology

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 β-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 Contra-indications

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

Cephalexin 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.

Cephalexin is contraindicated in patients with acute porphyria.

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.

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.

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.

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 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, glucose-galactose malabsorption or sucrose-isomaltase insufficiency should not take this medicine.

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.

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

Sunset yellow colour used in the formulation May cause allergic reactions.

4.5 Interaction with Other Medicinal Products and Other Forms of Interaction

Probenecid causes reduced excretion of Cephalexin 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 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 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 Cephalexin 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.

Skin and subcutaneous tissue disorders:

Not known – Acute generalised exanthematous pustulosis (AGEP)

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. 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 Cephalexin. 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 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 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.

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 calcoaceticus*. Penicillin-resistant *Strptococcus 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

Cephalexin is acid stable and may be given without regard to meals.

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.

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 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.

5.3 Preclinical Safety Data

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

6. Pharmaceutical Particulars

6.1 List of Excipients

Name of the Excipients	Pharmacopoeial reference
Xanthum Gum	USP
Sodium Benzoate	USP
Colloidal Silicon Dioxide	USP
Colour sunset yellow	IH
Flavour Strawberry **Ingredient Declaration** Maltodextrin 55-70% Nature Identical Flavoring Substances 15-30% Emulsifier (INS 414) 10-25% Artificial Flavoring Substances 0.5-5.0% Natural Flavoring Substances 0.01-0.15%	IH
Sugar	USP

6.2 Incompatibilities

Not Applicable

6.3 Shelf Life

36 Months

6.4 Special Precautions for Storage

Do not store above 30°C. Protect from light. Store reconstituted suspension in a refrigerator at a temperature between 2 to 8°C. The reconstituted suspension should be consumed within 7 days of preparation.

Keep out of the reach of children.

6.5 Nature and Contents of Container

100 ml White HDPE Bottle with LDPE measuring cup.

6.6 Special precautions for disposal and other handling

Instructions for Reconstitution:

The reconstituted suspension should be consumed within 7 days of preparation.

Any unused product or waste material should be disposed of in accordance with local requirements.

7. Marketing Authorisation Holder

Generics & Specialities Ltd.,
P.O. Box 1469, Mindu street, Upanga, Dar es salaam,
Tanzania

Manufacturer:

Scott-Edil Advance Research Laboratories & Education Ltd.,
Hill-Top, Industrial Area, Bhatoli Kalan, Baddi, Dist. Solan (HP), INDIA

8. Marketing Authorization Number

To be allocated

9. Date of Renewal of the Authorization

Not Applicable

10. Date of Revision of the Text

April, 2022