Summary of Product Characteristics for Pharmaceutical Products

1. Name of the medicinal product:

Leocef® 250 mg Capsule for oral administration.

2. Qualitative and quantitative composition

Each capsule contains: Cefalexin monohydrate BP equivalent to Cefalexin 250 mg.

Excipient(s) with known effect

Each capsule contains 26.6 mg lactose.

For full list of excipients, see section 6.1

3. Pharmaceutical form

Capsule for oral administration.

Leocef Capsules are size "2" capsules with Green/ Yellow hard gelatin capsule containing off white granular powder.

4. Clinical particulars

4.1 Therapeutic indications

Leocef® Oral preparations are indicated for the treatment of infections caused by gram-positive and gram-negative aerobic and anaerobic bacteria sensitive to cephalexin.

It is used for the treatment of respiratory tract infections such as bronchitis, pneumonia, pleurisy and other respiratory tract conditions such as empyema, lung abscesses and bronchiectasis.

Leocef® Oral preparations are also used in the treatment of urinogenital tract infections (UTI) including pyelonephritis, cystitis and acute prostatitis.

Leocef® Oral preparations have also proved to be effective in the treatment of bone, joints, skin and soft tissue infections such as osteomyelitis, infected wounds open fractures, pyodermatitis and abscesses. It is also used as a prophylactic measures pre and post operatively.

Leocef® Oral preparations are effective against infections caused by *Klebsiella pneumonia, Proteus mirabilis, Haemophillus influenazae, Moraxella catarrhalis, Escherichia coli,* Salmonella species and Shigella species.

The preparations are also effective against infections caused by sensitive Gram-positive cocci including both penicillinase producing Staphylococci and also most Streptococci.

4.2 Posology and method of administration

Leocef® Oral preparations are administered by the oral route.

Adults

The adult dosage ranges from 1-4g 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.

The elderly and patients with impaired renal function

As for adults. Reduce dosage if renal function is markedly impaired (see section 4.4).

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

Method of administration

For oral use.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

Cefalexin is contraindicated in patients with known allergy to the cephalosporin group of antibiotics.

4.4 Special warnings and precautions for use

Leocef® Oral preparations are contraindicated in patients with known hypersensitivity to cephalexin or cephalosporin group of antibiotics.
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.

Reports of neurotoxicity have been identified in association with cephalosporin treatment. Symptoms may include encephalopathy, myoclonus and seizures.

Elderly patients, patients with severe renal impairment or central nervous system disorders are particularly at risk. 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. If cefalexin associated neurotoxicity is suspected, discontinuation of cefalexin should be considered.

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 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 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 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 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 Pregnancy and Lactation

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 sensitization.

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 categorised below, according to system 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: Fever

Immune System disorders

Rare: Anaphylactic reaction

Hepatobiliary Disorders

Rare: Hepatitis, cholestatic icterus

Psychiatric Disorders

Frequency not known: Hallucinations, agitation, confusion

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 pharmacy and poisons board, Pharmacovigilance Electronic Reporting System (PvERS) https://pv.pharmacyboardkenya.org

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 cephalosporin.
ATC code: J01DB01.
Leocef® Oral preparations contain Cephalexin which is a first-generation cephalosporin antibiotic that exerts its bactericidal action on growing and dividing bacteria by inhibiting bacterial cell-wall synthesis. Cephalexin inhibits the final cross-linking stage of peptidoglycan production by binding to and inactivating transpeptidases and penicillin binding proteins on the inner surface of the bacterial cell membrane, in addition to causing bacterial lysis by inactivation of endogenous inhibitors of bacterial autolysins.
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 calcoaeticus. 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:

Absorption

Human pharmacology - 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 32 mg/L respectively were obtained at 1 hour. Measurable levels were present 6 hours after administration.

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.

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

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 250 mg, 500 mg and 1 g doses were approximately 1000, 2200 and 5000 mg/L respectively

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

- Lactose Monohydrate
- Purified Talc
- Sodium Lauryl Sulphate
- Aerosil 200 Pharma
- Magnesium stearate
- Empty Hard Gelatin shells Green size "2"

6.2 Incompatibilities

Not Applicable

6.3 Shelf life

30 Months.

6.4 Special precautions for storage

Store in a dry place below 30°C. Protect from light.Keep all medicines out of reach of children.

6.5 Nature and contents of container

Leocef® Capsules are packed in blisters of 10 x 10's in a unit box with literature insert.

6.6 Special precautions for disposal and other handling

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

7. MARKETING AUTHORIZATION HOLDER AND MANUFACTURING SITE ADDRESSES

Marketing Authorization Holder:
Company name: LABORATORY & ALLIED LTD
Address: PLOT NO: 209/10349 OFF MOMBASA ROAD,
P.O BOX 42875, CODE 00100 NAIROBI,
Country: KENYA
Telephone: + 254 – 20-8040306
Telefax: 254 – 020 – 8040309
E-Mail: info@laballied.com

Manufacturing Site Addresses:
Company name: LABORATORY & ALLIED LTD
Address: PLOT NO: 209/10349 OFF MOMBASA ROAD,
P.O BOX 42875, CODE 00100 NAIROBI,
Country: KENYA
Telephone: + 254 – 20-8040306
Telefax: 254 – 020 – 8040309
E-Mail: info@laballied.com

8. MARKETING AUTHORIZATION NUMBER
Kenya: Registration No. CTD8277

9. DATE OF FIRST <REGISTRATION> / RENEWAL OF THE <REGISTRATION>

Date of first authorization: 25/08/2023
Date of latest renewal: Not Applicable.

10. DATE OF REVISION OF THE TEXT
O7 MAY 2025.