1. Name of the Medicinal Product

(a) Product Name : Monacef-500 Capsules
(b) Strength : 500 mg
(c) Pharmaceutical Dosage Form : Capsules

2. Quality and Quantitative Composition

(a) Qualitative Declaration, the active substance should be declared by its recommended INN. Accompanied by its salt or hydrate form if relevant.

Composition:

Each hard gelatin capsule contains:
Cefalexin Monohydrate B.P.
Eq. to Anhydrous Cefalexin 500 mg

(b) Quantitative Declaration, the quantity of the active substance must be expressed per dosage unit

Sr. No.	Name of the Materials	Specification	Label Claim	Quantity (mg/caps)	Active/ Inactive
1	Cefalexin Monohydrate Eq. to Anhydrous Cefalexin	B.P.	500 mg	526.0 mg	Active

3. Pharmaceutical Form Visual description of the appearance of the product (colour, markings, etc.) e.g.: White body and green cap hard gelatin capsule containing white crystalline powder.

4. Clinical Particulars

4.1 Therapeutic Indications:

Monacef-500 Capsules is indicated for the treatment of respiratory tract infections (RTI's), urinary tract infections (UTI's), skin and soft tissue infections, otitis media and other infections due to sensitive organisms.

4.2 Posology and method of administration:

Posology

Adults

The dosage is 1-4 g daily in divided doses. Most infections will respond to 500 mg every 8 hours. For skin and soft tissue infections, streptococcal pharyngitis and mild uncomplicated UTI's, 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 dosages may be needed.

Older people

The dosage is as for adults. The dosage should be reduced if renal function is markedly impaired.

Paediatric population and adolescents

The usual recommended daily dosage for children is 25-50 mg/kg 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 75-100mg/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
Monacef-500 Capsules are for oral use. Each capsule should be swallowed whole with water.

4.3 Contraindications:
Monacef-500 Capsules is contra-indicated in patients with known allergy to the cephalosporin group of antibiotics. Severe systemic infections, which require parenteral cephalosporin treatment, should not be treated orally during the acute stage.

4.4 Special warning and precautions for use:
Monacef-500 Capsules 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 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 the patient experiences an allergic reaction cefalexin should be discontinued and treatment with the appropriate agents initiated.

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.Cefalexin should be administered with caution in the presence of markedly impaired renal function as it is excreted mainly by the kidneys. Careful clinical and laboratory studies should be made because the safe dosage may be lower than that usually recommended.

Positive direct Coombs' tests have been reported during treatment with cephalosporin antibiotics. For 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. Tests based on glucose oxidation reactions may be safely used.

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.

4.5 Interaction with other medicinal products and other forms of interactions:
As cephalosporins like cefalexin are only active against proliferating microorganisms, they should not be combined with bacteriostatic antibiotics.

Concomitant use of uricosuric drugs (e.g. probenicid) suppresses renal drug elimination. As a result, cefalexin plasma levels are increased and sustained for longer periods.

If associated with highly potent diuretics (ethacrynic acid, furosemide) or other potentially nephrotoxic antibiotics (aminoglycosides, polymyxin, colistin), cephalosprins may show higher nephrotoxicity.

Combined use of cephalosporins and oral anticoagulants may prolong prothrombin time.

A potential interaction between cefalexin and metformin may result in an accumulation of metformin and could result in fatal lactic acidosis.

Hypokalaemia has been described in patient taking cytotoxic drugs for leukaemia when they were given gentamicin and cefalexin.

4.6 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.

4.7 Effects on ability to drive and use machine:
Monacef-500 Capsules has negligible influence on the ability to drive and use machines.

4.8 Undesirable effects:
Side effects of cefalexin include gastro-intestinal disturbances such as nausea, vomiting, diarrhoea and abdominal discomfort. The most common of these effects is diarrhoea, but this is rarely severe enough to warrant cessation of therapy. Dyspepsia has also occurred. Transient hepatitis and cholestatic jaundice have rarely been reported.

Allergic reactions have been reported such as rash, urticaria, angioedema and rarely erythema multiforme, Stevens-Johnson syndrome and toxic epidermal necrolysis (exanthematic necrolysis). These reactions usually subsided upon discontinuation of the drug, although in some cases supportive therapy may be necessary. Anaphylaxis and Acute generalised exanthematous pustulosis (AGEP) have also been reported.

Other side effects such as genital and anal pruritus, genital candidiasis, vaginitis and vaginal discharge, dizziness, fatigue, headache, agitation, confusion, hallucinations, arthralgia, arthritis and joint disorders have been reported.

As with other cephalosporins interstitial nephritis has rarely been reported.

Eosinophilia, neutropenia, thrombocytopenia, haemolytic anaemia and slight elevations in AST and ALT have been reported.

As with other broad-spectrum antibiotics prolonged use may result in the overgrowth of non-susceptible organisms, e.g. candida. This may present a vulvo-vaginitis.

There is a possibility of development of pseudomembranous colitis and it is therefore important to consider its diagnosis in patients who develop diarrhoea while taking cefalexin. It may range in severity from mild to life threatening with mild case usually responding to cessation of therapy. Appropriate measures should be taken with moderate to severe cases.

4.9 Overdose:
Symptoms of oral overdose may include nausea, vomiting, epigastric distress, diarrhoea and haematuria. General management consists of close clinical and laboratory monitoring of haematological, renal and hepatic functions and coagulation status until the patient is stable.

Serum levels of Cefalexin can be considerably reduced by haemodialysis or peritoneal dialysis.

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: : Antibacterials for Systemic Use, Other Beta-Lactam antibacterials, First-generation cephalosporins,
ATC code: J01DB01

Cefalexin is an oral broad-spectrum antibiotic belonging to the group known as cephalosporins. In adequate concentrations it is bactericidal for sensitive proliferating microorganisms by inhibiting the biosynthesis of the cell wall. It is active against the following pathogens:

Gram Positive
Staphylococci (coagulase positive as well as penicillinase-producing strains), Streptococci, pneumococci, Corynebacterium diphtheriae, Baccillus anthracis, Clostridia, Listeria monocytogenes, Bacillus subtilis and Bacteroides melaninogenicus

Gram Negative
Escherichia coli, Salmonellae, Shigellae, Neisseria, Proteus mirabilis, Haemophilus influenzae (some strains), Brucellae, Klebsiella species, Treponema pallidum and actinomycetes

5.2 Pharmacokinetic Properties:

Cefalexin is almost completely absorbed from the gastrointestinal tract and produces peak plasma concentrations about 1 hour after administration.
A dose of 500 mg produces a peak plasma concentration of about 18 μg per ml; doubling the dose doubles the peak concentration. Cefalexin readily diffuses into tissues, including bone, joints and the pericardial as well as pleural cavities. Only 10-15 % of the dose is bound to plasma proteins.
Elimination is mainly renal with 80% of the dose, recovered from the urine, therapeutically active, in the first 6 hours. Cefalexin does not enter cerebrospinal fluid in significant quantities. Cefalexin crosses the placenta and small quantities are found in the milk of nursing mothers. Therapeutically effective concentrations may be found in the bile and some may be excreted by this route.

The half-life has been reported to range from 0.5 to 2 hours and this increases with reduced renal function.

5.3 Preclinical Safety Data:

None stated.

6. Pharmaceutical Particulars

6.1 List of Excipients:

Sr. No.	Name of the Materials
1	Maize Sarch
2	Methylparaben sodium
3	Propylparaben sodium
4	Magnesium Stearate
5	Colloidal Anhydrous Silica

6.2 Incompatibilities:
Not applicable

6.3 Shelf life:
36 Months

6.4 Special precautions for storage:
Store in a cool, dark & dry place.

6.5 Nature and contents of container:
10 Capsules in Alu-PVC Blister pack. Such 1 blister of 10 Capsules are packed in a mono carton along with pack insert. Further 10 mono cartons are packed in a printed outer carton.

6.6 Instructions for use and handling
No special requirements.

7. Applicant/Manufacturer

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