Cephalexin Oral Formulations

QUALITATIVE AND QUANTITATIVE COMPOSITION

**PHEXIN (Cephalexin Capsules IP 250 mg):**

Each capsule contains:
Cephalexin IP equivalent to anhydrous Cephalexin 250 mg
Colours: Tartrazine, Brilliant Blue FCF and Titanium Dioxide IP in empty capsule shells.

**PHEXIN (Cephalexin Capsules IP 500 mg):**

Each capsule contains:
Cephalexin IP equivalent to anhydrous Cephalexin 500 mg
Colours: Erythrosine, Titanium Dioxide IP, Sunset Yellow FCF, Ponceau 4R and Brilliant Blue FCF in empty capsule shells.

**PHEXIN KID TABLETS DISPERSIBLE TABLETS (Cephalexin Tablets IP 125 mg):**

Each uncoated dispersible tablet contains:
Cephalexin IP equivalent to anhydrous Cephalexin 125 mg
Colour: Sunset Yellow FCF.

**PHEXIN DISPERSIBLE TABLETS (Cephalexin Tablets IP 250 mg):**

Each uncoated dispersible tablet contains:
Cephalexin IP equivalent to anhydrous Cephalexin 250 mg
Colour: Sunset Yellow FCF.

**PHEXIN SUSPENSION (For Paediatric Use) (Cephalexin Oral Suspension IP):**

Each 5 ml of the reconstituted suspension contains:
Cephalexin IP equivalent to anhydrous Cephalexin 250 mg
Color: Sunset Yellow FCF.

**PHEXIN REDISYP 125mg / 5ml (Cephalexin Suspension 125 mg / 5 ml):**

Each 5 ml contains:
Cephalexin IP equivalent to 125 mg of anhydrous Cephalexin in a flavoured base
Colour: Quinoline Yellow Lake.

**PHEXIN REDISYP 250mg / 5ml (Cephalexin Suspension 250 mg / 5 ml):**

Each 5 ml contains:
Cephalexin IP equivalent to 250 mg of anhydrous Cephalexin in a flavoured base
Color: Quinoline Yellow Lake.
**PHEXIN PEDIATRIC DROPS (Cephalexin Oral Suspension IP):**

Each 1 ml of the reconstituted suspension contains:
Cephalexin IP equivalent to anhydrous Cephalexin 100 mg
Colour: Sunset Yellow FCF.

**PHARMACEUTICAL FORM**

**PHEXIN (Cephalexin Capsules IP 250 mg) and** **PHEXIN (Cephalexin Capsules IP 500 mg):**

Hard Gelatin Capsules;

**PHEXIN KID TABLETS** (Cephalexin Tablets IP 125 mg; Dispersible Tablets) and **PHEXIN DISPERSIBLE TABLETS** (Cephalexin Tablets IP 250 mg):

Dispersible Tablets;

**PHEXIN SUSPENSION (For Paediatric Use) (Cephalexin Oral Suspension IP) and** **PHEXIN PEDIATRIC DROPS (Cephalexin Oral Suspension IP):**

Dry powder for reconstitution in water, at the time of dispensing, to form an oral suspension;

**PHEXIN REDISYP 125mg / 5ml (Cephalexin Suspension 125 mg / 5 ml) and** **PHEXIN REDISYP 250mg / 5ml (Cephalexin Suspension 250 mg / 5 ml):**

Oral Suspension.

**CLINICAL PARTICULARS**

**Therapeutic Indications**

Cephalexin is a bactericidal antibiotic which is active against a wide range of Gram-positive and Gram-negative organisms. It is indicated for treatment of the following conditions, when caused by susceptible bacteria.

It is indicated for treatment of respiratory tract infections (RTIs), urinary tract infections (UTIs), skin and soft tissue infections, otitis media and other infections due to sensitive organisms.

**Posology and Method of Administration**

Each capsule should be swallowed whole with water.

**Route of Administration**

For oral use.

**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
UTIs (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.

**Children**

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.

**Elderly**

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

**Renal impairment**

The dosage should be reduced if renal function is markedly impaired (see *Special Warnings and Special Precautions for Use*).

**Hepatic impairment**

There are no relevant data available.

**Contraindications**

*PHEXIN* is contraindicated 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.

**Special Warnings and Special Precautions for Use**

**Hypersensitivity reactions**

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 cephalosporins. Patients have had severe reactions (including anaphylaxis) to both drugs. If the patient experiences an allergic reaction cephalexin should be discontinued and treatment with the appropriate agents initiated.
**Acute generalized exanthematous pustulosis (AGEP)**

Acute generalized 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.

**Pseudomembranous colitis**

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.

**Superinfection**

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.

**Renal impairment**

Cephalexin 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.

**Direct Coombs test**

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.

**False-positive glycosuria reaction**

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.

**Azo dye**

Some PHEXIN formulations may contain azo dye [Sunset Yellow / Tartrazine / Ponceau 4R] (see List of Excipients), which may cause allergic-type reactions.

**Aspartame**

Some PHEXIN formulations may contain a source of phenylalanine (see List of Excipients). May be harmful for people with phenylketonuria.
Interaction with Other Medicaments and Other Forms of Interaction

Bacteriostatic antibiotics

As cephalosporins like cephalexin are only active against proliferating microorganisms, they should not be combined with bacteriostatic antibiotics.

Uricosuric drugs

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

Metformin

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

Increased risk of nephrotoxicity

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

Oral anticoagulants

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

Typhoid vaccine

Cephalexin, like other antibiotics with antibacterial activity against salmonella typhi organisms, may interfere with the immunological response to the live typhoid vaccine. The appropriate period of time should elapse between the administration of the last dose of the antibiotic and the live typhoid vaccine.

Oral contraceptives

Cephalexin may reduce the effects of oral contraceptives.

Cytotoxic drugs

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

Pregnancy and Lactation

Fertility

There are no relevant data available.

Pregnancy

It should be administered with caution during pregnancy.
There is no experimental or clinical evidence of teratogenic effects attributable to cephalexin.

**Lactation**

Cephalexin is excreted in human milk in low concentrations and should be used with caution in nursing mothers.

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.

**Effects on Ability to Drive and Use Machines**

There are no effects on ability to drive or to operate machinery.

**Undesirable Effects**

**Clinical Trial and Post Marketing Data**

Side effects of cephalexin 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, toxic epidermal necrolysis (exanthematic necrolysis) and acute generalized exanthematous pustulosis (AGEP) (with unknown frequency). These reactions usually subsided upon discontinuation of the drug, although in some cases supportive therapy may be necessary. Anaphylaxis has 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 cephalexin. 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.

**Overdose**

**Signs and Symptoms**

Symptoms of overdosage may include nausea, vomiting, epigastric distress, diarrhoea and haematuria.
**Treatment**

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 cephalexin can be reduced by haemodialysis or by 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 cephalexin in a day. Treatment has been supportive (fluids) and no sequelae have been reported.

Further management should be as clinically indicated or as recommended by the national poisons centre, where available.

**PHARMACOLOGICAL PROPERTIES**

Pharmacotherapeutic group: First-generation cephalosporins; ATC Code: J01DB01.

**Pharmacodynamic Properties**

**Mechanism of Action**

Cephalexin is an oral broad-spectrum antibiotic. In adequate concentrations it is bactericidal for sensitive proliferating microorganisms by inhibiting the biosynthesis of the cell wall.

**Pharmacodynamic effects**

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*.

**Pharmacokinetic Properties**

**Absorption**

Cephalexin 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.
Distribution

Cephalexin 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

Elimination is mainly renal with 80% of the dose, recovered from the urine, therapeutically active, in the first 6 hours.

Cephalexin does not enter cerebrospinal fluid in significant quantities. Cephalexin 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.

Clinical Studies

There are no relevant data available.

Preclinical Safety Data

Cephalexin is not anticipated to cause any genotoxic or carcinogenic effects, although no specific studies have been performed to determine this.

PHARMACEUTICAL PARTICULARS

List of Excipients

PHEXIN (Cephalexin Capsules IP 250 mg and 500 mg):

Cephalexin Capsules IP 250 mg: Magnesium Stearate, Colours (in empty capsule shells) - Tartrazine, Brilliant Blue FCF and Titanium Dioxide.

Cephalexin Capsules IP 500 mg: Magnesium Stearate, Colours (in empty capsule shells) - Erythorsine, Titanium Dioxide, Sunset Yellow FCF, Ponceau 4R and Brilliant Blue FCF.

PHEXIN KID TABLETS DISPERSIBLE TABLETS (Cephalexin Tablets IP 125 mg):

Magnesium Stearate, Colour Sunset Yellow FCF, Flavour Trusil Orange, Pregelatinised Starch, Microcrystalline Cellulose, Crospovidone, Monoammonium Glycyrrhizinate, Sodium Starch Glycollate, Purified Talc.

PHEXIN DISPERSIBLE TABLETS (Cephalexin Tablets IP 250 mg):

Magnesium Stearate, Colour Sunset Yellow FCF, Flavor Trusil Orange, Pregelatinised Starch Microcrystalline Cellulose, Crospovidone, Monoammonium Glyrrhizinate, Sodium Starch Glycollate, Purified Talc.
**PHEXIN SUSPENSION (For Paediatric Use) (Cephalexin Oral Suspension IP):**

Acacia powder, Citric Acid Anhydrous, Colour Sunset Yellow FCF, Edetate Calcium disodium, Flavour Trusil Orange, Sodium Citrate, Sucrose, Isopropyl alcohol.

**PHEXIN REDISYP 125 mg / 5 ml (Cephalexin Suspension 125 mg / 5 ml):**

Polysorbate 80, Xanthan Gum, Microcrystalline Cellulose, Aerosil 200, Aspartame, Disodium Edetate, Sucrose, Quinoline Yellow Lake, Flavour Pineapple, Vanillin, Butylated Hydroxytoluene, Corn Oil.

**PHEXIN REDISYP 250 mg / 5 ml (Cephalexin Suspension 250 mg / 5 ml):**

Polysorbate 80, Xanthan Gum, Microcrystalline Cellulose, Aerosil 200, Aspartame, Disodium Edetate, Sucrose, Quinoline Yellow Lake, Flavour Banana, Vanillin, Butylated Hydroxytoluene, Corn Oil.

**PHEXIN PEDIATRIC DROPS (Cephalexin Oral Suspension IP):**

Acacia powder, Citric Acid Anhydrous, Colour Sunset Yellow FCF, Edetate Calcium disodium, Flavour Trusil Orange, Sodium Citrate, Sucrose, Isopropyl alcohol.

**Incompatibilities**

There are no relevant data available.

**Shelf Life**

The expiry dates are indicated on the label and packaging.

**Special Precautions for Storage**

**PHEXIN (Cephalexin Capsules IP 250 mg and 500 mg):**

Store protected from moisture, at a temperature not exceeding 30°C.

**PHEXIN KID TABLETS DISPERSIBLE TABLETS (Cephalexin Tablets IP 125 mg):**

Store at a temperature not exceeding 30°C protected from light and moisture.

**PHEXIN DISPERSIBLE TABLETS (Cephalexin Tablets IP 250 mg):**

Store at a temperature not exceeding 30°C protected from light and moisture.

**PHEXIN SUSPENSION (For Paediatric Use) (Cephalexin Oral Suspension IP):**

Store at a temperature not exceeding 30°C protected from light and moisture.

**PHEXIN REDISYP 125 mg / 5 ml and 250 mg / 5 ml (Cephalexin Suspension 125 mg / 5 ml and 250 mg / 5 ml):**
Store protected from direct sunlight in well closed containers at temperatures not exceeding 30°C. Do Not Refrigerate.

**PHEXIN PEDIATRIC DROPS (Cephalexin Oral Suspension IP):**

Store at a temperature not exceeding 30°C protected from light and moisture.

Keep out of reach of children.

**Nature and Specification of Container**

**PHEXIN (Cephalexin Capsules IP 250 mg and 500 mg):**

PVC/Aluminium blister strips in a carton.

**PHEXIN KID TABLETS DISPERSIBLE TABLETS (Cephalexin Tablets IP 125 mg):**

Aluminium foil strips in a carton.

**PHEXIN DISPERSIBLE TABLETS (Cephalexin Tablets IP 250 mg):**

Aluminium foil strips in a carton.

**PHEXIN SUSPENSION (For Paediatric Use) (Cephalexin Oral Suspension IP):**

HDPE bottles with a measuring cup.

**PHEXIN REDISYP 125 mg / 5 ml and 250 mg / 5 ml (Cephalexin Suspension 125 mg / 5 ml and 250 mg / 5 ml):**

Amber PET bottles with a spoon in a carton.

**PHEXIN PEDIATRIC DROPS (Cephalexin Oral Suspension IP):**

HDPE bottle with a dropper in a carton.

All presentations may not be marketed in the Country.

**Instructions for Use / Handling**

**PHEXIN (Cephalexin Capsules IP 250 mg and 500 mg):**

There are no special requirements for use and handling of this product.

**PHEXIN KID TABLETS DISPERSIBLE TABLETS (Cephalexin Tablets IP 125 mg):**

Disperse one tablet in 5 ml (one teaspoonful) of previously boiled and cooled water immediately before use.
PHEXIN DISPERSIBLE TABLETS (Cephalexin Tablets IP 250 mg):

Disperse one tablet in 5 ml (one teaspoonful) of previously boiled and cooled water immediately before use.

PHEXIN SUSPENSION (For Paediatric Use) (Cephalexin Oral Suspension IP):

Using the measure cup provided, add boiled and cooled water up to the ring mark on the bottle and shake vigorously. Adjust the volume up to the mark by adding more water, if necessary, to make 30 ml i.e. six standard doses.

Prepared suspension to be used within 4 days at room temperature.

Shake well before use.

PHEXIN REDISYP 125 mg / 5 ml and 250 mg / 5 ml (Cephalexin Suspension 125 mg / 5 ml and 250 mg / 5 ml):

Shake vigorously before use.
Do not mix with water.

PHEXIN PEDIATRIC DROPS (Cephalexin Oral Suspension IP):

Add boiled and cooled water up to the mark on the label of the bottle and shake vigorously.

Adjust the volume up to the mark by adding more water if necessary. This makes 10 ml of the suspension.

The prepared suspension to be stored at room temperature & be used within 4 days.

Shake well before use.

For further information please contact:
GlaxoSmithKline Pharmaceuticals Limited.
Registered Office
Dr. Annie Besant Road, Worli
Mumbai 400 030, India.

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