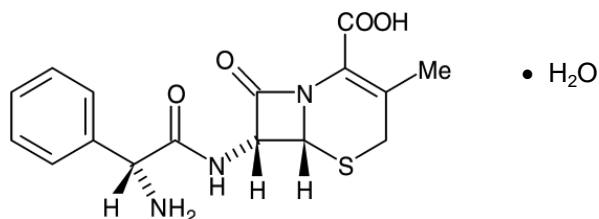


CHEMMART CEPHALEXIN CAPSULES**NAME OF THE MEDICINE**

Cephalexin monohydrate

Chemical Name: (6*R*,7*R*)-7-[[(*R*)-2-amino-2-phenylacetyl]amino]-3-methyl-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid monohydrate

Structural Formula:

Molecular Formula: C₁₆H₁₇N₃O₄S·H₂O

Molecular Weight: 365.41

CAS Registry Number: 23325-78-2

DESCRIPTION

A semi-synthetic cephalosporin antibiotic for oral administration. The nucleus of cephalexin is related to that of other cephalosporin antibiotics. The compound is a zwitterion; i.e. the molecule contains both a basic and an acidic group. The isoelectric point of cephalexin in water is approximately 4.5 to 5. The crystalline form of cephalexin, which is available, is a monohydrate. It is a white or almost white crystalline solid having a bitter taste. Solubility in water is about 1% at room temperature. It is practically insoluble in alcohol and in ether. The cephalosporins differ from penicillins in the structure of the bicyclic ring system. Cephalexin has a d-phenylglycyl group as substituent at the 7-amino position and an unsubstituted methyl group at the 3-position.

Each capsule contains cephalexin monohydrate equivalent to 250 mg or 500 mg cephalexin anhydrous as the active ingredient.

In addition, the capsules contain the following inactive ingredients: lactose, magnesium stearate, gelatin, iron oxide yellow, Brilliant blue FCF, Sunset yellow FCF, titanium dioxide, purified water, TekPrint SW-9008 black ink (Proprietary Ingredient No. 2328).

PHARMACOLOGY**Pharmacokinetics**

Cephalexin is acid stable and may be given without regard to meals. It is rapidly absorbed after oral administration. Following a dose of 500 mg, average peak serum levels of approximately 19 µg/mL were obtained at one hour. Measurable levels were present six hours after administration. Cephalexin is excreted in the urine by glomerular filtration and tubular secretion. Studies have shown that over 90% of the drug is excreted unchanged in the urine within 8 hours. During this period, reported peak urine concentrations following 250 mg, 500 mg and 1 g doses were approximately 1,000, 2,200 and 5,000 µg/mL respectively.

Microbiology

In vitro tests demonstrate that the cephalosporins are bactericidal because they inhibit cell wall synthesis. Cephalexin is active against the following organisms *in vitro*: β -haemolytic Streptococci, Staphylococci, including coagulase-positive, coagulase-negative, and penicillinase producing strains, *Streptococcus (Diplococcus) pneumoniae*, *Escherichia coli*, *Proteus mirabilis*, *Klebsiella* sp.

Note: Most strains of Enterococci (*Enterococcus faecalis*) and a few strains of Staphylococci are resistant to cephalexin. It is not active against most strains of Enterobacter sp., *Morganella morganii* (formerly *Pr. morganii*), and *Pr. vulgaris*.

It has no activity against *Pseudomonas* or *Acinetobacter calcoaceticus* (formerly *Mima* and *Herellea* sp.). When tested by *in vitro* methods, Staphylococci exhibit cross resistance between cephalexin and methicillin type antibiotics.

Disc Susceptibility Tests

Dilution or diffusion techniques – either quantitative (MIC) or breakpoint, should be used following a regularly updated, recognised and standardised method (e.g. NCCLS). Standardised susceptibility test procedures require the use of laboratory control microorganisms to control the technical aspects of the laboratory procedures.

A report of “Susceptible” indicates that the pathogen is likely to be inhibited if the antimicrobial compound in the blood reaches the concentrations usually achievable. A report of “Intermediate” indicates that the result should be considered equivocal, and if the microorganism is not fully susceptible to alternative, clinically feasible drugs, the test should be repeated. This category implies possible clinical applicability in body sites where the drug is physiologically concentrated or in situations where high dosage of drug can be used. This category also provides a buffer zone, which prevents small-uncontrolled technical factors from causing major discrepancies in interpretation. A report of “Resistant” indicates that the pathogen is not likely to be inhibited if the antimicrobial compound in the blood reaches the concentrations usually achievable; other therapy should be selected.

Note: The prevalence of resistance may vary geographically for selected species and local information on resistance is desirable, particularly when treating severe infections.

INDICATIONS

Cephalexin is indicated for the treatment of the following infections when caused by susceptible strains of the designated micro-organisms.

Respiratory Tract Infections

Caused by *S. pneumoniae* and group A β -haemolytic Streptococci (penicillin is the usual drug of choice in the treatment and prevention of streptococcal infections, including the prophylaxis of rheumatic fever. Cephalexin is generally effective in the eradication of Streptococci from the nasopharynx; however, substantial data establishing the efficacy of cephalexin in the subsequent prevention of rheumatic fever are not available at present).

Bacterial Sinusitis

Caused by Streptococci, *S. pneumoniae* and *S. aureus* (methicillin sensitive only).

Otitis Media

Due to *S. pneumoniae*, Staphylococci.

Skin and Skin Structure Infections

Caused by Staphylococci and/or Streptococci.

Genitourinary Tract Infections, Including Acute Prostatitis

Caused by *E. coli*, *P. mirabilis* and *Klebsiella* sp.

The effectiveness of cephalexin in the treatment of bacterial infections of the brain and spinal column has not been established and cephalexin is not indicated in these conditions.

Note: Appropriate culture and susceptibility tests should be initiated prior to and during therapy to determine susceptibility of the causative organism to cephalexin. Renal function studies should be performed when indicated.

CONTRAINDICATIONS

Cephalexin is contraindicated in patients with known allergy to the cephalosporin group of antibiotics or who have previously experienced a major allergy to penicillin (see **PRECAUTIONS**).

PRECAUTIONS

Before instituting therapy with cephalexin, every attempt should be made to determine if the patient has had previous hypersensitivity reactions to the cephalosporins, penicillins, or other drugs. This product should be given cautiously to penicillin sensitive patients.

There is some clinical and laboratory evidence of partial cross allergenicity of the penicillins and the cephalosporins. Patients have been reported to 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 usual agents (e.g. adrenaline or other pressor amines, antihistamines or corticosteroids).

Pseudomembranous colitis has been reported with virtually all broad spectrum antibiotics (including macrolides, semisynthetic penicillins and cephalosporins). A toxin produced with *Clostridium difficile* appears to be the primary cause. The severity of the colitis may range from mild to life-threatening. It is important to consider this diagnosis in patients who develop diarrhoea or colitis in association with antibiotic use (this may occur up to several weeks after cessation of antibiotic therapy). Mild cases usually respond to drug discontinuation alone. However, in moderate to severe cases appropriate therapy with a suitable oral antibacterial agent effective against *Cl. difficile* should be considered. Fluids, electrolytes and protein replacement therapy should be provided when indicated. Drugs that delay peristalsis, e.g. opiates and diphenoxylate with atropine (e.g. Lomotil), may prolong and/or worsen the condition and should not be used.

Broad spectrum antibiotics should therefore be prescribed with caution in individuals with a history of gastrointestinal disease, particularly colitis.

Patients should be followed carefully so that any side effects or unusual manifestations of drug idiosyncrasy may be detected.

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.

Impaired Renal Function

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.

Indicated surgical procedures should be performed in conjunction with antibiotic therapy.

Use in Pregnancy (Category A)

Laboratory experiments with animals and clinical experience show no evidence of teratogenicity with cephalexin, but as with all drugs, cephalexin should be administered with caution during all stages of pregnancy.

Category A: Drugs which have been taken by a large number of pregnant women and women of childbearing age without any proven increase in the frequency of malformations or other direct or indirect

harmful effects on the foetus having been observed.

Use in Lactation

Cephalexin is excreted in the milk. Caution should be exercised when cephalexin is administered to a breastfeeding woman. Alternative feeding arrangements for the infant should be considered.

Interactions with Other Medicines

Probenecid

Probenecid decreases the renal tubular secretion of cephalexin resulting in increased and prolonged serum concentrations and increased elimination half life and consequently an increased risk of toxicity.

As with other β -lactams, the renal excretion of cephalexin is inhibited by probenecid.

Metformin

In healthy subjects given single 500 mg doses of cephalexin and metformin, plasma metformin C_{max} and AUC increased by an average of 34% and 24%, respectively, and metformin renal clearance decreased by an average of 14%. The interaction of cephalexin and metformin following multiple dose administration has not been studied. Administration of a cephalosporin to a metformin-treated patient may result in increased metformin exposure.

Laboratory Tests

The quantitative determination of urinary protein excretion using strong acids is misleading during cephalexin therapy as precipitation of cephalexin in the urine may occur.

A false-positive reaction for glucose in the urine may occur with Benedict's or Fehling's solution or with Clinitest[®].

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 newborn infants whose mothers have received cephalosporin antibiotics before parturition, it should be recognised that a positive Coombs' test may be due to the drug.

ADVERSE EFFECTS

Adverse drug reactions reported with cephalexin are very rare (<0.01%) and are listed below:

Blood and Lymphatic System Disorders

Eosinophilia, neutropenia, thrombocytopenia and haemolytic anaemia.

Gastrointestinal Disorders

Nausea, vomiting, diarrhoea, dyspepsia, abdominal pain.

General Disorders and Administration Site Conditions

Fatigue.

Hepatobiliary Disorders

Cholestatic jaundice, transient hepatitis, elevated SGOT, elevated SGPT.

Immune System Disorders

Allergic reactions, urticaria, angioedema. These reactions usually subsided upon discontinuation of the drug. Anaphylaxis has also been reported.

Infections and Infestations

Pseudomembranous colitis.

Musculoskeletal and Connective Tissue Disorders

Arthralgia, arthritis and joint disorders.

Nervous System Disorders

Dizziness, headache.

Psychiatric Disorders

Hallucinations, agitation, confusion.

Renal and Urinary Disorders

Reversible interstitial nephritis.

Reproductive and Breast Disorders

Genital and anal pruritus, genital moniliasis, vaginitis and vaginal discharge.

Skin and Subcutaneous Tissue Disorders

Rash, erythema multiforme, Stevens Johnson syndrome, toxic epidermal necrolysis. These reactions usually subsided upon discontinuation of the drug.

DOSAGE AND ADMINISTRATION

Administered orally.

Adults

The adult dosage ranges from 1 to 4 g daily in divided doses. The usual adult dose is 250 mg every six hours.

For streptococcal pharyngitis or tonsillitis, mild, uncomplicated urinary tract infections, and skin and skin structure infections, a dosage of 500 mg may be administered every twelve hours.

For more severe infections or those caused by less susceptible organisms, larger doses may be needed. If daily doses of cephalexin greater than 4 g are required, parenteral cephalosporins, in appropriate doses, should be considered.

Twice daily dosing is not recommended when doses larger than 1 g daily are administered.

Children

The usual recommended daily dosage for children is 25 to 50 mg/kg in divided doses. For streptococcal pharyngitis in patients over 1 year of age, tonsillitis, mild, uncomplicated urinary tract infection, and skin and skin structure infections, the total daily dose may be divided and administered every twelve hours.

Part A: Four times daily dosage

Child's Weight	Suspension 125 mg / 5 mL	Suspension 250 mg / 5 mL
10 kg	2.5 to 5 mL 4 times daily	–
20 kg	5 to 10 mL 4 times daily	2.5 to 5 mL 4 times daily
40 kg	10 to 20 mL 4 times daily	5 to 10 mL 4 times daily

Part B: Twice daily dosage

Child's Weight	Suspension 125 mg / 5 mL	Suspension 250 mg / 5 mL
10 kg	5 to 10 mL twice daily	2.5 to 5 mL twice daily
20 kg	10 to 20 mL twice daily	5 to 10 mL twice daily
40 kg	20 to 40 mL twice daily	10 to 20 mL twice daily

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 four divided doses is recommended.

In the treatment of β -haemolytic streptococcal infections, a therapeutic dosage of cephalexin should be administered for at least 10 days.

Impaired Renal Function: see **PRECAUTIONS**

OVERDOSAGE**Symptoms**

There is no definite experience of poisoning or severe overdosage with cephalexin. However, clinical features of overdosage may be similar to those seen with other cephalosporins and penicillins, i.e. convulsions, hallucinations, hyperreflexia, electrolyte imbalance, gastrointestinal disturbances and haematuria.

Treatment

In the event of severe overdosage, general supportive care is recommended including close clinical and laboratory monitoring of haematological, renal, 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.

Contact the Poison Information Centre on 13 11 26 (Australia) for advice on the management of overdosage.

PRESENTATION AND STORAGE CONDITIONS**Chemmart Cephalexin 250 mg Capsules**

Dark green and white, self-locked hard gelatin capsules of size 2, imprinted with RX656 in black ink, containing white to off-white granular powder/pellets.

Blister packs of 20.

AUST R number 73868

Store below 25°C. Protect from moisture.

Chemmart Cephalexin 500 mg Capsules

Dark green and light green, self-locked hard gelatin capsules of size 0, imprinted with RX657 in black ink, containing white to off-white granular powder/pellets.

Blister packs of 20.

AUST R number 133853.

Store below 25°C. Protect from light and moisture.

Chemmart Cephalexin Capsules are intended for oral administration. Each capsule contains 250 mg or 500 mg cephalexin.

NAME AND ADDRESS OF THE SPONSOR

Apotex Pty Ltd
16 Giffnock Avenue
Macquarie Park NSW 2113

POISONS SCHEDULE OF THE MEDICINE

S4: Prescription Only Medicine.

Date of TGA approval:

250 mg Capsules: 26 May 2000
500 mg Capsules: 8 February 2007

Date of most recent amendment: 24 September 2015