PRODUCT INFORMATION

CEFALEXIN SANDOZ
250 mg & 500 mg capsules
125 mg/5 mL & 250 mg/5 mL powder for suspension

NAME OF THE MEDICINE
Active Cephalexin monohydrate

Chemical structure of cephalexin monohydrate

Chemical name (6R,7R)-7-[(R)-2-amino-2-phenylacetamido]-3-methyl-8-oxo-5-thia-
1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid monohydrate
Molecular formula C_{16}H_{17}N_{3}O_{4}S·H_{2}O
Molecular Weight 365.41
CAS 23325-78-2

DESCRIPTION
Inactive
Capsule 250 mg: Microcrystalline cellulose and magnesium stearate. The capsule shell and
body also contains gelatin, sodium lauryl sulphate, titanium dioxide, sunset yellow FCF, patent blue V, quinoline yellow, TekPrint SW-9008
black ink and water.

Capsule 500 mg: Magnesium stearate and cellulose-microcrystalline. The capsule shell also
contains gelatin and titanium dioxide.

Suspension: Saccharin sodium, iron oxide yellow CI77492, simethicone, citric acid-
anhydrous, strawberry, apple, raspberry and tutti frutti artificial
flavouring, guar gum, sodium benzoate, and sucrose.

A semisynthetic 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.
PHARMACOLOGY

Pharmacodynamics

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 (eg 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 with severe infections.

Pharmacokinetics

Cephalexin 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 1 g, average peak serum levels of approximately 9, 18 and 32 μg/mL respectively 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 showed that over 90% of the drug is 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 μg/mL, respectively.

CLINICAL TRIALS

Not applicable
INDICATIONS

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

Known allergy to the cephalosporin group of antibiotics or previous experience of a major allergy to penicillin (see PRECAUTIONS).

Cefalexin Sandoz is not indicated in the management of bacterial infections of the brain or spinal column.

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); therefore, it is important to consider its diagnosis in patients who develop diarrhoea in association with the use of antibiotics. Mild cases of pseudomembranous colitis usually respond to drug discontinuation alone. In moderate to severe cases, appropriate measures should be taken. Antibiotic associated pseudomembranous colitis has been reported with many antibiotics including cephalexin. 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 patient 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 be prescribed with caution in individuals with a history of gastrointestinal disease, particularly colitis. As with other broad-spectrum antibiotics, colitis, including rare instances of pseudomembranous colitis, has been reported in conjunction with therapy with cephalexin.

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 nonsusceptible organisms. Careful observation of the patient is essential. If superinfection occurs during therapy, appropriate measures should be taken.

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

**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.

**Use in pregnancy**
Australian 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 fetus having been observed.
Laboratory experiments with animals and clinical experience shown no evidence of teratogenicity with cephalexin, but as with all drugs, Cefalexin Sandoz should be administered with caution during all stages of pregnancy.

**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.

**Effects on 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 solutions or with Clinitest tablets, but not with Tes-Tape.

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.

**INTERACTIONS WITH OTHER MEDICINES**
As with other β-lactams, the renal excretion of cephalexin is inhibited by probenecid.

In healthy subjects given single 500mg doses of cephalexin and metformin, plasma metformin $C_{\text{max}}$ and AUC increased by an average 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. A potential interaction between cephalexin and metformin may result in accumulation of metformin.

**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, haemolytic anaemia

*Gastrointestinal disorders.* The most frequent side effect has been diarrhoea, which may rarely be severe enough to warrant cessation of therapy with cephalexin. Nausea and vomiting have been reported rarely. Dyspepsia and abdominal pain have also occurred.

*General disorders and administration site conditions*
- Fatigue

*Hepatobiliary disorders*
- Cholestatic jaundice, transient hepatitis, slight elevations in AST and ALT have been reported.

*Immune system disorders.* Allergic reactions in the form of urticaria, and angioedema have been observed. Anaphylaxis has also been reported.
Infections and infestations
Symptoms of pseudomembranous colitis may appear either during or after antibiotic treatment.

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 has been reported rarely.

Reproductive and breast disorders
Genital and anal pruritus, genital monillasis, 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 one 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. See table below.

### Part A: Four times daily dosage

<table>
<thead>
<tr>
<th>Child’s weight</th>
<th>Suspension 125 mg/5 mL</th>
<th>Suspension 250 mg/5 mL</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 kg</td>
<td>2.5 - 5 mL 4 times daily</td>
<td>-</td>
</tr>
<tr>
<td>20 kg</td>
<td>5 - 10 mL 4 times daily</td>
<td>2.5 - 5 mL 4 times daily</td>
</tr>
<tr>
<td>40 kg</td>
<td>10 - 20 mL 4 times daily</td>
<td>5 - 10 mL 4 times daily</td>
</tr>
</tbody>
</table>

### Part B: Twice daily dosage

<table>
<thead>
<tr>
<th>Child’s weight</th>
<th>Suspension 125 mg/5 mL</th>
<th>Suspession 250 mg/5 mL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight</td>
<td>Dosage</td>
<td>Dosage</td>
</tr>
<tr>
<td>--------</td>
<td>-------------------</td>
<td>-------------------</td>
</tr>
<tr>
<td>10 kg</td>
<td>5 - 10 mL twice daily</td>
<td>2.5 - 5 mL twice daily</td>
</tr>
<tr>
<td>20 kg</td>
<td>10 - 20 mL twice daily</td>
<td>5 - 10 mL twice daily</td>
</tr>
<tr>
<td>40 kg</td>
<td>20 - 40 mL twice daily</td>
<td>10 - 20 mL twice daily</td>
</tr>
</tbody>
</table>

*Note: 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**

Contact the Poisons Information Centre on 13 11 26 for advice on management of overdose.

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. 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.

**PRESENTATION AND STORAGE CONDITIONS**

*Capsules*
Cefalexin Sandoz capsules contains cephalexin (as monohydrate) equivalent to 250 mg or 500 mg of cephalexin anhydrous. Each pack contains 20 capsules.

250 mg - Size '2' capsules with dark green cap imprinted with "250" in black ink and white body

500 mg - The capsules are white opaque in colour, containing a white to yellowish powder.

*Powder for Oral Suspension*
Cefalexin Sandoz Powder for Oral Suspension contains cephalexin (as monohydrate) equivalent to 125 mg/5 mL or 250 mg/5 mL of cephalexin anhydrous. The suspension is orange-yellow in colour with a fruity flavour. It is available in 60 mL, 75 mL or 100 mL pack sizes.

*Not all presentations may be marketed in Australia*

*Storage*
- Capsule 250 mg: Store below 30°C
- Capsule 500 mg: Store below 25°C
**Powder for Oral Suspension**

**Before mixing**  
Store below 25°C. Protect from light and moisture.

**After mixing**  
Store at 2 to 8°C. (Refrigerate. Do not freeze) and discard unused portion 14 days after reconstitution.

**NAME AND ADDRESS OF THE SPONSOR**

Sandoz Pty Ltd  
ABN 60 075 449 553  
54 Waterloo Road  
Macquarie Park, NSW 2113  
Australia  
Tel: 1800 634 500

**POISON SCHEDULE OF THE MEDICINE**

Schedule 4 – Prescription Only Medicine

**Date of first inclusion in the Australian Register of Therapeutic Goods (the ARTG):**  
05/03/2008

**Date of most recent amendment:** 23/02/2016