1 PRODUCT NAME

Cefalexin Sandoz

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Cefalexin Sandoz capsules contain 250 mg or 500 mg cefalexin

Cefalexin Sandoz granules for oral suspension contain 125 mg or 250 mg cefalexin per 5mL when reconstituted

Excipient(s) with known effect: n/a

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Cefalexin Sandoz capsules, hard

250 mg: Capsule, powder filled, Size 2, orange opaque cap and grey opaque body, approximately 17.5 mm length and 6.3 mm diameter.

500 mg: Capsule, powder filled, Size 0, orange opaque cap and grey opaque body, approximately 21.2 mm length and 7.6 mm diameter.

Cefalexin Sandoz granules for oral suspension

125 mg/5 mL: Orange to yellow granules

250 mg/5 mL: Orange to yellow granules

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Cefalexin is indicated for the treatment of the following infections when caused by susceptible strains of the designated microorganisms:

- bacterial sinusitis caused by streptococci, S. pneumoniae, and Staphylococcus aureus (methicillin-sensitive only);
- respiratory tract infections caused by S. pneumoniae and S. pyogenes (penicillin is the usual medicine of choice in the treatment and prevention of streptococcal infections, including the prophylaxis of rheumatic fever - cefalexin is generally effective in the eradication of streptococci from the nasopharynx; however, substantial data establishing the efficacy of cefalexin in the subsequent prevention of either rheumatic fever or bacterial endocarditis are not available at present);
- otitis media due to S. pneumoniae, H. influenzae, staphylococci, streptococci, and M. catarrhalis;
- skin and skin-structure infections caused by staphylococci and/or streptococci;
- bone infections caused by staphylococci and/or P. mirabilis;
- genitourinary tract infections, including acute prostatitis, caused by E. coli, P. mirabilis, and Klebsiella pneumoniae;
- dental infections caused by staphylococci and/or streptococci.

Note - Culture and susceptibility tests should be initiated prior to and during therapy. Renal function studies should be performed when indicated.

4.2 Dose and method of administration

Dosage

Cefalexin Sandoz is administered orally.

Adults

The adult dosage ranges from 1 to 4 g daily in divided doses. The usual adult dose is 250 mg every 6 hours. For the following infections, a dosage of 500 mg may be administered every 12 hours: streptococcal pharyngitis, skin and skin-structure infections, and uncomplicated cystitis in patients over 15 years of age. Cystitis therapy should be continued for 7 to 14 days. For more severe infections or those caused by less susceptible organisms, larger doses may be needed. If daily doses of cefalexin greater than 4 g are required, parenteral cephalosporins, in appropriate doses, should be considered.

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, mild, uncomplicated urinary tract infections, and for skin and skin-structure infections, the total daily dose may be divided and administered every 12 hours.

Cefalexin Sandoz granules for oral suspension 125 mg/5 mL

For a child weighing about 10 kg, give prepared suspension 2.5 to 5 mL four times a day or 5 to 10 mL twice a day.

For a child weighing about 20 kg, give prepared suspension 5 to 10 mL four times a day or 10 to 20 mL twice a day.

For a child weighing about 40 kg, give prepared suspension 10 to 20 mL four times a day or 20 to 40 mL twice a day.

Cefalexin Sandoz granules for oral suspension 250 mg/5 mL

For a child weighing about 10 kg, give prepared suspension 1.25 to 2.5 mL four times a day or 2.5 to 5 mL twice a day.

For a child weighing about 20 kg, give prepared suspension 2.5 to 5 mL four times a day or 5 to 10 mL twice a day.

For a child weighing about 40 kg, give prepared suspension 5 to 10 mL four times a day or 10 to 20 mL twice a day.

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 dosage of cefalexin should be administered for at least 10 days.

Administration

Cefalexin Sandoz capsules should be taken with a glass of water. Cefalexin Sandoz granules for oral suspension were developed specially for paediatric use. For instructions on reconstitution of Cefalexin Sandoz granules for oral suspension, see section 6.6.

4.3 Contraindications

Cefalexin is contraindicated in patients who have had previous experience of a major allergy or anaphylaxis to a cephalosporin or penicillin.

Cefalexin is contraindicated in patients who have experienced hypersensitivity to any of the excipients listed in 6.1.

Limitations

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

4.4 Special warnings and precautions for use

Warnings

Cefalexin should not ordinarily be given to those allergic to cephalosporins or to penicillins, especially where an allergic or urticarial reaction has occurred. Before cefalexin therapy is instituted, careful inquiry should be made concerning previous hypersensitivity reactions to cephalosporins, penicillins or other drugs. Cephalosporin C derivatives should be given cautiously to penicillin-sensitive patients. Serious acute hypersensitivity reactions may require adrenaline or epinephrine and other emergency measures. 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 medicines. Any patient who has demonstrated some form of allergy, particularly to medicines, should receive antibiotics cautiously. No exception should be made with regard to cefalexin.

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 discontinuance alone. In moderate to severe cases, appropriate measures should be taken.

Antibiotic associated pseudomembranous colitis has been reported with many antibiotics including cefalexin. 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, may prolong and/or worsen the condition and should not be used.

Precautions

Cefalexin should be given with caution to patients who have experienced symptoms of allergy associated with a cephalosporin or penicillin.

Pseudomembranous colitis and delaying peristalsis – Pseudomembranous colitis has been reported with virtually all broad-spectrum antibiotics. It is important to consider this diagnosis in patients who develop diarrhoea in association with the use of cefalexin. Drugs which delay peristalsis may prolong and/or worsen the condition and should not be used.

Prothrombin time - Prolonged prothrombin time may occur in patients receiving protracted antimicrobial therapy.

Patients should be followed carefully so that any side effects or unusual manifestations of medicine idiosyncrasy may be detected. If an allergic reaction to cefalexin occurs, the medicine should be discontinued and the patient treated with the usual agents (e.g. adrenaline or epinephrine or other pressor amines, antihistamines, or corticosteroids).

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.

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

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

Impaired renal function

Cefalexin should be administered with caution in the presence of markedly impaired renal function. Under such conditions, careful clinical observation and laboratory studies should be made because safe dosage may be lower than that usually recommended.

Neurotoxicity

There have been reports of neurotoxicity associated with cephalosporin treatment. Symptoms include encephalopathy, seizures and/or myoclonus. Risk factors for developing neurotoxicity with cephalosporin treatment include being elderly, renal impairment, central nervous system disorders and intravenous administration. Withdrawal of the medicine should be considered if there are signs of neurotoxicity. Anticonvulsant therapy can be given if clinically indicated.

Severe cutaneous adverse reactions

Severe cutaneous adverse reactions (SCAR), such as Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), drug reaction with eosinophilia and systemic symptoms (DRESS), and acute generalised exanthematous pustulosis (AGEP) have been reported in patients taking beta-lactam antibiotics. When SCAR is suspected, cefalexin should be discontinued immediately and an alternative treatment should be considered.

4.5 Interaction with other medicines and other forms of interaction

Other medicines

As with other beta-lactams, the renal excretion of cefalexin is inhibited by probenecid. As a result, cefalexin plasma levels are increased and sustained for longer periods.

A potential interaction between cefalexin and metformin may result in accumulation of metformin. In healthy subjects given single 500 mg doses of cefalexin 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 cefalexin 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 cefalexin and metformin may result in accumulation of metformin.

As cephalosporins like cefalexin are only active against proliferating micro-organisms, they should not be combined with bacteriostatic antibiotics.

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

The combined use of cephalosporins and oral anticoagulants may prolong the prothrombin time.

Cephalosporins may reduce the effects of oral contraceptives.

Laboratory diagnostic tests

Positive direct Coombs' tests have been reported during treatment with the cephalosporin antibiotics. In haematologic 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 medicine.

Cefalexin may cause a false-positive glucose reaction in urine with Benedict's and Fehlings's solutions and also with tabletted reagents containing buffered copper (II) sulphate.

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

4.6 Fertility, pregnancy and lactation

Use in pregnancy

Assigned Category A by the Australian Drug Evaluation Committee. This category includes medicines 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.

The daily oral administration of cefalexin to rats in doses of 250 or 500 mg/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. Note that the safety of cefalexin during pregnancy in humans has not been established. Cefalexin showed no enhanced toxicity in weanling and newborn rats as compared with adult animals. Nevertheless, because the studies in humans cannot rule out the possibility of harm, cefalexin should be used during pregnancy only if clearly needed.

Use in lactation

The excretion of cefalexin in breast milk increased up to 4 hours after a 500 mg dose; the medicine reached a maximum level of 4 mg/l, 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 machines

During treatment with Cefalexin Sandoz, undesirable effects may occur (e.g. dizziness), which may influence the ability to drive and use machines. Patients should be cautious when driving or operating machinery.

4.8 Undesirable effects

Gastrointestinal

Symptoms of pseudomembranous colitis may appear either during or after antibiotic treatment. The most frequent side effect has been diarrhoea. However, it was very rarely severe enough to warrant cessation of therapy. Nausea and vomiting have been reported rarely. Dyspepsia and abdominal pain have also occurred. As with some penicillins and some other cephalosporins, transient hepatitis and cholestatic jaundice have been reported rarely.

Hypersensitivity

Allergic reactions in the form of rash, urticaria, angioedema, and, rarely, erythema multiforme, Stevens-Johnson Syndrome, or toxic epidermal necrolysis have been observed.

These reactions usually subsided upon discontinuation of the medicine. In some of the reactions, supportive therapy may be necessary. Anaphylaxis has also been reported.

Other

Other reactions have included genital and anal pruritis, genital moniliasis, vaginitis and vaginal discharge, dizziness, fatigue, headache, seizure, agitation, confusion, hallucinations, arthralgia, arthritis, cutaneous vasculitis, and joint disorders. Reversible interstitial nephritis has been reported rarely. Eosinophilia, neutropenia, thrombocytopenia, haemolytic anaemia and slight elevations in AST and ALT have been reported.

Encephalopathy, myoclonus (frequency not known)

Severe cutaneous adverse reactions, including Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), drug reaction with eosinophilia and systemic symptoms (DRESS), and acute generalised exanthematous pustulosis (AGEP) have been reported in beta-lactam antibiotics.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions https://pophealth.my.site.com/carmreportnz/s/

4.9 Overdose

Signs and symptoms

There is no definite experience of poisoning or severe overdosage with cefalexin. However, clinical features of overdosage may be similar to those seen with other cephalosporins and penicillins, i.e. convulsions, hallucinations, hyperreflexia, electrolyte imbalance, nausea, vomiting, epigastric distress, diarrhoea, and haematuria. If other symptoms are present, it is probably secondary to an underlying disease state, an allergic reaction, or toxicity due to ingestion of a second medication. The oral median lethal dose of cefalexin in rats is 5,000 mg/kg.

Management

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 cefalexin; however, it would be extremely unlikely that one of these procedures would be indicated.

For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764 766)

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group

J01DB01 – First generation cephalosporins.

Antibiotic class

Cefalexin is a semi-synthetic cephalosporin antibiotic intended for oral administration.

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.

Antibiotic nature and mode of action

In vitro tests demonstrate that the cephalosporins are bactericidal because of their inhibition of cell-wall synthesis. Cefalexin has been shown to be active against most strains of the following microorganisms both in vitro and in clinical infections as described in Indications.

Aerobes, Gram-positive: Staphylococcus aureus (including penicillinase-producing strains); Staphylococcus epidermidis (penicillin-susceptible strains); Streptococcus pneumoniae; Streptococcus pyogenes. Aerobes, Gram-negative: Escherichia coli; Haemophilus influenzae; Klebsiella pneumoniae; Moraxella catarrhalis; Proteus mirabilis.

Susceptibility data and clinically relevant MIC ranges

Susceptibility Tests - Diffusion techniques

Quantitative methods that require measurement of zone diameters provide reproducible estimates of susceptibility of bacteria to antimicrobial compounds. One such standardised procedure authorised by the National Committee for Clinical Laboratory Standards in Performance Standards for Antimicrobial Disc Susceptibility Tests--5th ed. as Approved Standard NCCLS Document M2-A5, Vol 13, No 24, NCCLS, Villanova, PA, 1993 has been recommended for use with discs to test the susceptibility of microorganisms to cefalexin and uses the 30 mcg cephalothin disc. Interpretation involves correlation of the diameter obtained in the disc test with the minimum inhibitory concentration (MIC) for cefalexin.

Reports from the laboratory providing results of the standard single-disc susceptibility test with a 30 mcg cephalothin disc should be interpreted according to the following criteria: a zone diameter NLT 18 mm is considered susceptible; a zone diameter between 15 and 17 mm is considered intermediate; a zone diameter NMT 14 mm is considered resistant.

A report of "Susceptible" indicates that the pathogen is likely to be inhibited by usually achievable concentrations of the antimicrobial compound in blood. A report of "Intermediate" indicates that the result should be considered equivocal, and, if the microorganism is not fully susceptible to alternative, clinically feasible medicine, 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 medicine can be used. This category also provides a buffer zone that prevents small uncontrolled technical factors from causing major discrepancies in interpretation. A report of "Resistant" indicates that usually achievable concentrations of the antimicrobial compound in the blood are unlikely to be inhibitory and that other therapy should be selected. Measurement of MIC or MBC and achieved antimicrobial compound concentrations may be appropriate to guide therapy in some infections (refer to Pharmacokinetics for information on drug concentrations achieved in infected body sites and other pharmacokinetic properties of this antimicrobial medicine.)

Standardised susceptibility test procedures require the use of laboratory control microorganisms. The 30 mcg cephalothin disc should provide the following zone diameters in these laboratory test quality control strains: for E. coli ATCC 25922, 15 to 21 mm; for S. aureus ATCC 25923, 29 to 37 mm.

Dilution techniques

Quantitative methods that are used to determine MICs provide reproducible estimates of the susceptibility of bacteria to antimicrobial compounds. One such standardised procedure authorised by National Committee for Clinical Laboratory Standards in Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically--3rd ed. as Approved Standard NCCLS Document M7-A3, Vol 13, No 25, NCCLS, Villanova, PA, 1993 uses a standardised dilution method (broth, agar, microdilution) or equivalent with cephalothin powder. The MIC values obtained should be interpreted according to the following criteria: a MIC NMT 8 mcg/mL is considered susceptible; a MIC of 16 mcg/mL is considered intermediate; a MIC NLT 32 mcg/mL is considered resistant. Interpretation should be as stated above for results using diffusion techniques.

As with standard diffusion techniques, dilution methods require the use of laboratory control microorganisms. Standard cephalothin powder should provide the following MIC values: for E. coli ATCC 25922, 4 to 16 mcg/mL; for E. faecalis ATCC 29212, 8 to 32 mcg/mL; for S. aureus ATCC 29213, 0.12 to 0.5 mcg/mL.

Resistance

Methicillin-resistant staphylococci and most strains of enterococci (Enterococcus faecalis) are resistant to cephalosporins including cefalexin. Penicillin-resistant Streptococcus pneumoniae is usually cross-resistant to beta-lactam antibiotics. It is not active against most strains of Enterobacter spp., Morganella morganii and Proteus vulgaris. It has no activity against Pseudomonas spp. or Acinetobacter calcoaceticus. When tested by in vitro methods, Staphylococci exhibit cross-resistance between cefalexin and methicillin type antibiotics.

5.2 Pharmacokinetic properties

Pharmacokinetics

Absorption

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 1 g, average peak serum levels of approximately 9, 18 and 32 mg/L respectively were obtained at one hour. Measurable levels were present six hours after administration.

Distribution

Cefalexin readily diffuses into tissues, including bone, joints and the pericardial as well as pleural cavities. Only 10 to 15% of a dose is bound to plasma protein.

Biotransformation

Cefalexin is excreted in the urine by glomerular filtration and tubular secretion. Almost the entire dose recovered from the urine is therapeutically active.

Elimination

Elimination is mainly renal. The half-life is approximately 50 min and this increases with reduced renal function. Studies showed that over 90% of the medicine 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.

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

5.3 Preclinical safety data

The daily oral administration of cefalexin to rats in doses of 250 or 500 mg/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 LD_{50} of cefalexin in rats is 5,000 mg/kg.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Cefalexin Sandoz capsules

Gelatin, microcrystalline cellulose, magnesium stearate, titanium dioxide pigment.

Cefalexin Sandoz granules for oral suspension

Sucrose, guar gum, tutti frutti flavour, sodium benzoate, apple flavour, raspberry flavour, strawberry flavour, citric acid, simethicone, iron oxide pigment, saccharin sodium.

6.2 Incompatibilities

None known.

6.3 Shelf life

Unopened container:

Cefalexin Sandoz capsules: 48 months.

Cefalexin Sandoz granules for oral suspension: 36 months.

After container first opened: Not applicable.

After dilution or reconstitution:

Cefalexin Sandoz capsules: not applicable.

Cefalexin Sandoz granules for oral suspension: 14 days when stored between 2 to 8°C (*refrigerate, do not freeze*).

6.4 Special precautions for storage

Cefalexin Sandoz capsules

Store below 30°C. Protect from light and moisture.

Cefalexin Sandoz granules for oral suspension

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

6.5 Nature and contents of container

Cefalexin Sandoz capsules

Packs of 20 or 100 capsules in blister strips.

Cefalexin Sandoz granules for oral suspension

Bottles of 100 mL.

6.6 Special precautions for disposal

No special requirements for disposal

Instructions for use/handling

Reconstitution of Cefalexin Sandoz granules for oral suspension 125 mg/5 mL

Add 64 mL of water to make up 100 mL. Close and shake well at once. Store the prepared suspension under refrigeration (2 to 8°C), and use within 14 days of preparation. Shake well before use.

Reconstitution of Cefalexin Sandoz granules for oral suspension 250 mg/5 mL

Add 63 mL of water to make up 100 mL. Close and shake well at once. Store the prepared suspension under refrigeration (2 to 8°C), and use within 14 days of preparation. Shake well before use

7 MEDICINE SCHEDULE

Prescription Medicine.

8 SPONSOR

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New Zealand
Telephone: 0800 726 369

9 DATE OF FIRST APPROVAL

Cefalexin Sandoz capsules: 21/02/2002

Cefalexin Sandoz granules for oral suspension: 04/10/2001

10 DATE OF REVISION OF THE TEXT

20/03/2024

SUMMARY TABLE OF CHANGES

Section changed	Summary of new information
4.2, 4.4, 4.5	Minor editorial changes.
4.4	Added Neurotoxicity, Severe cutaneous adverse reactions.
4.8	Added seizure, encephalopathy, myoclonus, severe cutaneous adverse reactions. Added suspected adverse reaction reporting information.