

New Zealand Data Sheet

1 CEPHALEXIN ABM

CEPHALEXIN ABM 250 mg and 500 mg capsules

This product may not be interchangeable with other products containing this ingredient in the New Zealand market.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains cephalexin monohydrate equivalent to 250 mg cephalexin or 500 mg cephalexin.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Cephalexin ABM 250 mg Capsules are Size ‘2’ capsules with a dark green cap imprinted with “250” in black ink and a white body.

Cephalexin ABM 500 mg Capsules are Size ‘0’ capsules with a dark green cap imprinted with “500” in black ink and a light green body.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Cephalexin capsules are 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. 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 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**

Dose

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 cephalexin 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.

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

Method of administration

Cephalexin capsules are administered orally.

4.3 **Contraindications**

Cephalexin ABM Capsules are contraindicated in patients who have had previous experience of a major allergy to a cephalosporin or penicillin, or those who have experienced hypersensitivity to any of the excipients.

4.4 **Special warnings and precautions for use**

Warnings

Before cephalexin therapy is instituted, careful inquiry should be made concerning previous hypersensitivity reactions to cephalosporins and penicillin. Cephalexin should be given with caution to patients who have experienced symptoms of allergy associated with a cephalosporin or penicillin. Serious acute hypersensitivity reactions may require adrenaline 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 cephalexin capsules.

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 including cephalosporin. Such colitis may range in severity from mild to life-threatening. Mild cases of pseudomembranous colitis usually respond to medicine discontinuance alone. In moderate to severe cases, appropriate measures should be taken. Drugs which delay peristalsis may prolong and/or worsen the condition and should not be used.

Precautions

General

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

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.

Cephalexin capsules 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.

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

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

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

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

As a result of administration of cephalexin, a false-positive reaction for glucose in the urine may occur. This has been observed with Benedict's and Fehling's solutions and also with Clinitest[®] tablets. 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.

Use in pregnancy

Safe use of this product during pregnancy has not been established (see Section 4.6 Fertility, pregnancy and lactation).

4.5 Interaction with other medicines and other forms of interaction

Cephalexin capsules may cause a false-positive glucose reaction in urine with Benedict's and Fehling's solutions and Clinitest[®] tablets.

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.

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

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%. No information is available about the interaction of cephalexin and metformin following multiple dose administration.

4.6 Fertility, pregnancy and lactation

Pregnancy

The daily oral administration of cephalexin 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 cephalexin during pregnancy in humans has not been established.

Cephalexin showed no enhanced toxicity in weaning and newborn rats as compared with adult animals. Nevertheless, because the studies in humans cannot rule out the possibility of harm, cephalexin capsules should be used during pregnancy only if clearly needed.

Breastfeeding

The excretion of cephalexin in the 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 cephalexin is administered to a nursing woman.

Fertility

No information held by the sponsor.

4.7 Effects on ability to drive and use machines

During treatment with cephalexin, 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. Nausea and vomiting have been reported rarely. The most frequent side effect has been diarrhoea. It was very rarely severe enough to warrant cessation of therapy. 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, agitation, confusion, hallucinations, arthralgia, cutaneous vasculitis, arthritis, and joint disorder. Reversible interstitial nephritis has been reported rarely. Eosinophilia, neutropenia, thrombocytopenia, haemolytic anaemia and slight elevations in AST and ALT have been reported.

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://nzphvc.otago.ac.nz/reporting/>

4.9 Overdose

Signs and Symptoms

Symptoms of oral overdose may include 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.

Treatment

In managing overdosage, consider the possibility of multiple medicine overdoses, interaction among medicines, and unusual medicine kinetics in your patient.

Unless 5 to 10 times the normal dose of cephalexin has been ingested, gastrointestinal decontamination should not be necessary. Protect the patient's airway and support ventilation and perfusion. Meticulously monitor and maintain, within acceptable limits, the patient's vital signs, blood gases, serum electrolytes, etc. Absorption of medicines from the gastrointestinal tract may be decreased by giving activated charcoal, which, in many cases, is more effective than emesis or lavage; consider charcoal instead of or in addition to gastric emptying. Repeated doses of charcoal over time may hasten elimination of some medicines that have been absorbed. Safeguard the patient's airway when employing gastric emptying or charcoal. Forced diuresis, peritoneal dialysis, haemodialysis, or charcoal haemoperfusion have not been established as beneficial for an overdose of cephalexin; however, it would be extremely unlikely that one of these procedures would be indicated. The oral median lethal dose of cephalexin in rats is 5,000 mg/kg.

For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: antibacterials, first generation cephalosporins
ATC code: J01DB01

Cephalexin is a 7-(D- α -amino- α -phenylacetamido)-3-methyl-3-cephem-4-carboxylic acid monohydrate. Cephalexin has the molecular formula $C_{16}H_{17}N_3O_4S \cdot H_2O$ and the molecular weight is 365.4.

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 crystalline solid having a bitter taste. Solubility in water is low at room temperature; 1 or 2 mg/mL may be dissolved readily, but higher concentrations are obtained with increasing difficulty.

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.

Mechanism of action

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

Microbiology - *In vitro* tests

In vitro tests demonstrate that the cephalosporins are bactericidal because of their inhibition of cell-wall synthesis. Cephalexin has been shown to be active against most strains of the following microorganisms both *in vitro* and in clinical infections as described in the Section 4.1 Therapeutic 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 influenza*
- Klebsiella pneumoniae*
- Moraxella catarrhalis*
- Proteus mirabilis*

Note: Methicillin-resistant staphylococci and most strains of enterococci (*Enterococcus faecalis*) are resistant to cephalosporins including cephalexin. 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*.

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 procedure¹ that has been recommended for use with discs to test the susceptibility of microorganisms to cephalexin uses the 30 mcg cephalothin disc. Interpretation involves correlation of the diameter obtained in the disc test with the minimum inhibitory concentration (MIC) for cephalexin.

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:

Zone Diameter (mm)	Interpretation
Greater than or equal to 18	(S) Susceptible
15-17	(I) Intermediate
Less than or equal to 14	(R) 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 (See Section 5.2 Pharmacokinetic properties 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:

Microorganism	Zone Diameter (mm)
<i>E. coli</i> ATCC 25922	15-21
<i>S. aureus</i> ATCC 25923	29-37

¹National Committee for Clinical Laboratory Standards. *Performance Standards for Antimicrobial Disc Susceptibility Tests--5th ed. Approved Standard NCCLS Document M2-A5, Vol 13, No 24, NCCLS, Villanova, PA, 1993.*

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 uses a standardised dilution method² (broth, agar, microdilution) or equivalent with cephalothin powder. The MIC values obtained should be interpreted according to the following criteria:

MIC (mcg/mL)	Interpretation
Greater than or equal to 8	(S) Susceptible
16	(I) Intermediate
Less than or equal to 32	(R) 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:

Microorganism	MIC (mcg/mL)
<i>E. coli</i> ATCC 25922	4-16
<i>E. faecalis</i> ATCC 29212	8-32
<i>S. aureus</i> ATCC 29213	0.12-0.5

²*National Committee for Clinical Laboratory Standards. Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically--3rd ed. Approved Standard NCCLS Document M7-A3, Vol 13, No 25, NCCLS, Villanova, PA, 1993.*

5.2 Pharmacokinetic properties

Absorption

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 mg/L respectively were obtained at one hour. Measurable levels were present six hours after administration.

Elimination

Cephalexin is excreted in the urine by glomerular filtration and tubular secretion. 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.

5.3 Preclinical safety data

No further data of relevance.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Microcrystalline cellulose
 Magnesium stearate

6.2 Incompatibilities

Not applicable

6.3 Shelf life

24 months

6.4 Special precautions for storage

Store below 30°C

6.5 Nature and contents of container

Blister packs of 20 capsules

6.6 Special precautions for disposal and other handling

No special requirements for disposal.

Any unused medicine or waste material should be disposed of in accordance with local requirements.

7 MEDICINE SCHEDULE

Prescription medicine

8 SPONSOR

BNM Group
39 Anzac Road
Browns Bay
Auckland 0753

Phone 0800 565 633

9 DATE OF FIRST APPROVAL

Date of publication in the New Zealand Gazette of consent to distribute the medicine:
24 April 2008

10 DATE OF REVISION OF TEXT

04 March 2019

Section changed	Summary of new information
All	Datasheet re-formatted in line with SPC style template
8	Change in sponsor from ABM Pharma Ltd to BNM Group