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 soft tissue infections caused by staphylococci and/or streptococci.

Genitourinary tract infections, including acute prostatitis, caused by *E. coli*, *P. mirabilis*, and *Klebsiella pneumoniae*.

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

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 or tonsillitis, mild, uncomplicated urinary tract infections, and skin and soft tissue infections. 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 infections, and for skin and soft- tissue 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.

Impaired renal function: see Section 4.4 Special warnings and precautions for use.

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 (see Precautions).

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.

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.

If an allergic reaction to cefalexin occurs, the drug should be discontinued and the patient treated with the usual agents (eg. 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 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.
However, in moderate to severe cases appropriate therapy with a suitable oral antibacterial agent effective against *Clostridium difficile* should be considered. Fluids, electrolytes and protein replacement should be provided when indicated.

Drugs which delay peristalsis, eg opiates and diphenoxylate with atropine (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 Cefalexin 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.

Neurotoxicity

There have been reports of neurotoxicity associated with cephalosporin treatment, including encephalopathy, seizures and/or myoclonus. Neurotoxicity is more likely observed in elderly patients and patients with renal impairment, central nervous system disorders and those receiving intravenous cephalosporins. Withdrawal of the medicine

should be considered if there are signs of neurotoxicity. Anticonvulsant therapy can be given if clinically indicated.

Use in renal impairment
Cefalexin 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 the elderly
No data available.

Paediatric use
No data available.

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, Cephalexin should be discontinued immediately and an alternative treatment 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 cefalexin 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 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 drug.

4.5 Interaction with other medicines and other forms of interaction

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. Administration of a cephalosporin to a metformin-treated patient may result in increased metformin exposure.

4.6 Fertility, pregnancy and lactation

Effects on fertility

No data available.

Use in pregnancy – Pregnancy Category A
Use in lactation

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

4.7 Effects on ability to drive and use machines

The effects of this medicine on a person's ability to drive and use machines were not assessed as part of its registration.

4.8 Undesirable effects

Adverse drug reactions reported with cefalexin are very rare (<0.01%) and are listed below:
Blood and Lymphatic System Disorders
Eosinophilia, Neutropenia, Thrombocytopenia, 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
Joint Disorder, Arthralgia, Arthritis

Nervous System Disorders
Dizziness, Headache, seizure
Encephalopathy, myoclonus (frequency not known)

Psychiatric Disorders
Hallucinations, Agitation, Confusion

Renal and Urinary Disorders
Reversible Interstitial Nephritis

Reproductive and Breast Disorders
Genital and Anal Pruritus, Genital Moniliasis, Vaginitis, Vaginal Discharge

Skin and Subcutaneous Tissue Disorders
Rash, Erythema Multiforme.
These reactions usually subsided upon discontinuation of the drug.
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), and symmetrical drug-related intertriginous and flexural exanthema (SDRIFE) (baboon syndrome) 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
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 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;

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 procedure[1] 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)
E. coli ATCC 25922	15-21
S. aureus ATCC 25923	29-37

[1]*National 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 method[2] (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)
E. coli ATCC 25922	4-16
E. faecalis ATCC 29212	8-32
S. aureus 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

15 November 2024

Section changed	Summary of new information
4.1, 4.2, 4.4, 4.5, 4.6, 4.7, 4.8 and 4.9	Updated information as per innovator product Keflex (Revised on: 10 May 2024).