AUSTRALIAN PRODUCT INFORMATION

IBILEX®

(cefalexin monohydrate) capsules and powder for oral liquid

1 NAME OF THE MEDICINE

Cefalexin monohydrate

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule (pulvule) contains cefalexin monohydrate equivalent to 250 mg or 500 mg of cefalexin.

Powder for oral liquid in bottle contains cefalexin monohydrate equivalent to 125 mg or 250 mg of cefalexin per 5 mL upon reconstitution.

Excipient with known effect: Powder for oral liquid contains sugars.

For the full list of excipients, see Section 6.1 LIST OF EXCIPIENTS.

3 PHARMACEUTICAL FORM

IBILEX 250 capsules	:	An opaque green and white capsule, size 1 containing 250 mg cefalexin.
IBILEX 500 capsules	:	An opaque dark green and light green capsule, size 0 containing 500 mg cefalexin.
IBILEX 125 powder for oral liquid	:	A white free-flowing powder before reconstitution and a red suspension after reconstitution containing 125 mg cefalexin per 5 mL.
IBILEX 250 powder for oral liquid	:	A white free-flowing powder before reconstitution and a red suspension after reconstitution containing 250 mg cefalexin per 5 mL.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

IBILEX is indicated in the treatment of the following infections when caused by susceptible strains of the designated microorganisms:

- Respiratory tract infections caused by *S. pneumoniae* and group A beta-haemolytic streptococci. (Penicillin is the usual drug of choice in the treatment and prevention of streptococcal infections, including the prophylaxis of rheumatic fever. Cefalexin monohydrate is generally effective in the eradication of streptococci from the nasopharynx; however, substantial data establishing the efficacy of cefalexin monohydrate 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 soft-tissue 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 IBILEX in the treatment of bacterial infections of the brain and spinal column has not been established and IBILEX 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 IBILEX. Renal function studies should be performed when indicated.

4.2 DOSE AND METHOD OF ADMINISTRATION

IBILEX 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 streptococcal pharyngitis or tonsillitis, mild, uncomplicated urinary tract infections, and skin and soft tissue infections, a dosage of 500 mg may be administered every 12 hours.

For more severe infections or those caused by less susceptible organisms, larger doses may be needed. If daily doses of IBILEX 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 soft-tissue infections, the total daily dose may be divided and administered every 12 hours.

IBILEX Suspension

Child's Weight	**125 mg/ 5 mL**	**250 mg/ 5 mL**
10 kg	2.5 – 5 mL q.i.d	
20 kg	5 – 10 mL q.i.d	2.5 – 5 mL q.i.d
40 kg	10 – 20 mL q.i.d.	5 – 10 mL q.i.d.

Or

Child's Weight	**125 mg/ 5 mL**	**250 mg/ 5 mL**
10 kg	5 – 10 mL b.i.d	2.5 – 5 mL b.i.d
20 kg	10 – 20 mL b.i.d.	5 – 10 mL b.i.d
40 kg	20 – 40 mL b.i.d.	10 – 20 mL b.i.d

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 recommended.

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

4.3 CONTRAINDICATIONS

IBILEX is contraindicated in patients with known allergy to the cephalosporin group of antibiotics or who have previously experienced a major allergy to penicillin (see Section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE).

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

BEFORE INSTITUTING THERAPY WITH CEFALEXIN MONOHYDRATE, 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 IBILEX occurs, the drug should be discontinued and the patient treated with the usual agents (e.g. adrenaline (epinephrine) or other pressor amines, antihistamines or corticosteroids).

Antibiotic associated 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 *Clostridium difficile* should be considered. Fluids, electrolytes and protein replacement should be provided when indicated.

Drugs which delay peristalsis, e.g. 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 IBILEX 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. Symptoms of neurotoxicity 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.

Use in Renal Impairment

IBILEX 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, IBILEX 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 IBILEX therapy as precipitation of cefalexin monohydrate 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 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

As with other ß-lactams, the renal excretion of IBILEX is inhibited by probenecid.

In healthy subjects given single 500 mg doses of cefalexin monohydrate 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 monohydrate 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.

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on Fertility

No data available

Use in Pregnancy

Pregnancy Category: A

Use in Lactation

Cefalexin monohydrate is excreted in the milk. Caution should be exercised when IBILEX 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 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

Adverse drug reactions reported with cefalexin monohydrate 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), acute generalised exanthematous pustulosis (AGEP), and symmetrical drug-related intertriginous and flexural exanthema (SDRIFE) (baboon syndrome) have been reported in beta-lactam antibiotics.

Reporting Suspected Adverse Effects

Reporting suspected adverse reactions after registration of the medicinal product is important. It allows continued monitoring of the benefit-risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions at www.tga.gov.au/reporting-problems.

4.9 OVERDOSE

There is no definite experience of poisoning or severe overdosage with cefalexin monohydrate. However, clinical features of overdosage may be similar to those seen with other cephalosporins and penicillins, i.e.

convulsions, hallucinations, hyper-reflexia, 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 cefalexin monohydrate.

For information on the management of overdose, contact the Poisons Information Centre on 13 11 26 (Australia).

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Mechanism of Action

In vitro tests demonstrate that the cephalosporins are bactericidal because of their inhibition of cell-wall synthesis. IBILEX is active against the following organisms *in vitro*:

- Beta-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 IBILEX. It is not active against most strains of Enterobacter sp., *Morganella morganii* (formerly *Proteus morganii*), and *Proteus 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 cefalexin monohydrate 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.

Minimal Inhibitory Concentration (MIC) Breakpoints

Zone diameters, reported off cefalotin discs, are provided with corresponding breakpoints:

Organisms	Zone Diameter	MIC Breakpoint*
Susceptible	18 mm or greater	8 mcg/mL or less
Moderately susceptible	15 – 17 mm	1 – 16 mcg/mL
Resistant	14 mm or less	More than 16 mcg/mL

* Please note that quality control strains are needed to assure that the procedure being run is consistent with expected results.

Clinical Trials

No data available.

5.2 PHARMACOKINETIC PROPERTIES

Absorption

IBILEX 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 mcg/mL, respectively, were obtained at 1 hour. Measurable levels were present 6 hours after administration.

Excretion

Cefalexin monohydrate is excreted in the urine by glomerular filtration and tubular secretion. Studies showed that over 90% of the drug 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 mcg/mL, respectively.

5.3 PRECLINICAL SAFETY DATA

Genotoxicity

No data available.

Carcinogenicity

No data available.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Each capsule (pulvule) contains Avicel RC 591 (ARTG PI No: 2530), dimeticone 350, magnesium stearate, patent blue V, quinoline yellow, titanium dioxide and gelatin.

Powder for oral liquid in bottle contains sodium lauryl sulfate, allura red AC, methylcellulose, dimeticone 350, xanthan gum, pregelatinised starch, Tuttifrutti 51880 TP0551 (ARTG PI No: 1775) and sucrose.

6.2 INCOMPATIBILITIES

See Section 4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS.

6.3 SHELF LIFE

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

IBILEX capsules:

IBILEX 250 mg and 500 mg: Store below 30 degrees Celsius.

IBILEX powder for oral liquid:

Store below 25 degrees Celsius and protect from light. Upon reconstitution, the suspension must be stored in a refrigerator between 2 and 8 degrees Celsius. Do not freeze. Discard unused portion 14 days after mixing.

6.5 NATURE AND CONTENTS OF CONTAINER

IBILEX 250 and 500 capsules : PVC/Al blister pack of 20.

IBILEX 125 and 250 Powder for oral liquid : HDPE bottle of 100 mL.

Australian Register of Therapeutic Goods (ARTG)

AUST R 73524 – IBILEX 250 cefalexin 250mg capsule blister pack

AUST R 73525 – IBILEX 500 cefalexin 500mg capsule blister pack

AUST R 92972 – IBILEX 125 cefalexin 125mg/5mL powder for oral liquid bottle

AUST R 92973 – IBILEX 250 cefalexin 250mg/5mL powder for oral liquid bottle

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

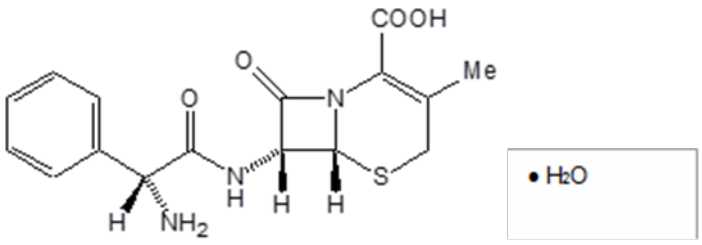
In Australia, any unused medicine or waste material should be disposed of by taking it to your local pharmacy.

6.7 PHYSICOCHEMICAL PROPERTIES

Chemical Structure

Chemical name: 7-(D-α-amino-α-phenyl-acetamido)-3-methyl-3-cephem-4-carboxylic acid, monohydrate

Structural:



Molecular formula: $C_{16}H_{17}N_3O_4S•H_2O$

Molecular weight: 365.41

CAS Number

23325-78-2

The nucleus of cefalexin monohydrate 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 cefalexin monohydrate in water is approximately 4.5 to 5.

The crystalline form of cefalexin 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. Cefalexin monohydrate has a D-phenylglycyl group as substituent at the 7-amino position and an unsubstituted methyl group at the 3-position.

7 MEDICINE SCHEDULE (POISONS STANDARD)

S4 (Prescription Only Medicine)

8 SPONSOR

Alphapharm Pty Ltd trading as Viatris

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Millers Point NSW 2000

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Phone: 1800 274 276

9 DATE OF FIRST APPROVAL

IBILEX capsule blister pack: 28/04/2000

IBILEX powder for oral liquid: 26/03/2003

10 DATE OF REVISION

17/07/2024

Summary Table of Changes

Section Changed	Summary of New Information
All	Minor editorial changes
4.8	Added symmetrical drug-related intertriginous and flexural exanthema (SDRIFE) (baboon syndrome)

IBILEX® is a Viatris company trade mark

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