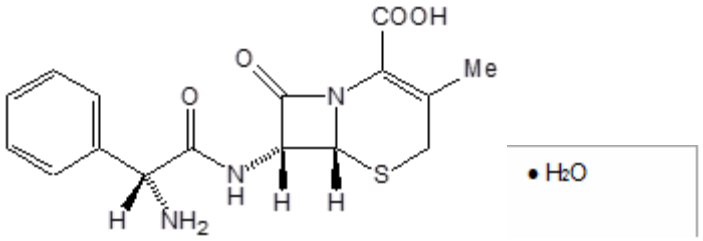
Ibilex

Cephalexin

PRODUCT INFORMATION

NAME OF THE MEDICINE

Active ingredient	:	Cephalexin (as monohydrate)
Chemical name	:	7-(D-α-amino-α-phenyl-acetamido)-3-methyl-3-cephem-4-carboxylic acid, monohydrate
Structural formula	:	

Molecular formula	:	$C_{16}H_{17}N_3O_4S•H_2O$	Molecular weight	:	365.41
			CAS Registry no.	:	23325-78-2

DESCRIPTION

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.

Each capsule (pulvule) contains cephalexin monohydrate equivalent to 250 mg or 500 mg of cephalexin. They also contain Microcrystalline cellulose, Carmellose Sodium, Dimethicone 350, Magnesium Stearate, Patent Blue V (CI42051), Quinoline Yellow (CI47005), Titanium Dioxide and Gelatin.

Powder for Suspensions in bottles contains cephalexin monohydrate equivalent to 125 mg or 250 mg of cephalexin per 5 mL upon reconstitution. They also contain Sodium Lauryl Sulphate, Allura Red AC CI16035, Methylcellulose 15, Dimeticone 350, Xanthan Gum, Pregelatinised Starch, Imitation Guarana Flavour 51880T and Sucrose.

PHARMACOLOGY

Human Pharmacology.

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. Cephalexin 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.

Microbiology.

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 cephalexin and methicillin-type antibiotics.

Disc Susceptibility Tests.

Dilution or diffusion techniques - either quantative (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 cephalothin 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.

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. 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 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.

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 **PRECAUTIONS**).

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 Ibilex occurs, the drug should be discontinued and the patient treated with the usual agents (e.g. adrenaline 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.

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.

Usage in Pregnancy

Pregnancy Category A

Use in Lactation

Cephalexin 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.

Effects on Laboratory Tests

The quantitative determination of urinary protein excretion using strong acids is misleading during Ibilex 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 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.

INTERACTIONS WITH OTHER DRUGS

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

In healthy subjects given single 500 mg doses of cephalexin and metformin, plasma metformin Cmax and AUC increased by an average of 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.

ADVERSE REACTIONS

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

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.

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, Stevens Johnson Syndrome, toxic epidermal Necrolysis.

These reactions usually subsided upon discontinuation of the drug.

DOSAGE AND 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.

Impaired renal function:

See **PRECAUTIONS**.

OVERDOSAGE

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, 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 cephalexin.

Contact the Poison Information Centre on 131126 for management of overdose.

STORAGE

Ibilex capsules:

Ibilex 250mg and 500mg: Store below 30 degrees Celsius

Ibilex powder for oral suspension:

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.

PRESENTATION

Ibilex 250, capsules containing cephalexin monohydrate equivalent to 250 mg cephalexin in packs of 20.

Ibilex 500, capsules containing cephalexin monohydrate equivalent to 500 mg cephalexin in packs of 20.

Ibilex 125 for Oral Suspension, containing cephalexin monohydrate equivalent to 125 mg cephalexin per 5 mL of reconstituted suspension in packs of 100 mL.

Ibilex 250 for Oral Suspension, containing cephalexin monohydrate equivalent to 250 mg cephalexin per 5 mL of reconstituted suspension in packs of 100 mL.

REFERENCES

1. Bauer, A.W., Kirby, W.M.M., Sherris, J.C., and Turck, M.: Antibiotic Susceptibility Testing by a Standardized Single Disk Method, Am. J. Clin. Pathol., 45: 493, 1966; Standardized Disc Susceptibility Test, Federal Register, 39: 19182-19184, 1974.

NAME AND ADDRESS OF SPONSOR

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POISONS SCHEDULE

S4

DATE OF FIRST INCLUSION IN THE AUSTRALIAN REGISTER OF THERAPEUTIC GOODS (THE ARTG)

Ibilex capsule blister pack: 28/04/2000

Ibilex powder for oral liquid: 26/03/2003

DATE OF MOST RECENT AMENDMENT

Jan 2019