APPROVED PROFESSIONAL INFORMATION

SCHEDULING STATUS

S4

PROPRIETARY NAME (and dosage form)

LIZORP SUSPENSION 125 mg/5 ml (Powder for suspension)

LIZORP SUSPENSION 250 mg/5 ml (Powder for suspension)

COMPOSITION

LIZORP SUSPENSION 125 mg/5 ml:

Each 5 ml (after reconstitution) contains cefprozil monohydrate equivalent to 125 mg anhydrous cefprozil and sodium benzoate 0,064 % *m/v* as preservative.

LIZORP SUSPENSION 250 mg/5 ml:

Each 5 ml (after reconstitution) contains cefprozil monohydrate equivalent to 250 mg anhydrous cefprozil and sodium benzoate 0,064 % *m/v* as preservative.

The other ingredients of the formulation are sucrose, sodium chloride, citric acid monohydrate, simethicone emulsion, polysorbate 80, aspartame, glycine, carmellose sodium, microcrystalline cellulose/carboxy methyl cellulose sodium, silica colloidal anhydrous, Bubble Gum Flavour (PWD # 730) and Colour FD&C Yellow No.6 (C.I. No: 15985).

PHARMACOLOGICAL CLASSIFICATION

A 20.1.1 Broad and medium spectrum antibiotics

PHARMACOLOGICAL ACTION

Cefprozil belongs to a sub-group of beta-lactam antibiotics, cephalosporins. It is bactericidal and acts by inhibiting synthesis of bacterial cell wall.

Microbiology

Cefprozil has *in vitro* activity against the following organisms. The bactericidal action of cefprozil results from inhibition of cell-wall synthesis.

Aerobes, gram-positive

NOTE: Cefprozil is inactive against methicillin-resistant staphylococci and *E. faecium*.

Aerobes, gram-negative

NOTE: Cefprozil is inactive against most strains of *Acinetobacter, Enterobacter, Morganella morganii, Proteus vulgaris, Providencia, Pseudomonas* and *Serratia.*

Anaerobes

Most strains of the *Bacteroides fragilis* group are resistant to cefprozil. Other resistant organisms include: *Clostridium difficile; C perfringens; Fusobacterium* spp.; *Peptostreptococcus* spp.; *Prevotella melaninogenica* (formerly known as *Bacteroides melaninogenicus*)

Propionibacterium acnes.

In vitro sensitivity does not necessarily imply clinical efficacy.

Pharmacokinetic properties

Cefprozil is an orally administered agent more active than first-generation cephalosporins against penicillin-sensitive streptococci, *E.coli*, *P. mirabilis*, *Klebsiella* spp., and *Citrobacter* spp. It has a serum half-life of 1,2 to 1,4 hours.

Cefprozil is approximately 96 % absorbed following oral administration in both fasting and non-fasting subjects.

Plasma protein binding is approximately 36 % and is independent of concentration in the range of 2 µg/ml to 20 µg/ml.

In individuals with normal renal function, cefprozil does not accumulate in the plasma.

The plasma half-life prolongation is related to the degree of renal dysfunction in patients with reduced renal dysfunction. In patients with complete absence of renal function, the plasma half-life of cefprozil has been shown to be as long as 5,9 hours.

The half-life is shortened during hemodialysis to 2,1 hours. Excretion pathways in patients with markedly impaired renal function have not been determined. (See **"WARNINGS AND SPECIAL PRECAUTIONS"** and **"DOSAGE AND DIRECTIONS FOR USE"**).

The average AUC observed in elderly subjects (65 years of age) is approximately 35 – 60 % higher than that of young adults and the average AUC in females is approximately 15 – 20 % higher than in males. The magnitude of these age and gender-related variations in the pharmacokinetics of cefprozil are not sufficient to necessitate dosage adjustments.

In patients with impaired hepatic function, no significant differences in pharmacokinetic parameters are observed, when compared to normal control subjects.

Adequate data on CSF levels of cefprozil are not available.

INDICATIONS

LIZORP is indicated for the treatment of patients with mild to moderately severe infections caused by susceptible strains of the designated micro-organisms listed below.

Upper respiratory tract:

Pharyngitis/tonsillitis caused by *Streptococcus pyogenes*. The usual agent of choice in the treatment and prevention of Streptococcal infections, including the prophylaxis of rheumatic fever, is penicillin. **LIZORP** is effective in the eradication of *Streptococcus pyogenes* from the nasopharynx. However, substantial data establishing the efficacy of **LIZORP** in the subsequent prevention of rheumatic fever are not available at present.

Otitis media:

Otitis media caused by *Streptococcus pneumoniae, Haemophilus influenza* and *Moraxella (Branhamella) catarrhalis.*

In the treatment of otitis media and sinusitis due to beta-lactamase producing organisms, **LIZORP** had bacteriologic eradication rates somewhat lower than those observed with a product containing a specific beta-lactamase inhibitor. In considering the use of **LIZORP**, lower overall eradication rates

should be balanced against the susceptibility patterns of the common microbes in a given geographic area and the increased potential for toxicity with products containing beta-lactamase inhibitors.

Lower respiratory tract:

Secondary bacterial infection of acute bronchitis and acute bacterial exacerbation of chronic bronchitis caused by *Streptococcus pneumonia, Haemophilus influenza* (beta-lactamase positive and negative strains) and *Moraxella* (*Branhamella) catarrhalis.*

Skin and skin structure:

Uncomplicated skin and skin structure infections caused by *Staphylococcus aureus* (including penicillinase-producing strains) and *Streptococcus pyogenes.*

Urinary tract:

Uncomplicated urinary tract infections including acute cystitis in women caused by *Escherichia coli, Klebsiella pneumonia* and *Proteus mirabilis.*

Culture and susceptibility testing should be performed when appropriate to determine susceptibility of the causative organism to **LIZORP**.

CONTRA-INDICATIONS

LIZORP is contraindicated in patients who have had previous hypersensitivity reactions to the cephalosporin class of antibiotics, penicillins or other beta-lactam antibiotics or any component of the formulation.

Children below the age of 1 year.

Pregnancy and lactation.

WARNINGS AND SPECIAL PRECAUTIONS

Before therapy with **LIZORP** is instituted, careful inquiry should be made to determine whether the

patients have had previous hypersensitivity reactions to **LIZORP**, other cephalosporins, penicillins, or other medicine. If **LIZORP** is to be given to penicillin-sensitive patients, caution should be exercised because cross-sensitivity among beta-lactam antibiotics has been documented. If an allergic reaction to **LIZORP** occurs, discontinue **LIZORP**. Serious acute hypersensitivity reactions may require emergency treatment measures.

Pseudomembranous colitis can occur.

Paediatric Use:

Safety and efficacy in children below the age of 1 year have not been established.

Accumulation of other cephalosporin antibiotics in newborn infants (resulting from prolonged medicine half-life in this age group) has been reported.

Evaluation of renal status before and during therapy is recommended, especially in seriously ill patients. In patients with known or suspected renal impairment (see **"DOSAGE AND DIRECTIONS FOR USE"**), careful clinical observation and appropriate laboratory studies should be done prior to and during therapy. The total daily dose of **LIZORP** should be reduced in these patients because high and/or prolonged plasma antibiotic concentrations can occur in such individuals from usual doses. Cephalosporins, including **LIZORP**, should be given with caution to patients receiving concurrent treatment with potent diuretics since these agents are suspected of adversely affecting renal function.

Prolonged use of **LIZORP** 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.

Positive direct Coombs tests have been reported during treatment with cephalosporin antibiotics.

Phenylketonurics: **LIZORP** (125 mg/5 ml and 250 mg/5 ml) contains phenylalanine (from aspartame) 8,4 mg per 5 ml reconstituted suspension.

Effects on ability to drive or use machinery

LIZORP may cause dizziness which may affect ability to drive or use machinery. These activities should not be performed until the influence of **LIZORP** on the individual has been determined.

INTERACTIONS

LIZORP can inhibit vitamin K synthesis by suppressing gut flora. Prophylactic vitamin K therapy is recommended when **LIZORP** are used for long periods in malnourished or seriously ill patients. Concomitant administration of **LIZORP** and aminoglycoside antibiotics causes nephrotoxicity.

Laboratory Test Interactions:

LIZORP may produce a false positive reaction for glucose in the urine with copper reduction tests (Benedict's or Fehling's solution or with Clinitest tablets), but not with enzyme-based tests (glucose oxidase) for glycosuria. A false negative reaction may occur in the ferricyanide test for blood glucose. The presence of **LIZORP** in the blood does not interfere with the assay of plasma or urine creatinine by the alkaline picrate method.

PREGNANCY AND LACTATION

Safety of use in pregnancy and lactation has not been established.

DOSAGE AND DIRECTIONS FOR USE

DIRECTIONS FOR RECONSTITUTION

LIZORP SUSPENSION 125 mg/5 ml:

For reconstitution to 60 ml, add purified water to the graduation mark on the bottle, invert the bottle and shake well until all the powder is dispersed.

LIZORP SUSPENSION 250 mg/5 ml:

For reconstitution to 60 ml, add purified water to the graduation mark on the bottle, invert the bottle and shake well until all the powder is dispersed.

Adults and children over 12 years:

LIZORP is administered orally for a period of 10 days in the treatment of infections due to susceptible bacteria in the following:

Upper respiratory infections	500 mg every 24 hours
Lower respiratory infections	500 mg every 12 hours
Sinusitis	250 mg every 12 hours or 500 mg every 12 hours
Uncomplicated urinary tract infections	500 mg every 24 hours
Skin & skin structure infections	250 mg every 12 hours or 500 mg every 12 or 24 hours

Children:

The recommended dosing of **LIZORP** for children between 1 year and 12 years of age is the following:

Upper respiratory tract infections, pharyngitis or tonsillitis:	7,5 mg/kg every 12 hours
Otitis media:	15 mg/kg every 12 hours
Skin and skin structure infections:	20 mg/kg once daily
Sinusitis:	7,5 – 15 mg/kg every 12 hours

Renal Impairment:

LIZORP may be administered to patients with impaired renal function. No dosage adjustment is necessary for patients with creatinine clearance values > 30 ml/min. For those with creatinine clearance values ≤30 ml/min, 50 % of the standard dose should be given at the standard dosing interval. **LIZORP** is in part removed by hemodialysis; therefore, **LIZORP** should be administered after the completion of hemodialysis.

Hepatic Impairment:

No dosage adjustment is necessary for patients with impaired hepatic function.

SIDE-EFFECTS

Blood and the lymphatic system disorders:

Frequent: Eosinophilia.

Less frequent: Neutropenia, thrombocytopenia. Prolonged PT/INR has been observed.

Immune system disorders:

Less frequent: Anaphylaxis, fever, serum sickness and pseudomembranous colitis.

Frequency unknown: Angioedema

Nervous system disorders:

The following side effects have been reported and frequencies are unknown:

Dizziness, hyperactivity, headache, nervousness, insomnia, confusion and somnolence.

Gastrointestinal disorders:

Frequent: Nausea, vomiting, diarrhoea and abdominal pain.

Hepato-biliary disorders:

Less frequent: Cholestatic jaundice.

The following side effects have been reported and frequencies are unknown:

Elevations of AST, ALT, alkaline phosphatase, bilirubin values.

Skin and subcutaneous tissue disorders:

Less frequent: Erythema multiforme, Stevens - Johnson syndrome, superinfection, rash, urticaria.

Renal and urinary disorders:

The following side effects have been reported and frequencies are unknown:

Elevations in blood urea and serum creatinine.

Reproductive system and breast disorders:

Less frequent: General pruritus and vaginitis.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT

(See **SIDE-EFFECTS**)

In case of severe overdosage, especially in patients with compromised renal function, haemodialysis will aid in the removal of **LIZORP** from the body.

IDENTIFICATION

LIZORP SUSPENSION 125 mg/5 ml:

For Dry Powder: White to off white granular powder with bubble gum flavour.

For Reconstituted Suspension: Light orange suspension with bubble gum flavour.

LIZORP SUSPENSION 250 mg/5 ml:

For Dry Powder: White to off white granular powder with bubble gum flavour.

For Reconstituted Suspension: Light orange suspension with bubble gum flavour.

PRESENTATION

LIZORP SUSPENSION 125 mg/5 ml:

The granules are packed in a colourless 115 ml HDPE translucent, round bottle with a 28 mm neck closed with a white opaque 28 mm child resistant closure with an induction sealing wad, together with a 20 ml measuring cup.

Pack size: 60 ml of suspension after reconstitution.

LIZORP SUSPENSION 250 mg/5 ml:

The granules are packed in a colourless 115 ml HDPE translucent, round bottle with a 28 mm neck closed with a white opaque 28 mm child resistant closure with an induction sealing wad, together with

a 20 ml measuring cup.

Pack size: 60 ml of suspension after reconstitution.

STORAGE INSTRUCTIONS

Store in a cool, dry place at or below 30 ºC.

Storage for Reconstituted Suspension:

Once reconstituted, the suspension should be kept in a refrigerator (2 to 8 ºC) and used within 14 days. SHAKE WELL BEFORE USE. Discard any unused solution. Keep the container well closed.

Protect from light.

KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBER

LIZORP SUSPENSION 125 mg/5 ml: 43/20.1.1/0535.

LIZORP SUSPENSION 250 mg/5 ml: 43/20.1.1/0536.

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION

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