4.75”

7.15”

Levoxsel Tablet

(L e v o f l o x a c i n)

لیووکسیل ٹیبلیٹ

(لیووفلوکساسین)

COMPOSITION
Levoxsel Tablet 250mg
Each film coated tablet contains:
Levofloxacin (as hemihydrate)..... 250mg
(USP Specifications)
Levoxsel Tablet 500mg
Each film coated tablet contains:
Levofloxacin (as hemihydrate)..... 500mg
(USP Specifications)
Levoxsel Tablet 750mg
Each film coated tablet contains:
Levofloxacin (as hemihydrate)..... 750mg
(USP Specifications)

DISCRIPTION
Levoxsel is a synthetic broad spectrum antibacterial fluoroquinolone containing levofloxacin, which is the S (-) enantiomer (levorotatory form) of the racemic drug substance ofloxacin for oral and intravenous administration. Levofloxacin acts on the DNA-DNA-gyrase complex by inhibiting DNA gyrase (bacterial topoisomerase II), an enzyme required for DNA replication, transcription, repair and recombination, and topoisomerase IV.

ANTIMICROBIAL SPECTRUM
Levoxsel is bactericidal in vitro. Its antibacterial spectrum covers many Gram-positive and Gram-negative bacteria.
Infections caused by the following organisms have been successfully treated with **Levoxsel** in clinical trials:
Gram-positive organisms: Staphylococcus aureus, Streptococcus pyogenes, Streptococcus faecalis.
Gram-negative organisms: Acinetobacter calcoaceticus, Enterobacter cloacae, Escherichia coli, Haemophilus influenzae, Haemophilus parainfluenzae, Klebsiella oxytoca, Klebsiella pneumoniae, Moraxella catarrhalis, proteus mirabilis, Pseudomonas aeruginosa.
Other organisms: Chlamydia pneumoniae, Legionella pneumophila, Mycoplasma pneumoniae.
In vitro there is cross-resistance between **Levoxsel** and other fluoroquinolones.
Due to the mechanism of action, there is generally no cross-resistance between **Levoxsel** and other classes of antibacterialagents.

PHARMACOKINETICS
food has little effect on the absorption of **Levoxsel** and the tablets may be taken during or between meals. The absorption of **Levoxsel** is significantly reduced when administered with iron salts, antacids and sucralfate.
Absorption: Orally administered **Levoxsel** is rapidly and almost completely absorbed with peak plasma concentrations being obtained within one hour. The absolute bioavailability is approximately 100%.
Levoxsel obeys linear pharmacokinetics over a range of 50 to 600 mg.
Distribution: Approximately 30 - 40% of **Levoxsel** is bound to serum protein. Multiple doses of 500mg once daily with **Levoxsel** showed negligible accumulation. There is modest but predictable accumulation of **Levoxsel** after doses of 500 mg twice daily. Steady state is achieved within three days.
Diffusion in fluids and tissues: **Levoxsel** diffuses well into bone tissue, bronchial mucosa, epithelial lining fluid, lung tissue and blister fluid. Metabolism and Elimination: **Levoxsel** is metabolised to a very small extent, the metabolites being desmethyl levefloxacin and levofloxacin N-oxide. Elimination of **Levoxsel** occurs primarily via the kidney. The elimination half-life is on average six to eight hours in patients following oral and intravenous administration.

INDICATIONS
In adults, treatment of bacterial infections due to levofloxacin-susceptible microorganisms:
Sinusitis: Due to H influenzae, S. pneummoniae, S. aureus, M. catarrhalis and H. Parainfluensae.
Acute exacerbations of chronic bronchitis: Due to H. influenzae, K. pneumoniae, S. aureus, M. catarrhalis, E coli, H parainfluenzae and S. Pneumoniae.
Community Acquired Pneumonia: Due to H. influenzae, S. Pneumoniae, S. aureus, M. catarrhalis, H. Parainfluenzae, K pneumoniae, E coli, Mycoplasma pneumoniae, Chlamydia pneumoniae and Legionella pneumophila.
Complicated urinary tract infections and acute pyelonephritis: Due E. coli, K. pneumoniae, S. faecalis, P. mirabilis, Enterobacter cloacae, P. Aeruginosa.
Uncomplicated skin and skin structure infections: Due to S. aureus, S. pyogenes, Acinetobacter calcoaceticus, E. cloacae, P. mirabilis, P. aeruginosa, E. coli, K. Pneumoniae, S. Faecalis.
Complicated skin and skin structure infections: Due to S. aureus, S. pyogenes, P. mirabilis, E. coli, K. pneumoniae, S. faecalis, E. cloacae, K oxytoca.
Intra-abdominal infections: Due to E. coli and anaerobic microorganisms.

CONTRA-INDITATIONS
Hypersensitivity to levofloxacin, other quinolones, or any of the excipients.
Epilepsy
History of tendon disorders related to fluoroquinolone administration.
Children or adolescents.
During pregnancy and lactation.

WARNINGS
Levoxsel should be used with caution in patients predisposed to seizures, such as patients with pre-existing central nervous system lesions, concomitant treatment with nonsteroidal anti-inflammatory drugs or with drugs which lower the cerebral seizure threshold, such as theophylline.
LEVOXSEL SHOULD NOT BE GIVEN TO PATIENTS UNDER 18 YEARS OF AGE.
Even when used as instructed, **Levoxsel** may alter reactivity to such an extent that the ability to drive or operate machinery may be impaired. Although photosensitization is extremely rare with **Levoxsel**, it is recommended that patients should not expose themselves unnecessarily to strong sunlight or to artificial UV rays (e.g. sunray lamp, solarium), in order to prevent photosensitization.
Levoxsel may inhibit the growth of Mycobacterium tuberculosis, and therefore may give false-negative results in the bateriological diagnosis of tuberculosis.

DOSAGE AND DIRECTIONS FOR USE
Levoxsel is administered once or twice daily.
The dosage depends on the type and severity of infection and sensitivity of the presumed causative pathogen. The duration of therapy varies according to the course of disease. Levoxsel should be continued for a minimum of 48 to 72 hours after the patient has become afebrile or evidence of bacterial eradication has been obtained.
The following daily dose recommendations can be given for **Levoxsel**
Reccomended daily dosage in patients with normal renal function:
Sinusitis: 500 mg once daily for 10 days.
Acute exacerbation of chronic bronchitis: 500 mg once daily for 5 - 10 days
Community acquired Pneumonia: 500 mg once or twice daily for 10 - 14 days

4.75”

7.15”

Complicated urinary tract infections and acute pyelonephritis: 250 mg once daily for 10 days.
Uncomplicated skin and skin structure infections: 250 to 500 mg once daily for 7 - 10 days.
Complicated skin and skin structure infections: 500 mg twice daily for 10 - 14 days.
Intra-abdominal infections: 500 mg once daily in combination with an antibiotic with anaerobic coverage for 10 - 14 days.
Above indications when bacteraemia or septicaemia is present 500 mg twice daily for 10 - 14 days.

RECOMMENDED DAILY DOSAGE IN PATIENTS WITH IMPAIRED RENAL FUNCTION
Dosage must be adjusted in patients with impaired renal function (creatinince clearance < 50 mL/min) according to the degree of impairment:
With a creatinine clearance between 20 and 50ml/min:
In patients meant to be taking 250 or 500 mg once daily, a normal single dose should be given intially and then reduced by half this dose once daily. In the patients is meant to be taking 500 mg twice daily, the initial dose should be 500 mg and then 250 mg should be administrated twelve hourly.
With a creatinine clearance between 10 and 19ml/min:
In patients meant to be taking 250 mg once daily, a normal single dose should be given initially and then reduced to 125 mg every 48 hours. Patients meant to be taking 500 mg once daily should be given a normal single dose initially and then this dose should be reduced to 125 mg every 24 hours.
Patients meant to be taking 500 mg twice daily should be given 500 mg initially and then this dose should be reduced to 125 mg every 12 hours. With a creatinine clearance of less than 10ml/min or in patients on haemodialysis or CAPD (Continuous Ambulatory Peritoneal Dialysis): If the prescribed dosage is 250 mg once daily, a normal single dose should be given initially and then this dose should be reduced to 125 mg every 48 hours. Patients meant to be taking 500 mg once daily should be given a normal single dose initially and then this dose should be reduced to 125 mg every 24 hours. Patients meant to be taking 500 mg twice daily should be given 500 mg initially and then this dose should be reduced to 125 mg every 24 hours. No adjustment of dosage is required in the elderly or in patients with impaired liver function.

NOTE
Levoxsel tablets should be swellowed whole, without crushing, and with sufficient amount of liquid. They may be taken on an empty stomach or with meals.
Levoxsel tablets should be taken two hours before iron salts, antacids and sucralfate administration since reduction of absorption may occur.

SIDE EFFECTS AND SPECIAL PRECAUTIONS
Gastro-intestinal symptoms may occur (gastric or abdominal symptoms, loss of appetite, nausea, vomiting, diarrhoea). The onset of diarrhoea, particulary if severe, persistent and / or bloody, during or after treatment with **Levoxsel,** may less frequently indicate the appearance of pseudomembranous colitis. Suspicion of pseudomembranous colitis requires immediate cessation of administration and treatment with appropriate specific antibiotic therapy. Products inhibiting peristalsis are contra-indicated in this clinical situation.
Disturbances of the nervous system, e.g. headaches, dizziness, sleep disturbances, unsteady gait and tremor (disturbances of mascular co-ordination), nubmness and tingling in the limbs (parasthesiae; visual and auditory disturbances, disturbances of taste and smell, hallucinations, convulsions and psychotic reactions such as restlessness, agitation, anxiety, depression and confusion. In some cases, these reactions have occurred already after the first dose. In the event of such adverse reactions, **Levoxsel** must be discontinued immediately.
Changes in the blood picture (leukopenia, eosinophilia, neutropenia, agranulocytosis, thrombocytopenia, pancytopenia, haemolytic anaemia), hepatitis and transient increases in liver enzymes and/or bilirubin and in serum creatinine have been observed. Interstitial nephritis and acute kidney failure may also occur.
Allergic manifestation may occus, in particular hypersensitivity reactions of the skin such as pruritus, rash, urticaria and vasculitis. Isolated cases of severe bullous eruptions such as Stevens' Johnson syndrome. Toxic epidermal necrolysis (Lyells syndrome) and erythema exsudativum multiforme have been reported. Photosensitivity reactions (skin reactions on exposure to strong sunlight and artificial UV rays) have been reported. There have been symptoms such as fever, allergic pneumonitis, angio-oedema, hypotension and anaphylactic-like shock. In the event of such reactions, **Levoxsel** should be discontinued immediately. Medical treatment (therapy for shock is imperative.
Tendinitis (e.g. Achilles tendon) is less frequently observed with quinolones and if its is suspected, treatment with **Levoxsel** must be halted immediately and appropriate treatment (e.g. Immobilisation) must be initiated for the affected tendon. Other musculoskeletal side effects such as arthralgia and myalgia have been less frequently observed and less frequent occurrences include:
Tendon rupture (Achilles tendon) - this undesirable effect may occur within 48 hours of starting treatment and may be bilateral.
Mascular weakness, which may be of special importance in patients with myasthenia gravis.
Isolated cases of rhabdomyolysis have been reported.
Hypoglycaemia, especially in diabetics, may occur.
Asthenia, fungal overgrowth and proliferation of other resistant microorganisms may occur.
Fluroquinolones are known to possible trigger attacks of porphyria in patients suffering from porphyria.

INTERACTIONS
If mineral-containing antacids or iron preparations are taken at the same time, absorption of **Levoxsel** tablets may be impaired. It is recommended that preparations containing divalent or trivalent cations such as iron salts, or magnesium or aluminium-containing antacids should not be taken 2 hours before or after **Levoxsel** tablet administration.
The bioavailability of **Levoxsel** tablets is significantly reduced when administered together with sucralfate. If the patient is to receive both sucralfate and **Levoxsel** tablets, it is best to administer sucralfate two hours after the **Levoxsel** tablet administration. No pharmacokinetic interactions of **Levoxsel** were found with theophylline in a clinical study. However there are indications of a pronounced lowering of ther cerebral seizure threshold when quinolones are given concurrently with other drugs that lower the seizure threshold (e.g. theophylline) or with fenbufen or similar non-steroidal anti-inflammatory drugs.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT
According to studies in animals, the most important signs to be expected following acute overdosage of **Levoxsel** are central nervous system symptoms such as confusion, dizziness, impairment of consciousness, and convulsive seizures.
Apart from symptomatic and supportive treatment, no specific therapeutic recommendation can be made in cases of overdosage.

STORAGE & INSTRUCTIONS
Store below 15-25°C.
Protect from heat, sunlight and moisture.
Keep away from the reach of children.
To be sold on prescription of registered medical practitioner only.

HOW SUPPLIED
Levoxsel Tablet 250mg
10's, 10x10's Tablets.
Levoxsel Tablet 500mg
10's, 10x10's Tablets.
Levoxsel Tablet 750mg
10's Tablets.

خوراک وطریقہ استعمال:

ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔

ہدایات:

دوا کو ۱۵-۲۵ ڈگری سینٹی گریڈ درجہ حرارت کے درمیان رکھیں۔
دھوپ، گرمی اور نمی سے بچائیں۔ بچوں کی پہنچ سے دور رکھیں۔
صرف رجسٹرڈ ڈاکٹر کے نسخے کے مطابق فروخت کریں۔

Manufactured by:
PHARMASOL
PRIVATE LIMITED
Plot # 549,Sundar Industrial Estate,
Lahore, Pakistan.