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LEVOCIL®

(Levofloxacin) Tablet

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COMPOSITION:
Levocil Tablet 250 mg:
Each film coated tablet contains:
Levofloxacin hemihydrate USP equivalent
to Levofloxacin ..... 250 mg.

Product Specs.: USP

Levocil Tablet 500 mg:
Each film coated tablet contains:
Levofloxacin hemihydrate USP equivalent
to Levofloxacin ..... 500 mg.

Product Specs.: USP

PHARMACOLOGY:
Antibacterial activity:
Levocil is a wide-spectrum antibacterial agent against gram-positive and gram-negative bacteria, including anaerobes. Levocil has shown strong antibacterial activities against Staphylococcus spp., Streptococcus pneumoniae, Streptococcus pyogenes, Streptococcus hemolyticus, Enterobacter spp., Escherichia coli, Klebsiella spp., Serratia spp., Enterococcus spp., Proteus spp., and other glucose non-fermentative gram-negative rods, Pseudomonas aeruginosa, Haemophilus influenzae, and Neisseria gonorrhoeae. Moreover, Levocil has shown antibacterial activity against Chlamydia trachomatis. Levocil has excellent protective and treatment effects in mice.
Mechanism of action:
The main mechanism of action of Levocil is the inhibition of DNA gyrase. It is two fold stronger than that of ofloxacin. There is not much difference between the MIC and MBC. The activity of Levocil is bactericidal. In the observation of bacterial morphology, bacteriolysis can be seen in the concentration around MIC.
Pharmacokinetics:
Absorption:
Orally administered Levofloxacin is rapidly and almost completely absorbed with peak plasma concentrations being obtained within 1hr. The absolute bioavailability is approximately 100%. Food has little effect on the absorption of Levofloxacin.
Distribution in plasma:
Approximately 30-40% of Levofloxacin is bound to serum protein. 500mg once daily multiple dosing with Levofloxacin showed negligible accumulation. There is modest but predictable accumulation of Levofloxacin after doses of 500mg twice daily. Steady-state is achieved within 3 days.
Penetration into tissues and body fluids:
Penetration into Bronchial mucosa, Epithelial Lining Fluid (ELF). Maximum Levofloxacin concentrations in bronchial mucosa and epithelia lining fluid were 8.3 ug/ml and 10.8ug/ml respectively. These were reached approximately one hour after administration.
Penetration into lung tissue:
Maximum Levofloxacin concentrations in lung tissue were approximately 11.3 ug/ml and were reached between 4 and 6 hours after administration. The concentration in the lungs consistently exceeded those in plasma.
Metabolism: Levofloxacin is metabolised to a very small extent, the metabolites being desmethyl-levofloxacin and levofloxacin N-oxide. These metabolites account for < 5% of the dose excreted in urine. Levofloxacin is stereochemically stable and does not undergo chiral inversion.
Elimination:
Following oral and intravenous administration, Levofloxacin is eliminated relatively slowly from the plasma ($t_{½}$: 6-8 h). Excretion is primarily by the renal route (> 85% of the administered dose). There are no major differences in the pharmacokinetics of Levofloxacin following intravenous and oral administration, suggesting that the oral and intravenous routes are interchangeable.
Subjects with renal insufficiency:
The pharmacokinetics of Levofloxacin are affected by renal impairment. With decreasing renal function, renal elimination and clearance are decreased, and elimination half-lives increased as shown in the table below.

Cl_{cr} [ml/min]	< 20	20 - 40	50 - 80
Cl_R [ml/min]	13	26	57
$t_{½}$ (h)	35	27	9

Elderly subjects:
There are no significant differences in Levofloxacin kinetics between young and elderly subjects, except those associated with differences in clearance.
Gender differences:
Separate analysis for male and female subjects did not show clinical relevant gender differences in Levofloxacin pharmacokinetics.

INDICATIONS:
The following infections caused by Staphylococcus spp., Streptococcus pneumoniae, Streptococcus pyogenes, Streptococcus hemolyticus, Enterococcus spp., Peptostreptococcus spp., Neisseria gonorrhoeae, Branhamella catarrhalis, Propionibacterium acnes, Escherichia coli, Citrobacter spp., Salmonella spp., Shigella spp., Klebsiella spp., Enterobacter spp., Serratia spp., Proteus spp., Vibrio cholerae, Pseudomonas aeruginosa, Haemophilus influenzae, Acinetobacter spp., Campylobacter spp., Chlamydia spp., Mycoplasma spp., Legionella spp., are susceptible to Levofloxacin.

- Pneumonia, chronic bronchitis, diffuse panbronchiolitis, bronchiectasis with infection, secondary infections in chronic respiratory disease.
- Laryngopharyngitis, tonsillitis (peritonsillitis, peritonsillar abscess), acute bronchitis.
- pyelonephritis, cystitis, prostatitis, epididymitis, gonococcal urethritis, non-gonococcal urethritis.
- Intrauterine infections, cervicitis, uterine adnexitis, bartholinitis.
- Folliculitis (including acne pustulosa), furuncle, furunculosis, carbuncle, impetigo contagiosa, hydradenitis, acn conglabata, infectious atheroma, periproctic abscess.
- Mastitis, (superficial) secondary infections in traumatic wounds, burns, operative wounds, etc.
- Cholecystitis, cholangitis.
- Otitis externa, otitis media, sinusitis, suppurative sialadenitis.
- Blepharitis, hordeolum, dacryocystitis, conjunctivitis, tarsadenitis.
- Bacterial dysentery, infectious enteritis, Salmonella enteritis, cholera.
- Periodontitis, pericoronitis, gnathitis.

DOSAGE AND ADMINISTRATION:
Method of administration: Levocil tablets should be swallowed without crushing and with sufficient amount of liquid. They may be divided at the score line to adapt the dosage. The tablets may be taken during meals or between meals. Levocil tablets should be taken two hours before iron salts, antacids and sucralfate administration since reduction of absorption can occur.
The following dose recommendations can be given for Levocil.
Dosage in patients with normal renal functions (Creatinine clearance > 50 ml/min)

INDICATION	DAILY DOSE (mg)	DURATION (DAY)
Acute Bacterial Exacerbation of Chronic Bronchitis	250 mg (1 Tab) bid or 500 mg (1 Tab) bid	7
Community Acquired Pneumonia	250 mg (1 Tab) bid or 500 mg (1 Tab) bid	7-14
Acute Maxillary Sinusitis	250 mg (1 Tab) bid or 500 mg (1 Tab) bid	10-14
Complicated Urinary Tract Infections	250 mg (1 Tab) od	10
Uncomplicated Skin and Soft Tissue Infections	250 mg (1 Tab) bid or 500 mg (1 Tab) bid	7-10
Acute Pyelonephritis	250 mg (1 Tab) od	10

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NOTE: Dosage may be adjusted according to the kind of infection and severity of the symptoms.
Dosage in patients with impaired renal function (Creatinine clearance ≤ 50 ml/min)

Creatinine clearance	**Dose regimen**		
	1 x 250 mg / 24 h	1 x 500 mg / 24 h	2 x 500 mg / 24 h
First dose / always	250 mg	500 mg	500 mg
50-20 ml/min	then: 125 mg / 24 h	then: 250 mg / 24 h	then: 250 mg / 12 h
19-10 ml/min	then: 125 mg / 48 h	then: 125 mg / 24 h	then: 125 mg / 12 h
< 10 ml/min (including hemodialysis and CAPD)	then: 125 mg / 48 h	then: 125 mg / 24 h	then: 125 mg / 24 h

No additional doses are required after hemodialysis or continuous ambulatory peritoneal dialysis (CAPD).
Dosage in elderly:
No adjustment of dosage is required in the elderly, other than imposed by consideration of renal function.

PRECAUTIONS:
To prevent the development of resistance, susceptibility to the drug should be determined before use. The duration of use should be limited to the minimum time required for treatment.

USE DURING PREGNANCY OR LACTATION:
- Since safety during pregnancy has not been established, this product should not be administered to women who are pregnant or suspected of being pregnant.
- Since Levofloxacin is excreted in breast milk, it is recommended that nursing mothers refrain from using this product. If use is necessary, breast feeding should be avoided.

Pediatric Use:
Since the product's safety for use by children has not been established, this product should not be administered to children.
Others:
Animal studies have shown that Levofloxacin can produce arthropathy in juvenile dogs, young mature dogs (13 months of age) and juvenile rats.

CONTRAINDICATIONS:
- Patients with a history of hypersensitivity to any ingredient in this product or to ofloxacin.
- Pregnant women or women suspected of being pregnant. (See "Use during pregnancy or lactation.")
- Children, (See "Pediatric use")

Careful administration:
- Patients with severe renal disorders.
- Patients with a history of convulsive disorders. (Convulsions may possibly occur).
- Patients with a history of hypersensitivity to quinolone antibacterial agents.
- The elderly. (See "Use in the elderly.")

DRUG INTERACTIONS:
- Since it has been reported that other quinolones (enoxacin, etc.) used in combination with nonsteroidal anti-inflammatory drugs of phenylacetic/propionic acid derivatives, such as fenbufen, may rarely cause convulsions, this product should be administered carefully.
- Since antacids containing aluminium or magnesium and drugs containing iron may interfere with the absorption of Levofloxacin resulting in attenuation of the efficacy of Levofloxacin, it is recommended to refrain from using this product with such products.

ADVERSE REACTIONS:
Shock:
Since shock symptoms may rarely occur, observe patients carefully. If any abnormalities are observed, discontinue the medication and take appropriate measures.
Hypersensitivity:
Anaphylactoid symptoms (erythema, chills, dyspnea), edema, urticaria, feeling of warmth or photosensitivity may rarely occur and rash or pruritus may infrequently occur. In the event of such symptoms, discontinue the medication.
Dermatologic:
It has been reported that Levofloxacin may rarely cause Lyell Syndrome or Stevens Johnson Syndrome.
Psychoneurologic:
Convulsion, tremor or numbness may rarely occur, and insomnia, dizziness or headache may infrequently occur.
Renal:
An increase in BUN may frequently occur. It has been reported that Levofloxacin may rarely cause acute renal failure.
Hepatic:
An increase in S-GOT, GPT, Al-Por γ-GTP or total bilirubin may infrequently occur.
Hematologic:
A decrease in leukocytes, erythrocytes, hemoglobin or hematocrit or an increase in eosinophils may infrequently occur. Observe patients carefully, and if any abnormality is observed, discontinue the medication.
Gastro-intestinal:
Nausea, vomiting, abdominal discomfort, diarrhea, anorexia, abdominal pain or enlarged feeling of the abdomen may infrequently occur. Since it has been reported that Levofloxacin may rarely cause severe colitis, with blood in the stool, such as pseudomembranous colitis, in the event of abdominal pain or frequent diarrhea take appropriate measures, including immediate discontinuation of the medication.
Muscular:
Since rhabdomyolysis with rapid deterioration of renal function characterized by myalgia, weakness, increase in CPK or myoglobin in blood or urine may occur, patients should be cautioned.
Others:
Since it has been reported that other new quinolones may rarely cause hypoglycemia (especially in elderly patients with renal disorders), this product should be administered carefully.
Malaise may rarely occur.
Use in the elderly:
This product is mainly excreted by the kidneys. (See "Pharmacokinetics.") Since the elderly often have a renal hypofunction and are in danger of continuous high blood concentration, observe dose and interval (e.g., 100 mg b.i.d.).

INSTRUCTIONS:
Store below 30°C. Protect from heat, sunlight & moisture. Keep out of the reach of children. To be sold on the prescription of a registered medical practitioner only.

PRESENTATION:
Levocil Tablet 250 mg : Pack of 1x10 tablets.
Levocil Tablet 500 mg : Pack of 1x10 tablets.

ہدایات:
۳۰ درجہ سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔
گرمی، دھوپ اور نمی سے بچائیں۔
بچوں کی پہنچ سے دور رکھیں۔
صرف مستند ڈاکٹر کے نسخہ پر فروخت کریں۔

FOR FURTHER INFORMATION PLEASE CONTACT.

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