Dlevo 250mg 500mg

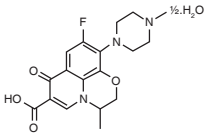
(Levofloxacin)
Tablets U.S.P.

QUALITATIVE AND QUANTITATIVE COMPOSITION:
Dlevo Tablets U.S.P. 250mg
Each film-coated tablet contains:
Levofloxacin hemihydrate eq. to
Levofloxacin U.S.P. 250mg

Dlevo Tablets U.S.P. 500mg
Each film-coated tablet contains:
Levofloxacin hemihydrate eq. to
Levofloxacin U.S.P. 500mg

WARNING:
Fluoroquinolones, including Dlevo, are associated with an increased risk of tendinitis and tendon rupture in all ages. This risk is further increased in older patients usually over 60 years of age, in patients taking corticosteroid drugs, and in patients with kidney, heart or lung transplants

DESCRIPTION:
Dlevo (Levofloxacin) is a synthetic broad-spectrum antibacterial agent. The molecular formula of levofloxacin is $C_{18}H_{20}FN_3O_4$ and the structural formula is:



CLINICAL PHARMACOLOGY:
Mechanism of Action
Levofloxacin is the L-isomer of the racemate, ofloxacin, a quinolone antimicrobial agent. The antibacterial activity of ofloxacin resides primarily in the L-isomer. The main mechanism of action of levofloxacin involves the inhibition of DNA gyrase (topoisomerase), which is essential in the reproduction of bacterial DNA. Levofloxacin has in-vitro activity against gram-negative and gram-positive microorganisms. It is often bactericidal at concentrations equal to or slightly greater than inhibitory concentration.
PHARMACOKINETICS:
Absorption: Levofloxacin is rapidly and essentially completely absorbed after oral administration. Peak plasma concentrations are attained 1-2 hours after oral dosing. The absolute bioavailability is approximately 99% demonstrating complete oral absorption of levofloxacin. Levofloxacin pharmacokinetics are linear and predictable after single and multiple dosing regimens. Steady state conditions are reached within 48 hours following a 500mg or 750 mg once daily dosage regimens. The mean ±SD peak and trough plasma concentrations attained following multiple once-daily oral dosage regimens were approximately 5.7±1.4 and 0.5±0.2µg/ml after the 500mg doses, and 8.6±1.9 and 1.1±0.4µg/ml after the 750mg doses, respectively. Oral administration of a levofloxacin with food slightly prolongs the time to peak concentration by approximately 1 hour and slightly decreases the peak concentration by approximately 14%. Therefore levofloxacin can be administered without regard to food.
Distribution: The mean volume of distribution generally ranges from 74 – 112 liters after single and multiple dosing of 500mg or 750mg doses. Levofloxacin is approximately 24 to 38% bound to serum proteins. Levofloxacin is mainly bound to serum albumin in humans. The binding of levofloxacin to serum proteins is independent of the drug concentration.
Metabolism and Elimination: Levofloxacin undergoes limited metabolism in human is primarily excreted as unchanged drug in the urine. Following oral administration approximately 87% of and administered dose was recovered as unchanged drug in urine within 48 hours. Whereas less than 4% of the dose was recovered in feces in 72 hours. Less than 5% of an administered dose was recovered in the urine as the desmethyl and N-oxide metabolites, the only metabolites indentified in humans. These metabolites have little relevant pharmacological activity. The mean terminal elimination half-life ($t_{1/2}$) of levofloxacin ranges from approximately 6 to 8 hours following single or multiple doses of levofloxacin. The mean apparent total body clearance and renal clearance range from approx. 144-226ml/min and 96-142,ml/min respectively.
Hepatic insufficiency: Pharmacokinetic studies in hepatically impaired patients have not been conducted. Due to the limited extent of levofloxacin metabolism, the pharmacokinetics of levofloxacin are not expected to be affected by hepatic impairment.
INDICATIONS:
Dlevo is indicated for the treatment of acute sinusitis, acute exacerbations of chronic bronchitis, and community-acquired pneumonia, but it should only be considered for these infections when first-line treatment cannot be used or is ineffective. It has greater activity against pneumococci than ciprofloxacin. It is also indicated for the treatment of urinary-tract infections and chronic prostatitis. Although is also indicated for skin and soft-tissue infections, many staphylococci are resistant to the quinolones and their use should be avoided in MRSA infections.
DOSAGE AND ADMINISTRATION
By mouth, acute sinusitis, 500 mg once daily for 10–14 days Acute exacerbation of chronic bronchitis, 500mg once daily for 7–10 days. Community-acquired pneumonia, 500 mg once or twice daily for 7–14 days.
Urinary-tract infections, 500 mg once daily for 7–14 days (250 mg once daily for 3 days in uncomplicated infection)
Chronic prostatitis, 500mg once daily for 28 days.
Complicated skin and soft tissue infections, 500mg once or twice daily for 7–14 days. Inhalation anthrax (treatment and post-exposure prophylaxis), 500mg once daily for 8 weeks.
Renal impairment: usual initial dose then use half normal dose if eGFR 20–50 mL/minute/1.73m2;consult product literature if eGFR less than 20 mL/minute/1.73m2
Pregnancy: Quinolones should be avoided in pregnancy because they have been shown to cause arthropathy in animal studies; safer alternatives are available; however, a single dose of ciprofloxacin may be used for the prevention of a secondary case of meningococcal meningitis.
Breast-feeding: Caution should be exercised.
SPECIAL WARNINGS AND PRECAUTIONS FOR USE:
Use in children Quinolones cause arthropathy in the weight-bearing joints of immature animals and are therefore generally not recommended in children and growing adolescents. However, the significance of this effect in humans is uncertain and in some specific circumstances short-term use of either ciprofloxacin or nalidixic acid may be justified in children.
Tendon damage: Tendon damage (including rupture) has been reported rarely in patients receiving quinolones.
Tendon rupture may occur within 48 hours of starting treatment; cases have also been reported several months after stopping a quinolone. Healthcare professionals are reminded that: quinolones are contra-indicated in patients with a history of tendon disorders related to quinolone use; patients over 60 years of age are more prone to tendon damage; the risk of tendon damage is increased by the concomitant use of corticosteroids; if tendinitis is suspected, the quinolone should be discontinued immediately.
Driving: May impair performance of skilled tasks (e.g. driving).
ADVERSE REACTIONS:
Side-effects of the quinolones include nausea, vomiting, diarrhoea (rarely antibiotic-associated colitis), headache, and dizziness. Less frequent side effects include dyspepsia, abdominal pain, anorexia, sleep disturbances, asthenia, confusion, anxiety, depression, hallucinations, tremor, blood disorders (including eosinophilia, leucopenia, thrombocytopenia), arthralgia, myalgia, rash (very rarely Stevens-Johnson syndrome and toxic epidermal necrolysis), disturbances in vision and taste. Other side-effects reported rarely or very rarely include hepatic dysfunction (including jaundice and hepatitis), hypotension, vasculitis, dyspnoea (more frequent with levofloxacin and moxifloxacin), convulsions, psychoses, symptoms of peripheral neuropathy (sometimes irreversible), renal failure, interstitial nephritis, tendon inflammation and damage, photosensitivity, disturbances in hearing and smell. The drug should be discontinued if psychiatric, neurological or hypersensitivity reactions (including severe rash) occur. Also flatulence, constipation, hyperhidrosis; rarely tachycardia, palpitation, abnormal dreams, tinnitus, hypoglycaemia; also reported potentially life-threatening hepatic failure, syncope, benign intracranial hypertension, pneumonitis, peripheral neuropathy, extrapyramidal symptoms, hyperglycaemia, rhabdomyolysis, stomatitis; local reactions and transient hypotension reported with infusion.
CONTRAINDICATIONS:
Quinolone hypersensitivity: Quinolones should be used with caution in patients with a history of epilepsy or conditions that predispose to seizures, in G6PD deficiency, myasthenia gravis (risk of exacerbation), and in children or adolescents (arthropathy has developed in weight-bearing joints in young animals).Exposure to excessive sunlight should be avoided (discontinue if photosensitivity occurs). Quinolones can prolong the QT interval. The CSM has warned that quinolones may induce convulsions in patients with or without a history of convulsions; taking NSAIDs at the same time may also induce them.
Drug interactions: Interaction with other medicinal products and other forms of interaction Effect of other medicinal products on levofloxacin Iron salts, magnesium- or aluminium-containing antacid, didanosines Levofloxacin absorption is significantly reduced when iron salts, or magnesium- or aluminium-containing antacids, or didanosine (only didanosine formulations with aluminium or magnesium containing buffering agents) are administered concomitantly with Levofloxacin tablets. Concurrent administration of fluoroquinolones with multi-vitamins containing zinc appears to reduce their oral absorption. It is recommended that preparations containing divalent or trivalent cations such as iron salts, zinc salts or magnesium- or aluminium-containing antacids, didanosine (only didanosine formulations with aluminium or magnesium containing buffering agents) should not be taken 2 hours before or after Levofloxacin tablet administration. Calcium salts have a minimal effect on the oral absorption of levofloxacin.
Sucralfate: The bioavailability of Levofloxacin tablets is significantly reduced when administered together with sucralfate. If the patient is to receive both sucralfate and levofloxacin, it is best to administer sucralfate 2 hours after the levofloxacin administration.
Theophylline, fenbufen or similar non-steroidal anti-inflammatory drugs No pharmacokinetic interactions of levofloxacin were found with theophylline in a clinical study. However a pronounced lowering of the cerebral seizure threshold may occur when quinolones are given concurrently with theophylline, non-steroidal anti-inflammatory drugs, or other agents which lower the seizure threshold. Levofloxacin concentrations were about 13% higher in the presence of fenbufen than when administered alone.
Probenecid and cimetidine: Probenecid and cimetidine had a statistically significant effect on the elimination of levofloxacin. The renal clearance of levofloxacin was reduced by cimetidine (24%) and probenecid (34%). This is because both drugs are capable of blocking the renal tubular secretion of levofloxacin. However, at the tested doses in the study, the statistically significant kinetic differences are unlikely to be of clinical relevance. Caution should be exercised when levofloxacin is coadministered with drugs that effect the tubular renal secretion such as probenecid and cimetidine, especially in renal impaired patients.
Other relevant information: Clinical pharmacology studies have shown that the pharmacokinetics of levofloxacin were not affected to any clinically relevant extent when levofloxacin was administered together with the following drugs: calcium carbonate, digoxin, glibenclamide, ranitidine.
Fertility, pregnancy and lactation
Pregnancy Category C: There are limited amount of data from the use of levofloxacin in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity. However, in the absence of human data and due to that experimental data suggest a risk of damage by fluoroquinolones to the weight-bearing cartilage of the growing organism, levofloxacin must not be used in pregnant women.
OVERDOSAGE:
Levofloxacin exhibits a low potential for acute toxicity. In the event of an acute overdosage, the stomach should be emptied. The patient should be observed and appropriate hydration maintained. Levofloxacin is not efficiently removed by hemodialysis or peritoneal dialysis.
INSTRUCTIONS:
Store below 30°C. Protect from heat, light & moisture. Keep all medicines out of the reach of children. To be sold on the prescription of a registered medical practitioner only.
PRESENTATION:
Dlevo (Levofloxacin) Tablets U.S.P. 250mg are available in Alu-Alu blister pack of 1x10's with leaf insert.
Dlevo (Levofloxacin) Tablets U.S.P. 500mg are available in Alu-Alu blister pack of 1x10's with leaf insert.

Manufactured for:
Daneen Pharma (Pvt.) Ltd.
27-Sundar Industrial Estate, Sundar Raiwind Road Lahore, Pakistan.
Tel: +92-42-35297781-2, **Email:** info@daneenpharma.com
ISO 9001:2015 ISO 14001:2015 ISO 45001:2018
www.daneenpharma.com

Manufactured by:
Genix Pharma (Pvt.) Ltd.
44,45-B, Korangi Creek Road, Karachi-75190, Pakistan.
UAN: +92-21-111-10-10-11, **Email:** info@genixpharma.com
ISO 9001:2015 ISO 14001:2015 ISO 45001:2018
www.genixpharma.com