LEVOFLOXACIN (Systemic)

Indications

Accepted

Bronchitis, bacterial exacerbations (treatment)¾Levofloxacin is indicated in the treatment of bacterial exacerbations of bronchitis caused by Haemophilus influenzae , Haemophilus parainfluenzae , Moraxella catarrhalis , Staphylococcus aureus , or Streptococcus pneumoniae1.

Pneumonia, community-acquired (treatment)¾Levofloxacin is indicated in the treatment of community-acquired pneumonia caused by Chlamydia pneumoniae , H. influenzae , H. parainfluenzae , Klebsiella pneumoniae , Legionella pneumophila , M. catarrhalis , Mycoplasma pneumoniae , S. aureus , or S. pneumoniae1.

Pyelonephritis (treatment)¾Levofloxacin is indicated in the treatment of pyelonephritis caused by Escherichia coli1.

Sinusitis (treatment)¾Levofloxacin is indicated in the treatment of sinusitis caused by H. influenzae , M. catarrhalis , or S. pneumoniae1.

Skin and soft tissue infections (treatment)¾Levofloxacin is indicated in the treatment of skin and soft tissue infections caused by S. aureus or Streptococcus pyogenes1.

Urinary tract infections, bacterial, complicated (treatment)¾Levofloxacin is indicated in the treatment of complicated bacterial urinary tract infections caused by Enterobacter cloacae , Enterococcus faecalis , E. coli , K. pneumoniae , Proteus mirabilis , or Pseudomonas aeruginosa1.

Precautions to Consider

Cross-sensitivity and/or related problems

Patients allergic to one fluoroquinolone or other chemically related quinolone derivatives (e.g., cinoxacin, nalidixic acid) may be allergic to other fluoroquinolones also 1.

Carcinogenicity/Tumorigenicity

In a long-term study in rats, levofloxacin did not show carcinogenic or tumorigenic potential after daily dietary administration for 2 years. The highest dose was two times the recommended human dose or 10 times the recommended human dose based on body surface area or body weight, respectively. 1

Mutagenicity

Levofloxacin was not mutagenic in the Ames test (Salmonella typhimurium and Escherichia coli ), CHO/HGPRT forward mutation assay, mouse micronucleus test, mouse dominant lethal assay, rat unscheduled DNA synthesis assay, and the mouse sister chromatid exchange assay. It was positive in the in vitro chromosomal aberration (CHL cell line) and sister chromatid exchange (CHL/IU cell line) assays. 1

Pregnancy/Reproduction

Fertility¾Levofloxacin had no effect on the fertility or reproductive performance of male and female rats at oral doses of up to 360 mg per kg of body weight (mg/kg), or 2124 mg per square meter of body surface area (mg/m 2), per day, corresponding to 18 and 3 times the maximum recommended human dose (MRHD) based on body weight and body surface area, respectively, or at intravenous doses of up to 100 mg/kg, or 590 mg/m 2, per day, corresponding to 5 and 1 times the MRHD based on body weight and body surface area, respectively. 1

Pregnancy¾Adequate and well-controlled studies in humans have not been done. Since levofloxacin has been shown to cause arthropathy in immature animals, use is recommended in pregnancy only if the potential benefit to the mother outweighs the potential risk to the fetus. 1

Levofloxacin was not teratogenic in rats at oral doses of up to 810 mg/kg, or 4779 mg/m 2, per day, corresponding to 82 and 14 times the MRHD based on body weight and body surface area, respectively, or at intravenous doses of up to 160 mg/kg, or 944 mg/m 2, per day, corresponding to 16 and 2.7 times the MRHD based on body weight and body surface area, respectively. Doses equivalent to 81 and 26 times the MRHD of levofloxacin, based on body weight and body surface area, respectively, caused decreased fetal body weight and increased fetal mortality in rats when administered orally at doses of 810 mg/kg, or 8910 mg/m 2, per day. No teratogenicity was observed when rabbits were given oral doses of up to 50 mg/kg, or 550 mg/m 2, per day, corresponding to 5 and 1.6 times the MRHD based on body weight and body surface area, respectively, or at intravenous doses of up to 25 mg/kg, or 275 mg/m 2, per day, corresponding to 2.5 and 0.8 times the MRHD based on body weight and body surface area, respectively. 1

FDA Pregnancy Category C 1.

Breast-feeding

It is not known whether levofloxacin is distributed into breast milk 1 ; however, based on data for ofloxacin, it is expected that levofloxacin is distributed into human milk 1.

Because of the potential for serious adverse effects in nursing infants, a decision should be made to either stop breast-feeding or discontinue taking levofloxacin 1.

Pediatrics

Safety and efficacy have not been established in patients up to 18 years of age 1.

Fluoroquinolones have been shown to cause arthropathy and osteochondrosis in immature animals of several species 1.

Geriatrics

The pharmacokinetics of levofloxacin are not altered in elderly patients with normal renal function 1.

Following a 500-mg oral dose of levofloxacin, the mean elimination half-life was approximately 7.6 hours in healthy elderly subjects, as compared with 6 hours in younger adults 1.

The difference was attributed to variation in renal function and was not believed to be clinically significant 1.

Drug interactions and/or related problems

The following drug interactions and/or related problems have been selected on the basis of their potential clinical significance (possible mechanism in parentheses where appropriate)¾not necessarily inclusive (>> = major clinical significance):

Note: Unlike other fluoroquinolones, levofloxacin does not alter the pharmacokinetics of cyclosporine, digoxin, theophylline, or warfarin 1.

Combinations containing any of the following medications, depending on the amount present, may also interact with this medication.
>> Antacids, aluminum-, calcium-, and/or magnesium-containing 1 or

>> Ferrous sulfate 1 or

>> Sucralfate 1 or

>> Zinc 1

(antacids, ferrous sulfate, sucralfate, and zinc may reduce absorption of levofloxacin by chelation, resulting in lower serum and urine concentrations 1 ; therefore, concurrent use is not recommended 1 ; it is recommended that levofloxacin be taken at least 2 hours before or 2 hours after taking any of these agents 1 )

>> Antidiabetic agents 1

(concurrent administration has resulted in hyperglycemia or hypoglycemia, usually in diabetic patients who are taking oral hypoglycemic agents or insulin 1 ; careful monitoring of blood glucose is recommended 1 )

>> Anti-inflammatory drugs, nonsteroidal 1

(concurrent use may increase the risk of central nervous system [CNS] stimulation and seizures 1 )

Cimetidine 1 or

Probenecid 1

(concurrent use of levofloxacin with cimetidine or probenecid increases the area under the plasma concentration-time curve [AUC] by 27 to 38% and 30%, respectively, and decreases the clearance by 21 to 35% 1 ; although these differences are statistically significant, the changes are not considered high enough to warrant a change in dose 1 )

Laboratory value alterations

The following have been selected on the basis of their potential clinical significance (possible effect in parentheses where appropriate)¾not necessarily inclusive (>> = major clinical significance):
With physiology/laboratory test values

>> Glucose, blood 1

(concentrations may be increased or decreased 1 )

Lymphocytes 1

(counts may be decreased 1 )

Medical considerations/Contraindications

The medical considerations/contraindications included have been selected on the basis of their potential clinical significance (reasons given in parentheses where appropriate)¾ not necessarily inclusive (>> = major clinical significance).
Except under special circumstances, this medication should not be used when the following medical problem exists

>> Previous allergic reaction to fluoroquinolones or other chemically related quinolone derivatives 1

Risk-benefit should be considered when the following medical problems exist

CNS disorders, including cerebral arteriosclerosis or epilepsy 1

(levofloxacin may cause CNS stimulation or toxicity, increasing the risk of seizures in patients with these conditions 1 )

>> Diabetes mellitus 1

(levofloxacin has been reported to cause hyperglycemia and hypoglycemia, usually in diabetic patients who are taking oral hypoglycemic agents or insulin 1 ; diabetic patients should be carefully monitored 1 )

>> Renal function impairment 1

(levofloxacin is renally excreted 1 ; it is recommended that patients with a creatinine clearance of less than 50 mL per minute receive a reduced dosage of levofloxacin 1 )

Side/Adverse Effects

Note: There have been reports of ruptures of the Achilles tendon and of tendons in the shoulder and hand that required surgical repair or resulted in prolonged disability in patients taking levofloxacin or other fluoroquinolones. Patients should discontinue levofloxacin if they experience pain, inflammation, or rupture of a tendon. They should rest and refrain from exercise until the diagnosis of tendinitis or

tendon rupture has been excluded. Tendon rupture can occur at any time during or after levofloxacin therapy. 1

The following side/adverse effects have been selected on the basis of their potential clinical significance (possible signs and symptoms in parentheses where appropriate)¾not necessarily inclusive:
Those indicating need for medical attention