

Size: 280 (L) x 420 (H) mm

Folding size: 30 x 150 mm

↓ Front side

Paper 35 to 50 gsm

Carton size: 36 x 18 x 90 mm



LEVOFLOXACIN

LEVOBACT

500 mg Film-Coated Tablet

750 mg Film-Coated Tablet

ANTIBACTERIAL

PRODUCT NAME:
Levobact

DOSAGE FORM AND STRENGTH:
Levofloxacin Tablets 500/750mg

PHARMACOLOGIC CATEGORY:
Antibacterial

PRODUCT DESCRIPTION
Levofloxacin Tablets 500/750mg: Brownish Pink coloured, oblong shaped, film-coated tablets with a breakline on one surface

FORMULATION/COMPOSITION:
Each film-coated tablet contains:
Levofloxacin Hemihydrate equivalent to
Levofloxacin500 mg /750 mg

PHARMACODYNAMICS/PHARMACOKINETICS:

Pharmacodynamics:
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 mechanism of action of Levofloxacin and other fluoroquinolone antimicrobials involves inhibition of bacterial topoisomerase IV and DNA gyrase (both of which are type II topoisomerases), enzymes required for DNA replication, transcription, repair and recombination.

Pharmacokinetics:

Absorption
Levofloxacin is rapidly and essentially completely absorbed after oral administration. Peak plasma concentrations are usually attained one to two hours after oral dosing. The absolute bioavailability of Levofloxacin from a 500 mg tablet and a 750 mg tablet of Levofloxacin are both approximately 99%, demonstrating complete oral absorption of Levofloxacin. Following a single intravenous dose of Levofloxacin to healthy volunteers, the mean \pm SD peak plasma concentration attained was 6.2 ± 1.0 mcg/mL after a 500 mg dose infused over 60 minutes and 11.5 ± 4.0 mcg/mL after a 750 mg dose infused over 90 minutes.

Levofloxacin pharmacokinetics is linear and predictable after single and multiple oral or IV dosing regimens. Steady-state conditions are reached within 48 hours following a 500 mg or 750 mg once-daily dosage regimen. The mean \pm SD peak and trough plasma concentrations attained following multiple once-daily oral dosage regimens were approximately 5.7 ± 1.4 and 5.0 ± 0.2 mcg/mL after the 500 mg doses, and 8.6 ± 1.9 and 1.1 ± 0.4 mcg/mL after the 750 mg doses, respectively. The mean \pm SD peak and trough plasma concentrations attained following multiple once-daily IV regimens were approximately 6.4 ± 0.8 and 6.0 ± 0.2 mcg/mL after the 500 mg doses, and 12.1 ± 4.1 and 1.3 ± 0.7 mcg/mL after the 750 mg doses, respectively. Oral administration of a 500 mg dose of Levofloxacin with food prolongs the time to peak concentration by approximately 1 hour and decreases the peak concentration by approximately 14% following tablet and approximately 25% following oral solution administration. Therefore, Levofloxacin Tablets can be administered without regard to food.

Distribution

The mean volume of distribution of Levofloxacin generally ranges from 74 to 112 L after single and multiple 500 mg or 750 mg doses, indicating widespread distribution into body tissues. Levofloxacin reaches its peak levels in skin tissues and in blister fluid of healthy subjects at approximately 3 hours after dosing. The skin tissue biopsy to plasma AUC ratio is approximately 2 and the blister fluid to plasma AUC ratio is approximately 1 following multiple once-daily oral administrations of 750 mg and 500 mg doses of Levofloxacin, respectively, to healthy subjects. Levofloxacin also penetrates well into lung tissues. Lung tissue concentrations were generally 2- to 5-fold higher than plasma concentrations and ranged from approximately 2.4 to 11.3 mcg/g over a 24-hour period after a single 500 mg oral dose.

In vitro, over a clinically relevant range (1 to 10 mcg/mL) of serum/plasma Levofloxacin concentrations, Levofloxacin is approximately 24 to 38% bound to serum proteins across all species studied, as determined by the equilibrium dialysis method. Levofloxacin is mainly bound to serum albumin in humans. Levofloxacin binding to serum proteins is independent of the drug concentration.

Metabolism

Levofloxacin is stereo chemically stable in plasma and urine and does not invert metabolically to its enantiomer, D-Ofloxacin. Levofloxacin undergoes limited metabolism in humans and is primarily excreted as unchanged drug in the urine. Following oral administration, approximately 87% of an 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 identified in humans. These metabolites have little relevant pharmacological activity.

Excretion

Levofloxacin is excreted largely as unchanged drug in the urine. The mean terminal plasma elimination half-life of Levofloxacin ranges from approximately 6 to 8 hours following single or multiple doses of Levofloxacin given orally or intravenously. The mean apparent total body clearance and renal clearance range from approximately 144 to 226 mL/min and 96 to 142 mL/min, respectively. Renal clearance in excess of the glomerular filtration rate suggests that tubular secretion of Levofloxacin occurs in addition to its glomerular filtration. Concomitant administration of either cimetidine or probenecid results in approximately 24% or 35% reduction in the Levofloxacin renal clearance, respectively, indicating that secretion of Levofloxacin occurs in the renal proximal tubule. No Levofloxacin crystals were found in any of the urine samples freshly collected from subjects receiving Levofloxacin.

Geriatric

There are no significant differences in Levofloxacin pharmacokinetics between young and elderly subjects when the subjects' differences in creatinine clearance are taken into consideration. Following a 500 mg oral dose of Levofloxacin to healthy elderly subjects (66 – 80 years of age), the mean terminal plasma elimination half-life of Levofloxacin was about 7.6 hours, as compared to approximately 6 hours in younger adults. The difference was attributable to the variation in renal function status of the subjects and was not believed to be clinically significant. Drug absorption appears to be unaffected by age. Levofloxacin dose adjustment based on age alone is not necessary.

Pediatrics

The pharmacokinetics of Levofloxacin following a single 7 mg/kg intravenous dose was investigated in pediatric patients ranging in age from 6 months to 16 years. Pediatric patients cleared Levofloxacin faster than adult patients, resulting in lower plasma exposures than adults for a given mg/kg dose. Subsequent pharmacokinetic analyses predicted that a dosage regimen of 8 mg/kg every 12 hours (not to exceed 250 mg per dose) for pediatric patients 6 months to 17 years of age would achieve comparable steady state plasma exposures (AUC₀₋₂₄ and C_{max}) to those observed in adult patients administered 500 mg of Levofloxacin once every 24 hours.

Gender

There are no significant differences in Levofloxacin pharmacokinetics between male and female subjects when subjects' differences in creatinine clearance are taken into consideration. Following a 500 mg oral dose of Levofloxacin to healthy male subjects, the mean terminal plasma elimination half-life of Levofloxacin was about 7.5 hours, as compared to approximately 6.1 hours in female subjects. This difference was attributable to the variation in renal function status of the male and female subjects and was not believed to be clinically significant. Drug absorption appears to be unaffected by the gender of the subjects. Dose adjustment based on gender alone is not necessary.

Race

The effect of race on Levofloxacin pharmacokinetics was examined through a covariate analysis performed on data from 72 subjects: 48 white and 24 non-whites. The apparent total body clearance and apparent volume of distribution were not affected by the race of the subjects.

Renal Impairment

Clearance of Levofloxacin is substantially reduced and plasma elimination half-life is substantially prolonged in patients with impaired renal function (creatinine clearance < 50 mL/min), requiring dosage adjustment in such patients to avoid accumulation. Neither hemodialysis nor continuous ambulatory peritoneal dialysis (CAPD) is effective in removal of Levofloxacin from the body, indicating that supplemental doses of Levofloxacin are not required following hemodialysis or CAPD.

Hepatic Impairment

Pharmacokinetic studies in hepatically impaired patients have not been conducted. Due to the limited extent of Levofloxacin metabolism, the pharmacokinetics of Levofloxacin is not expected to be affected by hepatic impairment.

INDICATIONS:

Levobact tablets are indicated for the treatment of adults (≥ 18 years of age) with mild, moderate, and severe infections caused by susceptible strains of the designated microorganisms in the conditions listed below:

Culture and susceptibility testing

Appropriate culture and susceptibility tests should be performed before treatment in order to isolate and identify organisms causing the infection and to determine their susceptibility to Levofloxacin. Therapy with Levofloxacin may be initiated before results of these tests are known; once results become available, appropriate therapy should be selected. As with other drugs in this class, some strains of *Pseudomonas aeruginosa* may develop resistance fairly rapidly during treatment with Levofloxacin. Culture and susceptibility testing performed periodically during therapy will provide information about the continued susceptibility of the pathogens to the antimicrobial agent and also the possible emergence of bacterial resistance.

Nosocomial Pneumonia

It is indicated for the treatment of Nosocomial pneumonia due to methicillin-susceptible *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Serratia marcescens*, *Escherichia coli*, *Klebsiella pneumoniae*, *Haemophilus influenzae*, or *Streptococcus pneumoniae*. Adjunctive therapy should be used as clinically indicated. Where *Pseudomonas aeruginosa* is a documented or presumptive pathogen, combination therapy with an anti-pseudomonal β -lactam is recommended.

Community-Acquired Pneumonia: 7–14 day Treatment Regimen

Levofloxacin is indicated for the treatment of community-acquired pneumonia due to methicillin-susceptible *Staphylococcus*

aureus, *Streptococcus pneumoniae* (including multi-drug-resistant *Streptococcus pneumoniae* [MDRSP]), *Haemophilus influenzae*, *Haemophilus parainfluenzae*, *Klebsiella pneumoniae*, *Moraxella catarrhalis*, *Chlamydophila pneumoniae*, *Legionella pneumophila*, or *Mycoplasma pneumoniae*.

Community-Acquired Pneumonia: 5-day Treatment Regimen

Levofloxacin is indicated for the treatment of community-acquired pneumonia due to *Streptococcus pneumoniae* (excluding multi-drug-resistant strains [MDRSP]), *Haemophilus influenzae*, *Haemophilus parainfluenzae*, *Mycoplasma pneumoniae*, or *Chlamydophila pneumoniae*.

Acute Bacterial Sinusitis: 5-day and 10–14 day Treatment Regimens

It is indicated for the treatment of acute bacterial sinusitis due to *Streptococcus pneumoniae*, *Haemophilus influenzae*, or *Moraxella catarrhalis*.

Acute Bacterial Exacerbation of Chronic Bronchitis

It is indicated for the treatment of acute bacterial exacerbation of chronic bronchitis due to methicillin-susceptible *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Haemophilus parainfluenzae*, or *Moraxella catarrhalis*.

Complicated Skin and Skin Structure Infections

It is indicated for the treatment of complicated skin and skin structure infections due to methicillin-susceptible *Staphylococcus aureus*, *Enterococcus faecalis*, *Streptococcus pyogenes*, or *Proteus mirabilis*.

Uncomplicated Skin and Skin Structure Infections

It is indicated for the treatment of uncomplicated skin and skin structure infections (mild to moderate) including abscesses, cellulitis, furuncles, impetigo, pyoderma, wound infections, due to methicillin-susceptible *Staphylococcus aureus*, or *Streptococcus pyogenes*.

Chronic Bacterial Prostatitis

It is indicated for the treatment of chronic bacterial prostatitis due to *Escherichia coli*, *Enterococcus faecalis*, or methicillin-susceptible *Staphylococcus epidermidis*.

Complicated Urinary Tract Infections: 5-day Treatment Regimen

Levofloxacin is indicated for the treatment of complicated urinary tract infections due to *Escherichia coli*, *Klebsiella pneumoniae*, or *Proteus mirabilis*.

Complicated Urinary Tract Infections: 10-day Treatment Regimen

It is indicated for the treatment of complicated urinary tract infections (mild to moderate) due to *Enterococcus faecalis*, *Enterobacter cloacae*, *Escherichia coli*, *Klebsiella pneumoniae*, *Proteus mirabilis*, or *Pseudomonas aeruginosa*.

Acute Pyelonephritis: 5 or 10-day Treatment Regimen

It is indicated for the treatment of acute pyelonephritis caused by *Escherichia coli*, including cases with concurrent bacteremia.

Uncomplicated Urinary Tract Infections

It is indicated for the treatment of uncomplicated urinary tract infections (mild to moderate) due to *Escherichia coli*, *Klebsiella pneumoniae*, or *Staphylococcus saprophyticus*.

Inhalational Anthrax (Post-Exposure)

Levofloxacin is indicated for inhalational anthrax (post-exposure) to reduce the incidence or progression of disease following exposure to aerosolized *Bacillus anthracis*. The effectiveness of it is based on plasma concentrations achieved in humans, a surrogate marker considered likely to predict clinical benefit. Levofloxacin has not been tested in humans for the post-exposure prevention of inhalation anthrax. The safety of Levofloxacin adults for durations of therapy beyond 28 days or in pediatric patients for durations of therapy beyond 14 days has not been studied. Prolonged Levofloxacin therapy in adults should only be used when the benefit outweighs the risk.

DOSAGE AND MODE ROUTE OF ADMINISTRATION:

Dosage in Adult Patients with Normal Renal Function

The usual dose of Levofloxacin Tablets or Oral Solution is 250 mg, 500 mg, or 750 mg administered orally every 24 hours, as indicated by infection and described in Table 1. These recommendations apply to patients with creatinine clearance ≥ 50 mL/min. For patients with creatinine clearance < 50 mL/min, adjustments to the dosing regimen are required.

Table 1: Dosage in Adult Patients with Normal Renal Function (creatinine clearance ≥ 50 mL/min)

Type of Infection*	Dosed Every 24 hours	Duration (days)†
* Due to the designated pathogens.		
‡ Sequential therapy (intravenous to oral) may be instituted at the discretion of the physician.		
§ Due to methicillin-susceptible <i>Staphylococcus aureus</i> , <i>Streptococcus pneumoniae</i> (including multi-drug-resistant isolates [MDRSP]), <i>Haemophilus influenzae</i> , <i>Haemophilus parainfluenzae</i> , <i>Klebsiella pneumoniae</i> , <i>Moraxella catarrhalis</i> , <i>Chlamydophila pneumoniae</i> , <i>Legionella pneumophila</i> , or <i>Mycoplasma pneumoniae</i> .		
¶ Due to <i>Streptococcus pneumoniae</i> (excluding multi-drug-resistant isolates [MDRSP]), <i>Haemophilus influenzae</i> , <i>Haemophilus parainfluenzae</i> , <i>Mycoplasma pneumoniae</i> , or <i>Chlamydophila pneumoniae</i> .		
■ This regimen is indicated for cUTI due to <i>Escherichia coli</i> , <i>Klebsiella pneumoniae</i> , <i>Proteus mirabilis</i> and AP due to <i>E. coli</i> , including cases with concurrent bacteremia.		
# This regimen is indicated for cUTI due to <i>Enterococcus faecalis</i> , <i>Enterococcus cloacae</i> , <i>Escherichia coli</i> , <i>Klebsiella pneumoniae</i> , <i>Proteus mirabilis</i> , and <i>Pseudomonas aeruginosa</i> ; and for AP due to <i>E. coli</i> .		
□ Drug administration should begin as soon as possible after suspected or confirmed exposure to aerosolized <i>B. anthracis</i> . This indication is based on a surrogate endpoint. Levofloxacin plasma concentrations achieved in humans are reasonably likely to predict clinical benefit.		
△ The safety of Levofloxacin in adults for durations of therapy beyond 28 days or in pediatric patients for durations beyond 14 days has not been studied. An increased incidence of musculoskeletal adverse events compared to controls has been observed in pediatric patients. Prolonged Levofloxacin therapy should only be used when the benefit outweighs the risk.		
▲ Drug administration should begin as soon as possible after suspected or confirmed exposure to <i>Yersinia pestis</i> . Higher doses of Levofloxacin typically used for treatment of pneumonia can be used for treatment of plague, if clinically indicated.		
Nosocomial Pneumonia	750 mg	7–14
Community Acquired Pneumonia‡	500 mg	7–14
Community Acquired Pneumonia§	750 mg	5
Acute Bacterial Sinusitis	750 mg	5
	500 mg	10–14
Acute Bacterial Exacerbation of Chronic Bronchitis	500 mg	7
Complicated Skin and Skin Structure Infections (SSSI)	750 mg	7–14
Uncomplicated SSSI	500 mg	7–10
Chronic Bacterial Prostatitis	500 mg	28
Complicated Urinary Tract Infection (cUTI) or Acute Pyelonephritis (AP)¶	750 mg	5
Complicated Urinary Tract Infection (cUTI) or Acute Pyelonephritis (AP)#	250 mg	10

MICRO LABS LIMITED, BANGALORE, INDIA					
1	Product Name	Levobact		Colours Used	
2	Strength	500 mg & 750 mg		<input checked="" type="checkbox"/> BLACK	
3	Component	Leaflet			
4	Category	Export - Philippines			
5	Dimension	280 (L) x 420 (H) mm			
6	Artwork Code	EXG-ML01I-0539/D			
7	Pharma Code	N/A			
8	Reason for Change	Size, text and Distributed by deleted			
		Prepared by (DTP)	Checked by (PD)	Approved by	
Sign	Date			Head CQA	Head Production/ Packing (Site)
	Kantharaju L.				
	26-07-2023				