Tavaquin® 250 mg, 500mg, 750mg
Film-coated tablets (levofloxacin).

Composition
Active ingredient: levofloxacin.
Each film – coated tablet contains 250 mg (marked 130), 500 mg (marked 131) and 750 mg (marked 132) of levofloxacin corresponding to 256.23 mg, 512.46 mg & 768.69 mg of levofloxacin hemihydrate, respectively.
Excipients: Core: Povidone, Croscarmellose Sodium, Microcrystalline Cellulose, Sodium Benzoate, and Magnesium Stearate.
Coating: Methylhydroxypropylcellulose, Titanium Dioxide, Polyethylene Glycol,

Properties
Pharmaco- therapeutic class: Antibacterial (J: Antiinfectives for systemic use).
Levofloxacin is a synthetic antibacterial fluoroquinolone for oral and intravenous use.
As a fluoroquinolone antibacterial agent, levofloxacin inhibits bacterial DNA synthesis by acting on the DNA gyrase complex and topoisomerase IV. Levofloxacin is highly bactericidal in vitro. Its spectrum covers many Gram-positive and Gram-negative bacteria such as staphylococci, streptococci including pneumococci, enterobacteriaceae, Haemophilus influenzae, non-fermentative Gram- negative bacteria and atypical microorganisms. There is generally no-cross resistance between levofloxacin and other classes of antibacterial agents. Nocosomial infections due to Pseudomonas aeruginosa may require combination therapy.
Following oral administration, levofloxacin is rapidly absorbed. The absolute bioavailability is approximately 100%. Food has little effect on the absorption of levofloxacin. Approximately 30-40% of levofloxacin are bound to serum protein. Steady state is achieved within 3 days. Penetration into bone tissue, blister fluid, and lung tissue is good but is poor into cerebro-spinal fluid. Levofloxacin is metabolized to a very small extent, the two metabolites account for < 5% of the dose excreted in urine. Levofloxacin is eliminated relatively slowly from the plasma (t½= 6-8h). Excretion is primarily by the renal route (> 85% of the administered dose). With decreasing renal function, renal elimination and clearance are decreased and elimination half-lives increased (for a creatinine clearance comprised between 20-40 ml /min, t½ is 27 hours). There are no major differences in the pharmacokinetic parameters following oral or intravenous administration, suggesting that the oral and intravenous routes are interchangeable.

When should this drug be used (Therapeutic indications)
Tavaquin is indicated for the treatment of the following infections due to levofloxacin susceptible microorganisms:
- Acute sinusitis,
- Acute exacerbation of chronic bronchitis,
  Community-acquired pneumonia,
  Complicated urinary tract infections including pyelonephritis,
- Skin and soft tissue infection,
- Prostatitis,

How should this drug be used
Strictly follow the recommended dosage unless directed otherwise by the physician.
The dosage depend on the type and severity of the infection and the sensitivity of the presumed causative pathogen.

DOSAGE AND ADMINISTRATION
Dosage in patients with Normal Renal Function
The usual dose of **Tavaquin** Tablets is 250mg, 500mg, or 750mg administered orally every 24 hours, as indicated by infection and described in Table(1).
Table(1): Dosage in patients with normal renal function (Creatinine clearance ≥ 50ml / min).

Type of Infection	Dosed Every 24 hours	Duration (days)
Nosocomial Pneumonia	750 mg	7-14
Community Acquired Pneumonia[1]	500 mg	7-14
Community Acquired Pneumonia[2]	750 mg	5
Acute Bacterial Sinusitis	750 mg	5
	500 mg	10-14
Acute Bacterial Exacerbation of Chronic Bronchitis	500 mg	
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)[3]	750 mg	5
Complicated Urinary Tract Infection (cUTI) or Acute Pyelonephritis (AP)[4]	250 mg	10
Uncomplicated Urinary Tract Infection	250 mg	3
Inhalational Anthrax (Post-Exposure), adult[5]	500 mg	60

1. Due to methicillin – susceptible Staphylococcus aureus, Streptococcus pneumoniae (including multi – drug-resistant strains [MDRSP], Haemophilus influenzae, Haemophilus parainfluenzae, Klebsiella pneumoniae, Moraxella catarrhalis, Chlamydophila pneumoniae, Legionella pneumophila, or Mycoplasma pneumoniae.
2. Due to Streptococcus pneumoniae (excluding multi-drug-resistant strains [MDRPS]), Haemophilus influenzae, Haemophilus parainfluenzae, Mycoplasma pneumoniae, or Chlamydophila pneumoniae .
3. This regimen is indicated for cUTI due to Escherichia coli, Klebsiella pneumoniae, Proteus mirabilis and AP due to E. coli, including cases with concurrent bacteremia.
4. This regimen is indicated for cUTI due t Enterococcus faecalis, Enterococcus cloacae, Escherichia coli, Klebsiella pneumoniae, Proters mirabilis, Pseudomonas aeruginosa; and for AP due to E. coli.
5. The safety of Levofloxacin in adults for durations of therapy beyond 28 days has not been studied. Prolonged Levofloxacin therapy in adults should only be used when the benefit outweighs the risk.

Table (2): Dosage adjustment in patients with renal impairment (creatinine clearance < 50 ml / min)

750 mg	750 mg every 48 hours	750 mg initial dose, then 500 mg every 48 hours.	750 mg initial dose, then 500 mg every 48 hours.
500 mg	500 mg initial dose, then 250 mg every 24 hours	500 mg initial dose, then 250 mg every 48 hours.	500 mg initial dose, then 250 mg every 48 hours.
250 mg	No dosage adjustment required	250 mg every 48 hours. If treating uncomplicated UTI, then no dosage adjustments is required.	No information on dosing adjustment is available.

Special populations
No dosage adjustment is required in patients with impaired liver function.
No dosage adjustment is necessary in elderly patients. However, special attention to renal function should be paid in elderly patients, and the dosage should be adapted accordingly.

Method of administration
Tavaquin tablets should be swallowed without crushing and with sufficient amount of liquid. Only **Tavaquin** 500 mg may be divided at the score line to adapt the dosage. The tablets may be taken during meals or between meals.

When should this drug not be used (Contraindications)
Tavaquin is contraindicated:
In patients hypersensitive (allergic) to levofloxacin, other quinolones or to any of its excipients,
In patients with epilepsy,
In patients with history of tendon disorders related to fluoroquinolone administration,
In children or adolescents,
During pregnancy and in breast – feeding women.

Warnings and precautions
In patients predisposed to seizures, for example in case of simultaneous medications (see Interactions), and as with other quinolones, levofloxacin should be used with extreme caution.
Diarrhea, particularly if severe, persistent and / or bloody, during or after treatment with levofloxacin, may be symptomatic of pseudo-membranous colitis due to Clostridium difficile. If pseudo-membranous colitis is suspected, levofloxacin must be stopped immediately.
Tendinitis, rarely observed with quinolones, may occasionally lead rupture involving Achilles tendon in particular. This undesirable effect may occur with 48 hous of starting of treatment and may be bilateral. Elderly patients are more prone to tendonitis. The risk of tendon rupture may be increased by coadministration of corticosteroids. If tendonitis is suspected, treatment with levofloxacin must be stopped IMMEDIATELY ant the affected tendons must be put at rest.
In patients with renal impairment, since levofloxacin is excreted mainly by the kidneys, the dose of levofloxacin should be adjusted.
- Although photosensitization is very rare with levofloxacin, it is recommended that patients should not expose themselves unnecessarily to strong sunlight or to artificial UV rays.
- As with other antibiotics, the use of levofloxacin, especially if prolonged, may result in overgrowth of non-susceptible organisms. Repeated evaluation of the patient's condition is essential. If superinfection occurs during treatment, appropriate measures should be taken.
  Patients with latent or actual defects in glucose-6-phosphate dehydrogenase activity may be prone to hemolytic reactions when treated with quinolone antibacterial agents. This has to be taken into consideration when using levofloxacin.

If you have diabetes and you develop a hypoglycemic reaction while taking **Tavaquin** tablets, you should stop taking it and call your doctor.

Driving
Levofloxacin may cause undesirable effects such as dizziness, vertigo, drowsiness and visual disturbances, which may constitute a risk in situations such as driving a car or operating machinery.

Overdose
In case of overdose, contact immediately your physician.
According to toxicity studies in animals, the most important signs to be expected following acute overdose of levofloxacin are central nervous system symptoms such as confusion, dizziness, impairment of consciousness, and convulsive seizures, gastro-intestinal reactions such as nausea and mucosal erosions.
In clinical pharmacology studies performed with a supra-therapeutic dose increase in QT interval has been seen.
In the event of overdose the patients should be carefully observed (including ECG monitoring) and symptomatic treatment should be implemented. In case of acute oral overdose, gastric lavage should also be considered and antacids may be used for protection of gastric mucosa. Haemodialysis, including peritoneal dialysis and CAPD, are not effective in removing levofloxacin from the body. No specific antidote exists.

Interactions
In order to avoid possible interactions with other medicines, inform your physician or pharmacist about any other current treatment.
There is no clinically relevant interaction with food. It is recommended that preparations containing divalent or trivalent cations such as iron salts or magnesium-or alumininum-containing antacids should not be taken 2 hours before or after levofloxacin administration, because of a possible reduction in absorption. The bioavailability of levofloxacin is significantly reduced when administered together with sucralfate, so it is recommended to administer sucralfate 2 hours after the levofloxacin administration.
No pharmacokinetic interaction 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, fenbufen or similar non-steroidal anti-inflammatory drugs or other agents, which lower the seizure threshold.
Caution should be exercised when levofloxacin is co-administered with drugs that affect the tubular renal secretion such as probenecid and cimetidine, especially in renally impaired patients.
Increased coagulation tests (PT/INR) and /or bleeding, which may be severe, have been reported in patients treated with levofloxacin in combination with a vitamin K antagonist (e.g. warfarin). Coagulation tests, therefore, should be monitored in patients treated with vitamin K antagonists.

Undesirable effects
Please tell your physician or pharmacist, if you experience any adverse effect with the use of this product.
Frequencies of undesirable effects: common (> 1/100 and < 1/10), uncommon (> 1/1000 and < 1/100), rare (1/10000> and < 1/1000), very rare (< 1/10000), including isolated reports.
The following undesirable effects may occur with the use of **Tavaquin**:
Gastrointestinal system: Common: Nausea, diarrhea, flatulence; Uncommon: Anorexia (loss of appetite), vomiting, dyspepsia (upset stomach), abdominal pain; Rare: bloody diarrhea which in very rare cases may be indicative of enterocolitis, including pseudomembranous colitis (severe bowel inflammation); Vary rare: Hypoglycemia (reduction in blood sugar) particularly in diabetic patients.
Skin and allergic reactions: vaginitis may be common in women; Uncommon: Rash, pruritus (itching); Rare: Urticaria (skin itching eruption), bronchospasm/ dyspnea (difficulty in breathing), Very rare: Quincke's oedema (swelling of the face, tongue, throat or larynx), hypotension (reduced blood pressure), anaphylactic/oid shock (severe allergic reaction of sudden onset), photosensitization; Isolated cases of severe bullous eruptions such as Steven's Johnson syndrome (skin and mucous membrane bullous reactions), toxic epidermal necrolysis (Lyell's syndrome, i.e., bullous reactions) and erythema exudativum multiforme (red inflammatory rash withformation of blisters). Muco-cutaneous and anaphylactic/anaphylactoid reactions may sometimes occur even after the first dose.
Nervous system: Uncommon: Headache, restlessness, dizziness/vertigo, drowsiness and insomnia, nightmares; Rare: Depression, anxiety, psychotic reactions (with e.g. hallucinations), paresthesia (abnormal sensations such as numbness, tingling and burning), tremor, agitation, confusion, convulsion, suicidal thoughts or acts Very rare: Hypoesthesia (decreased sensitivity to stimulation or sensations), visual and auditory disturbances, taste and smell disorders.
If neuropathy symptoms occur such as pain, burning, tingling, numbness, weakness, or other alterations of sensation (including feelings of vibration, temperature or touch sensitivity), you should stop taking **Tavaquin** tablets and contact your doctor immediately.
Cardiovascular system: Rare: Tachycardia (rapid heart rate), hypotension; Very rare: shock anaphylactic/anaphylactoid; Isolated cases: QT-interval prolongation (see section Overdose).
Muscle and skeleton: Rare Arthralgia (joint pain), myalgia (muscle pain), tendon disorders including tendonitis (inflammation of tendons, e.g. Achilles tendon); Very rare: Tendon rupture, muscular weakness which may be of special importance in patients with myasthenia gravis (chronic progressive muscle disease); Isolated case of rhabdomyolysis (dissolution of the muscle).
Liver and kidney: Common: Increase in liver enzymes (transaminases ALT and AST); Uncommon: Increase in bilirubin and serum creatinine; Very rare: Hepatitis and acute kidney failure.
Blood: Uncommon: Eosinophilia (increase in the number of certain white blood cells) and leucopenia (reduction in the number of white blood cells); Rare: Neutropenia (mild to severe reduction in the number of certain white blood cells) and thrombocytopenia (decrease in the number of platelets); Very rare: Agranulocytosis (insufficient number or absence of certain white blood cells); Isolated cases of hemolytic anemia (significant reduction in the number of red blood cells) and pancytopenia (pronounced reduction in the number of all blood cells).
Others: Uncommon: Asthenia (weakness), fungal overgrowth and proliferation of other resistant microorganisms; Very rare: Allergic pneumonitis (inflammation of the lung), fever. Other possible undesirable effects related to the class of fluoroquinolones: Very rare: Extrapyramidal symptoms and other disorders of musculare coordination, hypersensitivity vasculitis (inflammation of blood vessels) and attacks of porphyria (metabolic disease) in patients with porphyria.

Storage
Store at a temperature not to exceed 30°C.

Expiry date
Do not use later than the date of expiry indicated on the outer packaging.

Presentations
Film – coated tablets
250 mg tablets: pack of 7 tablets in PVC aluminium blisters.
500 mg scored tablets: pack of 7 tablets in PVC aluminium blisters.
750 mg tablets: pack of 7 tablets in PVC aluminium blisters.

This is a medicament:
- A medicament is a product that affects your health, and its consumption contrary to instructions is dangerous for you.
- follow strictly the doctors prescription, the method of use and the instructions of the pharmacist who sold the medicament.
- the doctor and pharmacist are expert in medicine , its benefits and risks.
- do not by yourself interrupt the period of treatment prescribed for you.
- do not repeat the same prescription without consulting your doctor.
- keep out of reach of children.

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