LEFLOX (Levofloxacin) is available for oral administration as film-coated tablets.

**LEFLOX (Levofloxacin) Tablets**

LEFLOX (Levofloxacin) is a synthetic broad-spectrum antibacterial agent. Chemically, levofloxacin, a chiral fluoroquinolone, is the (R)-5-fluoro-6-(pteridin-3-ylcarbonyl)-3-carboxylic acid hemihydrate. The molecular formula is C_{17}H_{18}FN_{2}O_{5} and the structural formula is:

![Chemical Structure]

**QUALITATIVE AND QUANTITATIVE COMPOSITION**

LEFLOX (Levofloxacin) Tablets contain levofloxacin as the active ingredient.

**CLINICAL PHARMACOLOGY**

**Mechanism of Action**

Levofloxacin is the L-isomer of the racemate, ofloxacin, a quinolone antibiotic. The antibacterial activity of ofloxacin resides primarily in the L-isomer. The main mechanism of action of levofloxacin involves the inhibition of bacterial topoisomerase IV and DNA gyrase (both of which are type II topoisomerases), enzymes required for DNA replication, transcription, repair, and recombination. Levofloxacin has in vitro activity against a broad range of gram-negative and gram-positive microorganisms. It is often used in the treatment of respiratory, urinary, and skin infections.

**Microbiology**

Levofloxacin has been shown to be active against most strains of the following microorganisms both in vitro and in clinical infections:

- Common susceptible species: *Acinetobacter baumannii*, *Aerobic Gram-negative bacteria*, *Bacteroides fragilis*, *Bacteroides vulgatus*, *B. fragilis group C* and *G. Staphylococcus aureus*, *Streptococcus pneumoniae*, *Streptococcus pyogenes*.
- Aerobic Gram-negative bacteria: *Escherichia coli*, *Enterobacter aerogenes*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*.
- Anaerobic bacteria: *Peptostreptococcus*.
- Other: *Chlamydia pneumoniae*, *Chlamydia psittaci*, *Chlamydia trachomatis*, *Legionella pneumophila*, *Mycoplasma pneumoniae*, *Streptococcus pneumoniae*, *Streptococcus pyogenes*.

**Species for which acquired resistance may be a problem**

Aerobic Gram-positive bacteria: *Staphylococcus aureus*, *Streptococcus pyogenes*, *Streptococcus pneumoniae*.

**Anaerobic Gram-negative bacteria**

*Aeromonas hydrophila*, *Citrobacter freundii*, *Enterobacter aerogenes*, *Enterobacter agglomerans*, *Enterobacter cloacae*, *Escherichia coli*, *Morganella morganii*, *Proteus mirabilis*, *Providencia stuartii*, *Pseudomonas aeruginosa*, *Serratia marcescens*.

**Anaerobic bacteria**

*Prevotella melaninogenica*, *Bacteroides ovatus*, *Bacteroides thetaiotaomicron*, *Bacteroides vulgatus*.

**Dosage in normal renal function**

**Dosage in patients with impaired renal function**

**Dosage in patients with normal renal function**

<table>
<thead>
<tr>
<th>INDICATIONS</th>
<th>DAILY DOSE</th>
<th>DURATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute Bacterial Sore Throat</td>
<td>750mg</td>
<td>3 - 7</td>
</tr>
<tr>
<td>Acute Bacterial Exacerbation of Chronic Bronchitis</td>
<td>750mg</td>
<td>3 - 5</td>
</tr>
<tr>
<td>Community Acquired Pneumonia</td>
<td>750mg</td>
<td>7 - 14</td>
</tr>
<tr>
<td>Uncomplicated Skin and Soft Tissue Infections</td>
<td>750mg</td>
<td>7 - 10</td>
</tr>
<tr>
<td>Uncomplicated Urinary Tract Infections</td>
<td>750mg</td>
<td>3 - 10</td>
</tr>
<tr>
<td>Complicated Skin and Soft Tissue Infections</td>
<td>750mg</td>
<td>7 - 14</td>
</tr>
<tr>
<td>Uncomplicated Urinary Tract Infections</td>
<td>750mg</td>
<td>3 - 10</td>
</tr>
<tr>
<td>Acute Pyelonephritis</td>
<td>750mg</td>
<td>3 - 10</td>
</tr>
<tr>
<td>Intestinal Bacterial Prostate</td>
<td>750mg</td>
<td>26</td>
</tr>
</tbody>
</table>

**Dosage in adults patients with impaired renal function**

**Dosage in normal renal function**

<table>
<thead>
<tr>
<th>DOSAGE</th>
<th>DAILY DOSE</th>
<th>CREATIVE CLAIRANCE (KmL/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute Bacterial Sore Throat</td>
<td>750mg</td>
<td>50 to 80</td>
</tr>
<tr>
<td>Acute Bacterial Exacerbation of Chronic Bronchitis</td>
<td>750mg</td>
<td>50 to 80</td>
</tr>
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<td>750mg</td>
<td>50 to 80</td>
</tr>
</tbody>
</table>

**Drug interactions**

Levofloxacin concentrations were about 13% higher in the presence of fenbufen than without fenbufen. Levofloxacin is metabolized in the liver by oxidation to form an active metabolite, which is the primary drug responsible for the antibacterial activity. Levofloxacin is excreted in the urine and is not removed by hemodialysis or peritoneal dialysis.

**Adverse Reactions**

- Levetac is usually well tolerated. However, following are the adverse effects reported during therapy:
  - Common: Abdominal pain, nausea, diarrhea, vomiting, dyspepsia, rash, pruritus, mnmalia, abdominal pain, vomiting, dyspepsia, rash, pruritus, vangitis, edema, chest pain.
Levofloxacin is the pure (-)-(S)-enantiomer of ofloxacin, a quinolone antimicrobial agent. It is the L-isomer of the racemate, ofloxacin, a fluorinated carboxyquinolone. Levofloxacin is the pure enantiomer of ofloxacin and is available as a single-entity product.

**CONTRAINDICATIONS**
- Patients with a history of hypersensitivity to this drug and/or quinolone antibacterials.
- Children or growing adolescents.

**WARNING**
- Fluoroquinolones, including Levofloxacin 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 corticosteroids, drugs, and/or in patients with kidney, heart or lung transplant patients.
- Fluoroquinolones, including Levofloxacin may exacerbate muscle weakness in persons with myasthenia gravis. Acute in patients with known history of myasthenia gravis.
- Serious adverse events requiring ventilatory support have been associated with fluoroquinolones use, in persons with myasthenia gravis.

**PRECAUTIONS**
- Although levofloxacin is more soluble than other quinolones, adequate hydration of patients receiving levofloxacin should be maintained to prevent the formation of highly concentrated urine.
- Tendinitis and tendon rupture: Tendinitis may rarely occur. It most frequently involves the Achilles tendon and may lead to tendon rupture. The risk of tendinitis and tendon rupture is increased in the elderly and in patients using corticosteroids. Close monitoring of these patients is therefore necessary if they are prescribed levofloxacin. All patients should consult their physician if they experience symptoms of tendinitis.
- Closstridium difficile-associated disease: Although levofloxacin is more soluble than other quinolones, adequate hydration of patients receiving levofloxacin should be maintained to prevent the formation of highly concentrated urine.
- Clostridium difficile-associated disease: Although levofloxacin is more soluble than other quinolones, adequate hydration of patients receiving levofloxacin should be maintained to prevent the formation of highly concentrated urine.
- Prevention of photodermatosis: Although photodermatosis is very rare with levofloxacin, it is recommended that patients should not expose themselves unnecessarily to strong sunlight or to artificial UV rays (e.g. sunray lamp, solarium), in order to prevent photodermatosis.
- Patients treated with Vitamin K antagonists: Due to possible increase in coagulation tests (PT/INR) and/or bleeding in patients treated with levofloxacin, concomitant treatment with warfarin and similar non-steroidal anti-inflammatory drugs or with drugs which lower the cerebral seizure threshold, such as theophylline.

**THERAPEUTIC INDICATIONS**
- Treatment of acute bacterial sinusitis.
- Treatment of acute exacerbation of chronic bronchitis in patients with known risk factors for prolongation of the QT interval such as, for example:
  - Congential long QT syndrome
  - Congential use of drugs that are known to prolong the QT interval (e.g. Class IA and III antiarrhythmics, tricyclic antidepressants, macrolides, antipsychotics).
  - Uncorrected electrolyte imbalance (e.g., hypokalemia, hypomagnesemia).
  - Asthma.
  - Cardiac disease (e.g., heart failure, myocardial infarction, bradycardia).

**Peripheral neuropathy**
Sensory or sensorimotor peripheral neuropathy has been reported in patients receiving fluoroquinolones, including Levofloxacin, which can be rapidly in its onset. Le floxacin should be discontinued if the patient experiences symptoms of neuropathy in order to prevent the development of an irreversible condition.

**Impotence**
In patients treated with Levofloxacin, determination of erectile function may give false positive results. It may be necessary to confirm positive erectile function by methods more specific method.

**Hepatobiliary disorders**
Patients should be advised to stop treatment and contact their doctor if signs and symptoms suggestive of hepatic disease develop such as anorexia, jaundice, dark urine, pruritus or tender abdomen.

**Renal Insufficiency**
Clearance of levofloxacin is substantially reduced and plasma elimination half-life is substantially prolonged in patients with impaired renal function (creatinine clearance <50mL/min), requiring dosage adjustment in such patients to avoid accumulation. Neither intermittent nor continuous ambulatory peritoneal dialysis (CAPD) is effective in removal of levofloxacin from the body, indicating that supplemental doses of levofloxacin are impractical following hemodialysis or CAPD.

**Geriatric Use**
Caution should be used when prescribing Levofloxacin to elderly patients especially those on concurrent drugs. Patients should be informed of these potential side-effects and advised to discontinue levofloxacin and contact their healthcare provider if any symptoms of tendinitis or tendon rupture occur.

**Pregnancy**
There are no adequate and well-controlled studies in pregnant women. Levofloxacin should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

**Nursing Mothers**
Because of the potential for serious adverse reactions from levofloxacin in nursing infants, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

**Drug Interactions**
Antibiotics, Surfactants, Metal Cations: Concurrent administration of levofloxacin with antibiotics containing maganese, or aluminum, as well as surfactable metal cations such as iron and multivitamin preparations with zinc or diezomal can interfere with the gastrointestinal absorption of levofloxacin resulting in systemic levels considerably lower than desired. These agents should be taken at least 2 hours before or 2 hours after levofloxacin administration.

Thyroid, anti-estrogen, or similar non-steroidal anti-inflammatory drugs: Pronounced lowering of the cerebral seizure threshold may occur when quinolones are given concomitantly 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 fenbital than when administered alone.

Probenecid and Cimetidine: 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.

**Cyclosporine:** The half-life of ciclosporine was increased by 33% when co-administered with levofloxacin.

**Lithium:** There have been reports in patients that levofloxacin enhances the effects of warfarin. Prothrombin time, international normalized Ratio (INR) or other suitable anticoagulation tests should be closely monitored if Levofloxacin is administered concomitantly with warfarin. Patients should also be monitored for evidence of bleeding.

**OVERDOSAGE**
In the event of overdose, symptomatic treatment should be implemented. ECG monitoring should be undertaken, because of the possibility of QT interval prolongation. In these cases, Levofloxacin, is a quinolone antibacterials agent and so levofloxacin should be used with caution.

**STORAGE**
Store below 30°C.
Protect from sunlight.
The expiration date refers to the product correctly stored at the required conditions.

Keep out of reach of children.
To be sold on prescription of a registered medical practitioner only.