Summary of Product Characteristics for Pharmaceutical Products

1. Name of the medicinal product:

ZLEVO 500, film coated tablets

2. Qualitative and quantitative composition

Each film coated tablet contains: 500 mg of Levofloxacin Hemihydrate For one film coated tablet

3. Pharmaceutical form

Red colored caplet shape film coated tablets break line on one side and plain on other side.

4. Clinical particulars

4.1 Therapeutic indications

Levofloxacin Tablets USP 500mg is indicated in below conditions -
Acute bacterial sinusitis
In above-mentioned infections, Levofloxacin tablets product should be used only when it is considered inappropriate to use other antibacterial agents that are commonly recommended for the treatment of these infections
Community-acquired pneumonia
Complicated skin and soft tissue infections / Complicated skin and skin structure infection. For the above-mentioned infections, Levofloxacin tablets should be used only when it is considered inappropriate to use antibacterial agents that are commonly recommended for the treatment of these infections.
Acute pyelonephritis and complicated urinary tract infections (see section 4.4)
Chronic bacterial prostatitis
Uncomplicated cystitis (see section 4.4) In above-mentioned infections, Levofloxacin tablets product should be used only when it is considered inappropriate to use other antibacterial agents that are commonly recommended for the treatment of these infections • Inhalation Anthrax: postexposure prophylaxis and curative treatment (see section 4.4)
Acute exacerbation of chronic obstructive pulmonary disease including bronchitis. In above- mentioned infections, Levofloxacin tablets product should be used only when it is considered inappropriate to use other antibacterial agents that are commonly recommended for the treatment of these infections
Levofloxacin tablets may also be used to complete a course of therapy in patients who have shown improvement during initial treatment with intravenous levofloxacin. Consideration should be given to official guidance on the appropriate use of antibacterial agents.

4.2 Posology and method of administration

Posology

Weight (Age)	Dose per administration	Administration interval	**Maximum daily dose**
Adults and children ≥ 15 years (≥50 Kg)	500 mg (1 tablet)	Every 24 hours	500 mg/day

Usual dose: 500 mg once daily depending on infection and clinical response.

Do not exceed 500 mg/day.

Renal impairment

Dose adjustment required:

Creatinine clearance (CrCl) Recommended dosing

≥ 50 mL/min- 500 mg once daily

20–49 mL/min - 500 mg every 48 hours or 500 mg once, then 250 mg daily

< 20 mL/min- 500 mg initially, then 250 mg every 48 hours

Hemodialysis/Peritoneal dialysis- Same as < 20 mL/min (not dialyzable)

Hepatic impairment : No adjustment required.

Use caution in severe liver disease due to QT prolongation risk or interacting medicines. Special clinical situations

Use with caution in:

- Elderly patients (tendon rupture, CNS effects)
- Patients receiving corticosteroids
- Seizure disorders or concomitant pro-convulsant drugs
- G6PD deficiency (hemolysis risk)
- QT prolongation or use of QT-prolonging agents

Method of administration

Oral use

Swallow tablets whole with water May be taken with or without foodFrequency of administration

- Once daily at the same time each day
- Maintain adequate hydration

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1. Levofloxacin tablets USP 500mg must not be used: in patients hypersensitive to levofloxacin or other quinolones or to any of the excipients in patients with epilepsy, in patients with history of tendon disorders related to fluoroquinolone administration, in children or growing adolescents, during pregnancy, in breast-feeding women.

4.4 Special warnings and precautions for use

Levofloxacin should be used only when antibacterial treatment is clearly indicated to limit the risk of resistance.

Use with extreme caution in:

- elderly patients (higher susceptibility to tendon injury and CNS adverse effects)
- patients with renal impairment (dose adjustment required)

Tendinitis and tendon rupture may occur, sometimes during the first 48 hours or months after treatment. Risk is increased in:

- patients over 60 years
- those on corticosteroids
- transplant recipients (kidney, heart, lung)

Treatment should be stopped immediately at the first sign of tendon pain, swelling or inflammation.

QT interval prolongation has been reported. Risk is increased in patients with:

- known QT prolongation
- uncorrected electrolyte imbalance (e.g., hypokalemia)
- cardiac disease (heart failure, MI, bradycardia),concomitant QT prolonging medicines
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Levofloxacin may cause:

- CNS reactions including confusion, hallucinations, tremor and seizures
- peripheral neuropathy (potentially irreversible; discontinue if symptoms develop)

Patients should avoid driving or operating machinery if dizziness, visual disturbances or CNS effects occur (see section 4.7).

Photosensitivity is rare but patients should avoid excessive sunlight or UV

exposure.
Clostridioides difficile–associated diarrhea may occur; discontinue treatment if suspected.

Precautions for use

Levofloxacin should be used cautiously in patients with:

- renal impairment (reduce dose according to creatinine clearance)

a history of seizures or on drugs lowering seizure threshold

- diabetes mellitus, particularly when receiving insulin or oral hypoglycemics (risk of dysglycaemia)
- glucose-6-phosphate dehydrogenase (G6PD) deficiency (risk of hemolysis)
- myasthenia gravis (may exacerbate muscle weakness)
- CNS disorders, including stroke

history or psychiatric illness Avoid use in:

- patients with documented tendon disorders related to fluoroquinolone use
- known QT prolongation unless no alternative is suitablerug interactions that may increase adverse effects include:

- corticosteroids (tendon rupture risk)
- NSAIDs and theophylline (lower seizure threshold)
- antiarrhythmics, antipsychotics, macrolides, tricyclic antidepressants (QT prolongation risk)

Maintain hydration to prevent crystalluria and renal complications.

Warnings related to excipients

- Microcrystalline cellulose, maltodextrin, croscarmellose sodium, polacrillin potassium May cause gastrointestinal discomfort in sensitive individuals.
  PVP K30, sodium starch/cross povidone

  Rare risk of hypersensitivity reactions (rash, pruritus).

- Magnesium stearate, sodium stearyl fumarate, talc, colloidal silicon dioxide

  Generally well tolerated; may cause mild GI effects at high levels.

- Iron oxide yellow

  May trigger rare allergic reactions in predisposed patients.

 Film coating polymers (Pure coat/Ansh Coat)

  Possible hypersensitivity, especially in patients allergic to coating materials.

Purified water, IPA, MDC (evaporates)

Residual solvents are below safety thresholds; no expected clinical risk.

4.5 Interaction with other medicinal products and other forms of interaction

Central nervous system (CNS) effects
Concomitant administration with:

- NSAIDs (e.g., ibuprofen, diclofenac)
- Theophylline
- Tramadol

May lower the seizure threshold, increasing risk of convulsions, particularly in predisposed patients.

Drugs prolonging the QT interval

Levofloxacin may enhance QT prolongation when given with:

- Antiarrhythmics (e.g., amiodarone, sotalol)
- Macrolides (e.g., erythromycin)
- Antipsychotics (e.g., haloperidol, olanzapine)
- Tricyclic antidepressants

Use cautiously in patients with known QT prolongation or electrolyte disturbances.

Corticosteroids
Systemic corticosteroids increase the risk of tendonitis and tendon rupture, especially in elderly patients. Avoid co-use unless necessary.

Antidiabetic agents

Insulin and oral hypoglycemics (e.g., glibenclamide) Risk of dysglycaemia (hypo- or hyperglycemia). Monitor blood glucose closely during therapy.

Warfarin and other vitamin K antagonists

Co-administration may increase INR and bleeding risk.

Monitor coagulation parameters, particularly in elderly or frail patients.

Antacids and multivalent cation products

- Antacids containing aluminum/magnesium
- Iron salts
- Zinc supplements

- Sucralfate

These reduce levofloxacin absorption.

Administer levofloxacin at least 2 hours before or after these products.

Probenecid and cimetidine

Reduce renal tubular secretion of levofloxacin → may increase plasma levels. Use with caution in renal impairment.

4.6 Pregnancy and Lactation

Pregnancy

There is 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 the experimental risk of damage by fluoroquinolones to the weight-bearing cartilage of the growing organism, Levofloxacin tablets must not be used in pregnant women.

Breast-feeding

Levofloxacin is contraindicated in breast-feeding women. There is insufficient information on the excretion of levofloxacin in human milk; however other fluoroquinolones are excreted in breast milk. In the absence of human data and due to the experimental data suggest a risk of damage by fluoroquinolones to the weight-bearing cartilage of the growing organism, Levofloxacin tablets must not be used in breast-feeding women.

Fertility

Levofloxacin caused no impairment of fertility or reproductive performance in rats.

4.7 Effects on ability to drive and use machines

Certain undesirable effects (e.g. dizziness / vertigo, drowsiness, visual disturbances) may impair the patient's ability to concentrate and react, and therefore may constitute a risk in situations where these abilities are of special importance (e.g. driving a car or operating machinery).

4.8 Undesirable effects

Levofloxacin may cause gastrointestinal upset and CNS effects. Most reactions are mild to moderate and reversible.

Immune system disorders

- Rare: hypersensitivity reactions (rash, pruritus, urticaria)
- Very rare: anaphylaxis
  → Discontinue immediately if signs of allergy occur.

Nervous system

- Common: headache, dizziness, insomnia
- Uncommon: tremor, paraesthesia
- Rare: seizures (particularly in predisposed patients), peripheral neuropathy (may be irreversible) → Stop treatment if neuropathic symptoms occur.

Gastrointestinal

- Common: nausea, diarrhea, abdominal pain
- Uncommon: vomiting, dyspepsia
- Rare: antibiotic-associated colitis including *C. difficile* colitis → Discontinue and treat appropriately if suspected.

Psychiatric

- Uncommon: anxiety, agitation, confusion
- Rare: hallucinations, depression, psychotic reactions
- Very rare: suicidal thoughts/behavior (usually reversible on withdrawal)

Skin

- Uncommon: rash, pruritus
- Rare: photosensitivity reactions
- Very rare: severe cutaneous reactions (SJS, TEN) → Stop treatment if skin reactions develop.

Musculoskeletal

- Uncommon: arthralgia, myalgia
- Rare: tendinitis and tendon rupture (Achilles tendon most common) Risk increased in elderly and corticosteroid use.

Blood

- Rare: leukopenia, eosinophilia
- Very rare: neutropenia, thrombocytopenia, hemolytic anemia

Genitourinary

- Uncommon: dysuria, candidiasis
- Very rare: acute renal failure secondary to interstitial nephritis

Hepatic

- Uncommon: transient elevation of liver enzymes
- Rare: hepatitis
- Very rare: fulminant hepatic failure (mostly in patients with serious underlying disease)

Individuals should report any adverse reactions to National Regulatory authorities. Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product.

4.9 Overdose

Overdose risk is higher in patients with renal impairment, the elderly, and those taking interacting medicines (e.g., NSAIDs, theophylline).

Symptoms

Symptoms usually occur within several hours and may include:

- gastrointestinal symptoms: nausea, vomiting, abdominal pain
- central nervous system effects: dizziness, confusion, tremor, drowsiness
- seizures, particularly in predisposed patients or with NSAID co-use
- QT interval prolongation, palpitations or arrhythmias
- hallucinations, anxiety or agitation

Severe toxicity may lead to CNS depression, hypotension and metabolic disturbances.

Management

There is no specific antidote to levofloxacin. Emergency management should include:

- Immediate medical evaluation
- Maintenance of airway, adequate oxygenation and ventilation
- ECG monitoring due to risk of QT prolongation

- Seizure control with benzodiazepines if required
- Hydration support to enhance renal elimination

Hemodialysis or peritoneal dialysis are ineffective in removing levofloxacin.

Management is largely supportive and symptomatic until clinical recovery. Monitor renal function, electrolytes and ECG until stable.

Most patients recover with appropriate supportive care.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Quinolone Antibacterials-Fluroquinolone

ATC code: J01MA12

Levofloxacin is a broad-spectrum fluoroquinolone antibacterial (ATC J01MA12) that exerts a rapid bactericidal effect. It inhibits bacterial DNA gyrase and topoisomerase IV, enzymes essential for DNA replication, transcription and repair. Activity is concentration-dependent and associated with a post antibiotic effect. Levofloxacin is active against a range of respiratory and urinary pathogens, including Streptococcus pneumoniae, Hemophilus

5.2 Pharmacokinetic properties

Absorption

Orally administered levofloxacin is rapidly and almost completely absorbed with peak plasma concentrations being obtained within 1-2 hr. The absolute bioavailability is approximately 99- 100%.

Food has little effect on the absorption of levofloxacin.

Steady state conditions are reached within 48 hours following a 500 mg once or twice daily dosage regimen.Distribution

Approximately 30 – 40 % of levofloxacin is bound to serum protein.

The mean volume of distribution of levofloxacin is approximately 100 l after single and repeated 500 mg doses, indicating widespread distribution into body tissues.
Penetration into tissues and body fluids:

Levofloxacin has been shown to penetrate into in bronchial mucosa, epithelial lining fluid, alveolar macrophages, lung tissue, skin (blister fluid), prostatic tissue and urine. However, levofloxacin has poor penetration intro Cerebro-spinal fluid.

Metabolism

Levofloxacin is metabolized to a very small extent, the metabolites being desmethyl- levofloxacin and levofloxacin N-oxide. These metabolites account for < 5 % of the dose excreted in urine. Levofloxacin is stereo chemically stable and does not undergo chiral inversion.

Elimination

Following oral and intravenous administration of levofloxacin, it is eliminated relatively slowly from the plasma (t1/2 : 6 – 8 h). Excretion is primarily by the renal route > 85 % of the administered dose).

The mean apparent total body clearance of levofloxacin following a 500 mg single dose was 175 +/-29.2 ml/min.
There are no major differences in the pharmacokinetics of levofloxacin following intravenous and oral administration, suggesting that the oral and intravenous routes are interchangeable.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of single dose toxicity, repeated dose toxicity, carcinogenic potential and toxicity to reproduction and development.

Levofloxacin caused no impairment of fertility or reproductive performance in rats and its only effect on fetuses was delayed maturation as a result of maternal toxicity.
Levofloxacin did not induce gene mutations in bacterial or mammalian cells but did induce chromosome aberrations in Chinese hamster lung cells in vitro. These effects can be attributed to inhibition of topoisomerase II. In vivo tests (micronucleus, sister chromatid exchange, unscheduled DNA synthesis, dominant lethal tests) did not show any genotoxic potential.
Studies in the mouse showed levofloxacin to have phototoxic activity only at very high doses. Levofloxacin did not show any genotoxic potential in a photomutagenicity assay, and it reduced tumor development in a photocarcinogen study.
In common with other fluoroquinolones, levofloxacin showed

effects on cartilage (blistering and cavities) in rats and dogs. These findings were more marked in young animals.

6. Pharmaceutical Particulars

6.1 List of Excipients

Microcrystalline cellulose, Maltodextrine, Cross povidone, PVP K30, Purified water, Sodium stearyl fumarate, Magnesium stearate, Talcum, Croscarmellose sodium, Polacrillin potassium, Colloidal silicone dioxide, Pure coat Wt. 101 White Film Coating/Ansh Coat White, Col. Iron Oxide Yellow, ***IPA, ***MDC

6.2 Incompatibilities

Not applicable

6.3 Shelf-Life

36 months

6.4 Special Precautions for storage

Store below 30°C and protect from light.

6.5 Nature and Content of container

Ten tablets packed in one blister. One such blister packed in monocarton with package insert.

6.6 Special precautions for disposal and other handling

No special requirements.

7. Marketing Authorization Holder

Lexine Technochem Pvt. Ltd. Opp Ramakaka Deri, Chhani, Vadodara- 391 740, Gujarat, India.

8. Marketing Authorization Number

CTD2156

9. Date of first authorization/renewal of the authorization

14/10/2015

10. Date of revision of the text

27/02/2026