Summary of Product Characteristics for Pharmaceutical Products

1. Name of the medicinal product:

Safloxa® 500
Levofloxacin Tablets 500 mg
Safloxa® 750
Levofloxacin Tablets 750 mg

2. Qualitative and quantitative composition

Safloxa® 500
Each film coated tablet contains:
Levofloxacin Hemihydrate USP
Equivalent to Levofloxacin 500 mg
Excipients q.s.
(for the full list of excipients, see section 6.1)
Safloxa® 750
Each film coated tablet contains:
Levofloxacin Hemihydrate USP
Equivalent to Levofloxacin 750 mg
Excipients q.s.
(for the full list of excipients, see section 6.1)

3. Pharmaceutical form:

Safloxa® 500
Film coated tablet
Brick red colour, elongated shape, biconvex, film coated tablets, having break line on one sides & plain on other side.

Safloxa® 750
Film coated tablet
Brick red colour, elongated shape, biconvex, film coated tablets, having break line on one sides & plain on other side.

4. Clinical particulars

4.1 Therapeutic indications

Safloxa® is indicated for the treatment of the following bacterial infections in adults

- Community-acquired pneumonia
- Acute bacterial sinusitis
- Acute exacerbation of chronic obstructive pulmonary disease including bronchitis
- Complicated skin and soft tissue infections
- Acute pyelonephritis and complicate urinary tract infections
- Chronic bacterial prostatitis
- Uncomplicated cystitis
- Inhalation anthrax

4.2 Posology and method of administration

Posology

Levofloxacin tablets are administered once or twice daily for 7-14 days. The dosage depends on the type and severity of the infection and the sensitivity of the presumed causative pathogen. In cases such as chronic bacterial prostatitis it can be taken once daily for 28 days.

Method of administration

Oral use

Levofloxacin tablets should be swallowed without crushing and with sufficient amount of liquid. The tablets may be taken during meals or between meals, levofloxacin tablets should be taken at least 2 hours before or after iron salts, zinc salts, magnesium-or aluminium containing antacids or didanosine (only didanosine formulations with aluminium or magnesium containing buffering agents), and sucralfate administration since reduction of absorption can occur.

4.3 Contraindications

- in patients hypersensitive to levofloxacin or other quinolones or to any of the excipients listed in section 6.1
- 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

Tendinitis and Tendon Rupture

Fluoroquinolones, including ofloxacin, 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 corticosteroid drugs, and in patients with kidney, heart or lung transplants.

Myasthenia gravis

Fluoroquinolones, including levofloxacin, have neuromuscular blocking activity and may exacerbate muscle weakness in patients with myasthenia gravis. Levofloxacin is not recommended in patients with a known history of myasthenia gravis.

Peripheral neuropathy

Cases of sensory or sensorimotor polyneuropathy resulting in paraesthesia, hypaesthesia, dysesthesia, or weakness have been reported in patients receiving fluoroquinolones. Patients under treatment with Levofloxacin Tablets should be advised to inform their doctor prior to continuing treatment if symptoms of neuropathy such as pain, burning, tingling, numbness, or

weakness develop in order to prevent the development of potentially irreversible condition

Hepatobiliary disorders
Cases of hepatic necrosis up to life threatening hepatic failure have been reported with levofloxacin, primarily in patients with severe underlying diseases, e.g. sepsis. Patients should be advised to stop treatment and contact their doctor if signs and symptoms of hepatic disease develop such as anorexia, jaundice, dark urine, pruritus or tender abdomen.

QT interval prolongation
Caution should be taken when using fluoroquinolones, including levofloxacin, in patients with known risk factors for prolongation of the QT interval such as, for example:
- congenital long QT syndrome
- concomitant 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)
- Elderly patients and women may be more sensitive to QTc-prolonging medications.
- Therefore, caution should be taken when using fluoroquinolones, including levofloxacin, in these populations.

4.5 Interaction with other medicinal products and other forms of interaction.
Antidiabetic agents
Disturbances of blood glucose, including hypeglycemia and hypoglycaemia, have been reported in patients treated concomitantly with quinolones and an antidiabetic agent. Therefore, careful monitoring of blood glucose is recommended when these agents are co-administered.

NSAIDs: the concomitant administration with a quinolone, including levofloxacin, may increase the risk of CNS stimulation and convulsive seizures.

Cyclosporine: No significant effect of levofloxacin on the peak plasma concentrations, AUC, and other parameters for cyclosporine was detected in a clinical study involving healthy volunteers, elevated serum levels of cyclosporin have been reported in the patient population when coadministered with some quinolones. Levofloxacin Cma and ke were slightly lower while Tmax and t1/2 were slightly longer in the presence of cyclosporine than those observed in other studies without concomitant medication. The differences, however, are not considered, to be clinically significant. Therefore, no dosage adjustment is required for levofloxacin or cyclosporin when coadministered concomitantly.

Digoxin: No significant effect of levofloxacin on the peak plasma concentrations, AUC, and other disposition parameters for digoxin was

detected in a clinical study involving healthy volunteers. Levofloxacin absorption and disposition kinetics were similar in the presence of or absence of digoxin. Therefore, no dosage adjustment for administered concomitantly.

Probenecid and Cimetidine: No significant effect of probenecid or cimetidine on the Cmax of levofloxacin was observed in a clinical study involving healthy volunteers. The AUC and t1/2 of levofloxacin were higher while CL/F and CLR were lower during concomitant treatment of levofloxacin with probenecid or cimetidine compared to levofloxacin alone. However, these changes do not warrant dosage adjustment for Levofloxacin, probenecid or cimetidine when co-administered.

4.5 Fertility, pregnancy and lactation

Pregnancy

There are 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.

Breastfeeding

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

4.6 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed. However, undesirable effects may occur (e.g. allergic reactions, dizziness), which may influence the ability to drive and use machines.

4.8 Undesirable effects

Frequencies are defined using the following convention: very common (≥1/10), common (≥1/100, <1/10), uncommon (≥1/1000, ≤1/100), rare (≥1/10000, ≤1/1000), very rare (≤1/10000), not known (cannot be estimated from the available data).

System Organ Class	**Common (≥1/100 to <1/10)**	**Uncommon (≥1/1,000 to <1/100)**	**Rare (≥1/10,000 to <1/1,000)**	**Not known (cannot be estimated from available data)**
Infections and Infestations		Fungal infection including Candida infection;		

		Pathogen resistance		
Blood and Lymphatic system disorder		Leukopenia; Eosinophilia	Thrombocytopenia; Neutropenia	Bone marrow failure including aplastic anaemia, pancytopenia, agranulocytosis, haemolytic anaemia
Immune system Disorders			Angioedema; Hypersensitivity	Anaphylactic shock; Anaphylactoid shock
Metabolism and nutrition disorders		Anorexia	Hypoglycaemia (particularly in diabetic patients); Hypoglycaemic coma	Hyperglycaemia
Psychiatric Disorders	Insomnia	Anxiety; Confusional state; Nervousness	Psychotic reactions; Depression; Agitation; Abnormal dreams; Nightmares	Psychotic disorders with self-endangering behaviour; Mania
Nervous system Disorders	Headache; Dizziness	Somnolence; Tremor; Dysgeusia	Paraesthesia; Convulsion; Memory impairment	Peripheral sensory neuropathy; Peripheral sensorimotor neuropathy; Parosmia including anosmia; Dyskinesia; Extrapyramidal disorder
Eye disorders			Visual disturbances such as blurred vision	Transient vision loss; Uveitis
Ear and Labyrinth disorders		Vertigo	Tinnitus	Hearing loss; Hearing impaired
Cardiac Disorders			Tachycardia; Palpitation	Ventricular tachycardia; Ventricular

				arrhythmia and torsade de pointes; QT prolonged
Vascular Disorders			Hypotension	
Respiratory, thoracic and mediastinal disorders		Dyspnoea		Bronchospasm; Pneumonitis allergic
Gastrointestinal disorders	Diarrhoea; Vomiting; Nausea	Abdominal pain; Dyspepsia; Flatulence; Constipation		Pancreatitis; Diarrhoea – haemorrhagic
Hepatobiliary Disorders	Hepatic enzyme increased (ALT/AST, alkaline phosphatase, GGT)	Blood bilirubin increased		Jaundice and severe liver injury; Hepatitis
Skin and subcutaneous tissue disorders		Rash; Pruritus; Urticaria; Hyperhidrosis	DRESS; Fixed drug eruption	Toxic epidermal necrolysis; Stevens-Johnson syndrome; Erythema multiforme; Photosensitivity reaction; Leukocytoclastic vasculitis; Stomatitis; Skin hyperpigmentation
Musculoskeletal and connective tissue disorders		Arthralgia; Myalgia	Tendon disorders including tendinitis	Tendon rupture; Rhabdomyolysis; Ligament rupture; Muscle rupture; Arthritis
Renal and Urinary disorders		Blood creatinine increased	Renal failure acute	
General disorders and administration site conditions		Asthenia	Pyrexia	Pain (including pain in back, chest, and extremities)

Endocrine disorders			Syndrome of inappropriate secretion of antidiuretic hormone (SIADH)	

a Anaphylactic and anaphylactoid reactions may sometimes occur even after the first dose
b Mucocutaneous reactions may sometimes occur even after the first dose
Other undesirable effects which have been associated with fluoroquinolone administration include:
- attacks of porphyria in patients with porphyria

* Very rare cases of prolonged (up to months or years), disabling and potentially irreversible serious drug reactions affecting several, sometimes multiple, system organ classes and senses (including reactions such as tendonitis, tendon rupture, arthralgia, pain in extremities, gait disturbance, neuropathies associated with paraesthesia, fatigue, psychiatric symptoms memory and concentration impairment, and impairment of hearing, vision, taste and smell) have been reported in association with the use of quinolones and fluoroquinolones in some cases irrespective of pre-existing risk factors.

A range of psychiatric symptoms may occur as part of these side effects, which may include, but are not necessarily limited to, sleep disorders, anxiety, panic attacks, confusion, or depression. There are no pharmacological treatments established to be effective treatments of the symptoms of long lasting or disabling side effects associated with fluoroquinolones. The frequency of these prolonged, disabling and potentially irreversible serious drug reactions cannot be estimated with precision using available data, but the reporting incidence from adverse drug reaction reports indicates the frequency is at minimum between 1/1,000 and 1/10,000 (corresponding to the rare frequency category).

** Cases of aortic aneurysm and dissection, sometimes complicated by rupture (including fatal ones), and of regurgitation/incompetence of any of the heart valves have been reported in patients receiving fluoroquinolones.

Reporting of suspected adverse reactions
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. Healthcare professionals are asked to report any suspected adverse reactions via pharmacy and poisons board, Pharmacovigilance Electronic Reporting System (PvERS) https://pv.pharmacyboardkenya.org.

4.9 Overdose
According to toxicity studies in animals or clinical pharmacology studies performed with supra- therapeutic doses, the most important signs to be expected following acute overdosage of Levofloxacin tablets are central nervous system symptoms such as confusion, dizziness, impairment of consciousness, and convulsive seizures, increases in QT interval as well as gastro- intestinal reactions such as nausea and mucosal erosions.
CNS effects including confusional state, convulsion, hallucination, and tremor have been observed in post marketing experience.
In the event of overdose, symptomatic treatment should be implemented, ECG monitoring should be undertaken, because of the possibility of QT interval prolongation. 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.

5. Pharmacological properties
5.1 Pharmacodynamic properties
Pharmacotherapeutic group: Quinolone antibacterials - Fluroquinolone
ATC code: J01MA12

Mechanism of action
Levofloxacin is a broad-spectrum antibiotic that is active against both Gram-positive and Gram-negative bacteria. It functions by inhibiting DNA gyrase, a type II topoisomerase, and topoisomerase iv, which is an enzyme necessary to separate replicated DNA, thereby inhibiting cell division.

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.

Biotransformation
Levofloxacin is metabolised 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 stereochemically 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
None available

6. Pharmaceutical particulars
6.1 List of Excipients:
Safloxa® 500

- Microcrystalline cellulose
- Starch
- Sodium Starch Glycollate
- Methyl Paraben sodium
- Propyl Paraben Sodium
- Croscarmellose sodium
- Aerosil
- Purified Talc
- Magnesium Stearate
- Film coat
- Methylene Dichloride
- PEG 6000
- Red Oxide of Iron Lake

Safloxa® 750

- Microcrystalline cellulose
- Starch
- Sodium Starch Glycollate
- Methyl Paraben sodium
- Propyl Paraben Sodium
- Croscarmellose sodium
- Aerosil
- Purified Talc
- Magnesium Stearate
- Kyron-T 314
- Film coat
- Methylene Dichloride
- PEG 6000
- Red Oxide of Iron Lake

6.2 Incompatibilities
Not applicable

6.3 Shelf life
Safloxa® 500 & Safloxa® 750
36 months.

6.4 Special precautions for storage
Store below 30°C, Protect from direct sunlight, heat & moisture.

6.5 Nature and contents of container
Safloxa® 500 is available as 1 x 10 tablets in Alu-Alu blister pack.
Safloxa® 750 is available as 1 x 10 tablets in Alu-Alu blister pack.

6.6 Special precautions for disposal and other
Any unused medicine product or waste material should be disposed of in accordance with the local requirements.

7. Marketing authorization holder and manufacturing site addresses
Safloxa® 500 & Safloxa® 750
Manufactured in India by:
MAGBRO HEALTHCARE PVT. LTD
Village Mehsa Tibba,
P.O. Manjholi, Teh. Nalagarh,
Distt. Solan-174 101 (HP) India

Manufactured For & Marketed by:
KRISHNA CHEMISTS LTD.
P.O. BOX 3328-00506
NAIROBI, KENYA.

8. Marketing authorisation number(s)
Safloxa® 500
CTD4447
Safloxa® 750
CTD4448
9. Date of first Registration/ Renewal of Registration
10. Date of revision of text
06/01/2025