PROPOSED PROFESSIONAL INFORMATION FOR

LEVOFLOXACIN UNICORN

SCHEDULING STATUS

S4

1. NAME OF THE MEDICINE

LEVOFLOXACIN UNICORN 250 film coated tablet

LEVOFLOXACIN UNICORN 500 film coated tablet

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film coated **LEVOFLOXACIN UNICORN 250** tablet contains levofloxacin hemihydrate equivalent to 250 mg levofloxacin.

Each film coated **LEVOFLOXACIN UNICORN 500** tablet contains levofloxacin hemihydrate equivalent to 500 mg levofloxacin.

Sugar free.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

LEVOFLOXACIN UNICORN 250: Light peach coloured, capsule shaped, film coated tablet, scored on both sides and debossed with “J” and “250” on either side of the score line on one side of tablet.

LEVOFLOXACIN UNICORN 500: Light peach coloured, capsule shaped, film coated tablet, scored on both sides and debossed with “J” and “500” on either side of the score line on one side of tablet.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

LEVOFLOXACIN UNICORN can be used in adults, in the treatment of the following bacterial infections:

Acute exacerbations of chronic bronchitis: caused by *H. influenzae*, *K. pneumoniae*, methicillin-sensitive *S. aureus*, *M. catarrhalis*, *E. coli*, *H. parainfluenzae* or *S. pneumoniae*.

Pneumonia (community acquired): caused by *H. influenzae*, *S. pneumoniae*, methicillin-sensitive *S. aureus*, *M. catarrhalis*, *H. parainfluenzae*, *K. pneumoniae*, *E. coli*, *Mycoplasma pneumoniae*, *Chlamydia pneumoniae* or *Legionella pneumophila*.

Sinusitis: caused by *H. influenzae*, *S. pneumoniae*, methicillin-sensitive *S. aureus*, *M. catarrhalis* or *H. parainfluenzae*.

Urinary tract infections (complicated) and acute pyelonephritis: caused by *E. coli*, *K. pneumoniae*, *E. faecalis*, *P. mirabilis*, *Enterobacter cloacae* and *P. aeruginosa**.

Uncomplicated urinary tract infections in women: caused by *E. coli*.

Skin and soft tissue infections (uncomplicated): caused by methicillin-sensitive *S. aureus*, *S. pyogenes*, *Acinetobacter calcoaceticus*, *E. cloacae*, *P. mirabilis*, *P. aeruginosa**, *E. coli*, *K. pneumoniae* or *E. faecalis*.

Skin and soft tissue infections (complicated): caused by methicillin-sensitive *S. aureus*, *S. pyogenes*, *P. mirabilis*, *E. coli*, *K. pneumoniae*, *E. faecalis*, *E. cloacae* and *K. oxytoca*.

Intra-abdominal infections: caused by *E. coli* and anaerobic micro-organisms.

Chronic bacterial prostatitis: caused by *Eschericia coli, Enterrococcus faecalis,* methicillin-sensitive *Staphylococcus epidermidis,* and *Staphylococcus haemolyticus, Streptococcus agalactiae* or *Streptococcus mitis.*

*In the treatment of infections caused by *P. aeruginosa,* an aminoglycoside should be administered concomitantly.

4.2 Posology and method of administration

Posology

LEVOFLOXACIN UNICORN tablets should be taken two hours before medicines containing iron salts, antacids and sucralfate. These medicines will reduce the absorption of levofloxacin.

LEVOFLOXACIN UNICORN is to be taken once or twice daily in a usual dose of 250 or 500 mg. The dosage will depend on the type of pathogen and the severity of the infection. The use of **LEVOFLOXACIN UNICORN** should be continued for a minimum of 48 to 72 hours after the patient has become afebrile or evidence of bacterial eradication has been obtained. The duration of therapy varies according to the course of the disease.

The following daily doses are recommended for **LEVOFLOXACIN UNICORN**:

Daily dosage recommended in patients with normal renal function:

Sinusitis due to *H. influenzae, S. pneumoniae,* methicillin-sensitive *S. aureus, M. catarrhalis* and *H. parainfluenzae:* 500 mg once daily for 10 days.

Acute exacerbation of chronic bronchitis due to *H. influenzae, K pneumoniae,* methicillin-sensitive *S. aureus, M. catarrhalis, E. coli, H. influenzae* and *S. pneumoniae:* 500 mg once daily for 5 – 10 days.

Community acquired pneumonia due to *H. influenzae, S. pneumoniae,* methicillin-sensitive *S. aureus, M. catarrhalis, H. parainfluenzae, K. pneumoniae, E. coli, Mycoplasma pneumoniae, Chlamydia pneumoniae* and *Legionella pneumophila:* 500 mg once or twice daily for 10 – 14 days. (The higher dosage should be chosen in the presence of complicating factors e.g. comorbidity, advanced age).

Chronic bacterial prostatitis due to *Eschericia coli, Enterrococcus faecalis,* methicillin-sensitive *Staphylococcus epidermidis* and *Staphylococcus haemolyticus, Streptococcus agalactiae, Streptococcus mitis:* 500 mg once a

day for 28 days.

Complicated urinary tract infections and acute pyelonephritis due to *E. coli, K. pneumoniae, E. faecalis, P. mirabilis, Enterobacter cloacae, P. aeruginosa:* 250 mg once daily for 10 days.

Uncomplicated urinary tract infections in women due to *E. coli:* 250 mg once daily for 3 days.

Uncomplicated skin and skin structure infections due to methicillin-sensitive *S. aureus, S. pyogenes, Acinetobacter calcoaceticus, E. cloacae, P mirabilis, P aeruginosa, E.coli, K. pneumoniae, E. faecalis:* 250 to 500 mg once daily for 7 – 10 days.

Complicated skin and skin structure infections due to methicillin-sensitive *S. aureus, S. pyogenes, P. mirabilis, E. coli, K. pneumoniae, E. faecalis, E. cloacae, K. oxytoca:* 500 mg twice daily for 10 – 14 days.

Intra-abdominal infections due to *E. coli* and anaerobic microorganisms: 500 mg once daily in combination with an antibiotic with anaerobic coverage for 10 – 14 days.

Above indications when bacteraemia or septicaemia is present: 500 mg twice daily for 10 – 14 days.

Special populations

Daily dosage recommended in patients with impaired renal function:

Dosage must be adjusted in patients with impaired renal function according to the degree of impairment (creatinine clearance ≤ 50 ml/min):

Patients with a creatinine clearance between 20 and 50 ml/min:

Patients to be taking 250 or 500 mg once daily: a normal single dose should be given initially and then reduced by half this dose once daily.

Patients to be taking 500 mg twice daily: the initial dose should be 500 mg and

then 250 mg should be taken twelve-hourly.

Patients with a creatinine clearance between 10 and 19 ml/min:

Patients to be taking 250 mg once daily: a normal single dose should be given initially and then reduced to 125 mg every 48 hours.

Patients to be taking 500 mg once daily: should be given a normal single dose initially and then this dose should be reduced to 125 mg every 24 hours.

Patients to be taking 500 mg twice daily: should be given 500 mg initially and then this dose should be reduced to 125 mg every 12 hours.

Patients with a creatinine clearance of less than 10 ml/min or in patients on haemodialysis or CAPD (continuous ambulatory peritoneal dialysis):

In patients where the prescribed dosage is 250 mg once daily: a normal single dose should be given initially and then this dose should be reduced to 125 mg every 48 hours.

Patients to be taking 500 mg once daily: should be given a normal single dose initially and then this dose should be reduced to 125 mg every 24 hours.

Patients to be taking 500 mg twice daily: should be given 500 mg initially and then this dose should be reduced to 125 mg every 24 hours.

No adjustment of dosage is required in the elderly or in patients with impaired liver function.

Paediatric population

Levofloxacin is not recommended for use in children and adolescents below 18 years of age due to a lack of data on safety and efficacy. (see section 4.3).

Method of administration:

LEVOFLOXACIN UNICORN tablets should be swallowed whole, without

crushing, and with a sufficient amount of liquid.

LEVOFLOXACIN UNICORN tablets may be taken on an empty stomach or with meals.

4.3 Contraindications

The use of **LEVOFLOXACIN UNICORN** is contraindicated in:

- Hypersensitivity reaction to levofloxacin, other quinolones, or any other ingredients of **LEVOFLOXACIN UNICORN** (see sections 2 & 6.1).
- Epilepsy.
- Patients with history of tendon disorders associated with fluoroquinolone administration.
- Children or adolescents (under 18 years of age).
- During pregnancy and lactation (see section 4.6).
- Co-administration of fluoroquinolones with ACE inhibitors/angiotensin-receptor blockers in patients with moderate to severe renal impairment (creatinine clearance ≤ 30 mL/min) and in the elderly.
- Patients with mitral valve and/or aortic valve regurgitation unless no safer appropriate alternative antibiotic is available, has failed, or is not well tolerated.

4.4 Special warnings and precautions for use

Fluoroquinolones, including LEVOFLOXACIN UNICORN, 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, in patients taking corticosteroid medicines, and in patients who have undergone a kidney, heart or lung transplant.

Tendinitis and tendon rupture:

Tendinitis may occur with **LEVOFLOXACIN UNICORN** use. It most frequently involves the Achilles tendon and may lead to tendon rupture, which may require surgical repair. Tendinitis and tendon rupture in the rotator cuff, the hand, the biceps, the thumb, and other tendon sites, sometimes bilateral, may occur within 48 hours of starting treatment with **LEVOFLOXACIN UNICORN** and has been reported up to several months after discontinuation of treatment.

The risk of tendinitis and tendon rupture is increased in patients aged over 60 years, in patients receiving daily doses of 1 000 mg, in patients using corticosteroids. The daily dose should be adjusted in elderly patients based on creatinine clearance (see section 4.2). In addition to age and corticosteroid use, there are independent factors that may increase the risk of tendon rupture. Close monitoring of these patients is therefore necessary if they are prescribed **LEVOFLOXACIN UNICORN**. All patients should consult their doctor if they experience symptoms of tendinitis. If tendinitis is suspected, treatment with **LEVOFLOXACIN UNICORN** must be halted immediately, and appropriate treatment (e.g. immobilisation) must be initiated for the affected tendon, including rest.

Methicillin-resistant *S. aureus* (MRSA) infections

Methicillin-resistant *S. aureus* (MRSA) is very likely to possess co-resistance to fluoroquinolones, including **LEVOFLOXACIN UNICORN**. Therefore, **LEVOFLOXACIN UNICORN** is not recommended for the treatment of known or suspected MRSA infections unless laboratory results have confirmed susceptibility of the organism to **LEVOFLOXACIN UNICORN**.

Hypersensitivity reactions:

LEVOFLOXACIN UNICORN can cause serious, potentially fatal hypersensitivity

reactions (e.g. angioedema up to anaphylactic shock), following the initial dose (see section 4.8).

***Clostridium difficile*-associated disease:**

Diarrhoea, particularly if severe, persistent and/or bloody, during or after treatment with **LEVOFLOXACIN UNICORN** (including several weeks after treatment), may be symptomatic of *Clostridium difficile*-associated disease (CDAD). CDAD may range in severity from mild to life-threatening, the most severe form of which is pseudomembranous colitis (see section 4.8). It is therefore important to consider this diagnosis in patients who develop serious diarrhoea during or after treatment with **LEVOFLOXACIN UNICORN**. If CDAD is suspected or confirmed, **LEVOFLOXACIN UNICORN** should be stopped immediately and appropriate treatment initiated without delay. Antiperistaltic medicines are contraindicated in this clinical situation.

Hepato-biliary disorders:

Cases of hepatic necrosis up to fatal hepatic failure have been reported with **LEVOFLOXACIN UNICORN**, 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.

Cardiac disorders:

Caution should be taken when using **LEVOFLOXACIN UNICORN** in patients with known risk factors for prolongation of the QT interval, for example:

- Congenital long QT syndrome.
- Concomitant use of medicines that are known to prolong the QT interval (e.g. Class IA and III antidysrhythmics, tricyclic antidepressants,

macrolides, antipsychotics) (see section 4.5).

- Uncorrected electrolyte imbalance (e.g. hypokalaemia, hypomagnesaemia).
- Cardiac disease (e.g. heart failure, myocardial infarction, bradycardia).

Elderly patients and women may be more sensitive to QTc-prolonging medicines. Therefore, caution should be taken when using fluoroquinolones, including **LEVOFLOXACIN UNICORN**, in these patients.

There is some evidence, although inconclusive, of a possible association between the use of fluoroquinolones and mitral valve and/or aortic valve regurgitation. A thorough cardiovascular examination including an echocardiogram should be performed before oral fluoroquinolones are prescribed. Fluoroquinolones should not be prescribed to patients with confirmed mitral valve and/or aortic valve regurgitation (see section 4.3).

Peripheral neuropathy:

Peripheral sensory neuropathy and peripheral sensory motor neuropathy have been reported in patients receiving fluoroquinolones, including **LEVOFLOXACIN UNICORN**, which can be rapid in its onset (see section 4.8). **LEVOFLOXACIN UNICORN** should be discontinued if the patient experiences symptoms of neuropathy in order to prevent the development of an irreversible condition.

Psychotic reactions:

Psychotic reactions have been reported in patients receiving **LEVOFLOXACIN UNICORN**. These may progress to suicidal thoughts and self-endangering behaviour – sometimes after only a single dose of **LEVOFLOXACIN UNICORN** (see section 4.8). In the event that the patient develops these reactions, **LEVOFLOXACIN UNICORN** should be discontinued and appropriate measures

instituted. Caution is recommended if **LEVOFLOXACIN UNICORN** is to be used in psychotic patients or in patients with history of psychiatric disease.

Exacerbation of myasthenia gravis:

LEVOFLOXACIN UNICORN have neuromuscular blocking activity and may exacerbate muscle weakness in patients with myasthenia gravis. Post marketing serious adverse reactions, including deaths and the requirement for respiratory support, have been associated with fluoroquinolone use in patients with myasthenia gravis. **LEVOFLOXACIN UNICORN** is not recommended in patients with a known history of myasthenia gravis.

Severe bullous reactions:

Cases of severe bullous skin reactions such as Stevens-Johnson syndrome or toxic epidermal necrolysis have been reported with **LEVOFLOXACIN UNICORN** (see section 4.8). Patients should be advised to contact their doctor immediately prior to continuing treatment if skin and/or mucosal reactions occur.

Patients predisposed to seizures:

Fluoroquinolones, such as **LEVOFLOXACIN UNICORN**, may lower the seizure threshold and may trigger seizures. It is therefore contraindicated in patients with a history of epilepsy (see section 4.3) and should be used with extreme caution in patients predisposed to seizures or concomitant treatment with other medicines that lower the cerebral seizure threshold, such as theophylline. In case of convulsive seizures, treatment with **LEVOFLOXACIN UNICORN** should be discontinued.

Vision disorders:

If vision becomes impaired or any effects on the eyes are experienced, an eye

specialist should be consulted immediately.

Dysglycaemia:

Disturbances in blood glucose, including both hypoglycaemia and hyperglycaemia have been reported, usually in diabetic patients receiving concomitant treatment with an oral hypoglycaemic medicine (e.g. glibenclamide) or with insulin. Cases of hypoglycaemic coma have been reported. In diabetic patients, careful monitoring of blood glucose is recommended.

Prevention of photosensitisation:

Photosensitisation has been reported with **LEVOFLOXACIN UNICORN** (see section 4.8). It is recommended that patients should not expose themselves unnecessarily to strong sunlight or to artificial UV rays (e.g. sunray lamp, solarium), during treatment and for 48 hours following treatment discontinuation in order to prevent photosensitisation.

Patients with glucose-6-phosphate dehydrogenase deficiency:

Patients with latent or actual defects in glucose-6-phosphate dehydrogenase activity may be prone to haemolytic reactions when treated with **LEVOFLOXACIN UNICORN**. Therefore, if **LEVOFLOXACIN UNICORN** has to be used in these patients, potential occurrence of haemolysis should be monitored.

Patients with renal impairment:

Since levofloxacin is excreted mainly by the kidneys, the dose should be adjusted in patients with renal impairment (see section 4.2).

Concomitant use with ACE inhibitors/Angiotensin-receptor blockers

The co-administration of fluoroquinolones and ACE inhibitors/Angiotensin-receptor blockers may precipitate acute kidney injury in patients, especially those with moderate to severe renal impairment and elderly patients (see section 4.3). Renal function should be assessed before starting treatment and monitored during treatment with fluoroquinolones or ACE inhibitors/angiotensin-receptor blockers whether used separately or concomitantly.

Patients treated with vitamin K antagonists:

Due to possible increase in coagulation tests (PT/INR) and/or bleeding in patients treated with **LEVOFLOXACIN UNICORN** in combination with a vitamin K antagonist (e.g. warfarin), coagulation tests should be monitored when these medicines are given concomitantly (see section 4.5).

Superinfection:

The use of **LEVOFLOXACIN UNICORN**, especially if prolonged, may result in overgrowth of non-susceptible organisms. If superinfection occurs during therapy, appropriate measures should be taken.

Interference with laboratory tests:

In patients treated with **LEVOFLOXACIN UNICORN**, determination of opiates in urine may give false-positive results. It may be necessary to confirm positive opiate screens by more specific method.

LEVOFLOXACIN UNICORN may inhibit the growth of *Mycobacterium tuberculosis* and, therefore, may give false-negative results in the bacteriological diagnosis of tuberculosis.

4.5 Interaction with other medicines and other forms of interaction

Iron salts, magnesium- or aluminium- containing antacids and sucralfate:

The absorption of levofloxacin is significantly reduced when administered with iron salts, antacids and sucralfate. It is recommended that preparations containing iron salts, sucralfate, magnesium- or aluminium-containing antacids should not be taken 2 hours before or after **LEVOFLOXACIN UNICORN** tablet administration.

Theophylline, fenbufen or similar nonsteroidal anti-inflammatory drugs:

LEVOFLOXACIN UNICORN is known to inhibit hepatic metabolism and may interfere with the clearance of medicines, such as theophylline, fenbufen or similar nonsteroidal anti-inflammatory drugs that lower the seizure threshold (see section 4.4).

Probenecid and cimetidine:

Caution should be exercised when **LEVOFLOXACIN UNICORN** is coadministered with medicines that affect the tubular renal secretion, such as probenecid and cimetidine, especially in renally impaired patients.

Ciclosporin:

The half-life of ciclosporin is increased by 33 % when coadministered with **LEVOFLOXACIN UNICORN**.

Vitamin K antagonists:

Increased coagulation tests (PT/INR) and/or bleeding which may be severe, have been reported in patients treated with **LEVOFLOXACIN UNICORN** in combination with a vitamin K antagonist (e.g. warfarin). Coagulation tests should be monitored in patients treated with vitamin K antagonists (see section 4.4).

QT interval prolonging medicines:

LEVOFLOXACIN UNICORN should be used with caution in patients receiving medicines known to prolong the QT interval (e.g. Class IA and III antidysrhythmics, tricyclic antidepressants, macrolides, antipsychotics) (see section 4.4).

ACE inhibitors and angiotensin-receptor blockers

The co-administration of fluoroquinolones and ACE inhibitors/angiotensin-receptor blockers may precipitate acute kidney injury. The mechanism of the possible interaction between the different classes of medicines, over and above different mechanisms of kidney damage, is not known (see section 4.3).

4.6 Fertility, pregnancy and lactation

The use of **LEVOFLOXACIN UNICORN** during pregnancy and lactation is contraindicated.

There is a risk of damage caused by **LEVOFLOXACIN UNICORN** to the weight-bearing cartilage.

4.7 Effects on the ability to drive and use machines

Some undesirable effects (e.g. dizziness/vertigo, drowsiness, visual disturbances) may impair the patient's ability to concentrate and react. Patients should be advised not to drive or use machines until it is established that their ability to perform such activities is not affected.

4.8 Undesirable effects

Infections and infestations:

Less frequent: Fungal infection including *Candida* infection, pathogen resistance.

Blood and the lymphatic system disorders:

Less frequent: Leukopenia, eosinophilia, Neutropenia, thrombocytopenia

Frequency unknown: agranulocytosis, pancytopenia, and haemolytic anaemia.

Immune system disorders:

Less frequent: Hypersensitivity reactions of the skin such as pruritus and rash, urticaria, severe bullous eruptions such as Stevens-Johnson syndrome, toxic epidermal necrolysis (Lyell's syndrome) and erythema exsudativum multiforme, vasculitis, angioedema.

Frequency unknown: Anaphylactic and anaphylactoid shock.

Metabolism and nutrition disorders:

Less frequent: Anorexia, hypoglycaemia, especially in diabetics

Frequency unknown: hypoglycaemic coma, hyperglycaemia.

Psychiatric disorders:

Frequent: Insomnia

Less frequent: Anxiety, confusional state, nervousness, psychotic reactions (e.g. with hallucination, paranoia), depression, agitation, abnormal dreams, nightmares.

Frequency unknown: Psychotic disorders with self-endangering behaviour, including suicidal ideation or suicidal attempt.

Nervous system disorders:

Frequent: Headaches, dizziness

Less frequent: Paraesthesia, tremors, convulsions, disturbances of the senses of taste and smell, somnolence.

Frequency unknown: Peripheral sensory neuropathy, including motor neuropathy; parosmia, including anosmia, dyskinesia, extrapyramidal disorder, ageusia, syncope, benign intracranial hypertension.

Eye disorders:

Less frequent: Visual disturbances (such as blurred vision).

Frequency unknown: Transient vision loss.

Ear and labyrinth disorders:

Less frequent: Vertigo, tinnitus.

Frequency unknown: Impaired hearing and loss.

Cardiac disorders:

Less frequent: Tachycardia, palpitation.

Frequency unknown: Ventricular tachycardia (which may result in cardiac arrest), ventricular dysrhythmia, torsades de pointes (reported predominantly in patients with risk factors of QT prolongation), prolonged electrocardiogram QT. Cases of mitral valve and/or aortic valve regurgitation were reported in patients treated with oral fluoroquinolones. Due to insufficient post-marketing information in the reported cases, it is not known whether fluoroquinolone use was the causative factor, or a contributory factor, or played no role in the reported cases where mitral valve and/or aortic valve regurgitation was diagnosed.

Vascular disorders:

Less frequent: Hypotension.

Respiratory, thoracic and mediastinal disorders:

Less frequent: Dyspnoea.

Frequency unknown: Bronchospasm, allergic pneumonitis.

Gastrointestinal disorders:

Frequent: Nausea, diarrhoea, vomiting.

Less frequent: Loss of appetite, abdominal pain, dyspepsia, pseudomembranous colitis, flatulence, constipation.

Frequency unknown: Haemorrhagic (bloody) diarrhoea (which in very rare cases may be indicative of enterocolitis, including pseudomembranous colitis), pancreatitis, stomatitis.

Hepato-biliary disorders:

Frequent: Transient increase in liver enzymes (ALT/AST, alkaline phosphatase, GGT).

Less frequent: Hepatitis, transient increase in bilirubin and in serum creatinine.

Frequency unknown: Jaundice, severe liver injury (including fatal acute liver failure, primarily in patients with severe underlying diseases).

Skin and subcutaneous tissue disorders:

Less frequent: Photosensitivity reactions (skin reactions to sunlight and other UV rays), rash, pruritus, urticaria, hyperhidrosis, Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) (see section 4.4), Fixed drug eruption.

Frequency unknown: Toxic epidermal necrolysis, Stevens-Johnson syndrome, Erythema multiforme photosensitivity reaction (see section 4.4), leukocytoclastic

vasculitis, stomatitis.

Endocrine disorders:

Less frequent: Syndrome of inappropriate secretion of antidiuretic hormone (SIADH).

Musculoskeletal, connective tissue and bone disorders:

Less frequent: Arthralgia, myalgia, tendonitis, muscular weakness, which may be of special importance in patients with myasthenia gravis

Frequency unknown: Rhabdomyolysis, tendon rupture (Achilles tendon), ligament rupture, muscle rupture, arthritis.

Renal and urinary disorders:

Less frequent: Interstitial nephritis and acute kidney failure, increased blood creatinine.

General disorders and administrative site conditions

Less frequent: Asthenia, fungal overgrowth and proliferation of other resistant microorganisms, fever.

Frequency unknown: Pain (in the back, chest and extremities).

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of LEVOFLOXACIN UNICORN is important. It allows continued monitoring of the benefit/risk balance of LEVOFLOXACIN UNICORN. Health care providers are asked to report any suspected adverse reactions via the "**6.04 Adverse Drug Reaction Reporting Form**", found online under SAHPRA's publications:

https://www.sahpra.org.za/Publications/Index/8

Report all side effects to Unicorn Pharmaceuticals (Pty) Ltd to enquiries@unicornpharma.co.za

By reporting side effects, you can help provide more information on the safety of **LEVOFLOXACIN UNICORN**.

4.9 Overdose

The symptoms that can be expected from an acute overdosage of **LEVOFLOXACIN UNICORN** are central nervous system symptoms such as confusion, dizziness, impairment of consciousness and convulsive seizures.
The treatment of an overdosage is symptomatic and supportive.
LEVOFLOXACIN UNICORN is not effectively removed by haemodialysis or peritoneal dialysis.

5. PHARMACOLOGICAL PROPERTIES

Pharmacological Class: A 20.1.1 Broad and medium spectrum antibiotics

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Fluoroquinolones
ATC code: J01MA12

Levofloxacin is a broad spectrum bactericidal medicine from the chemical group fluoroquinolone. Levofloxacin is the pure (S)-(–)-enantiomer of ofloxacin.

Pharmacodynamic properties:

Levofloxacin's bactericidal action results from interference with the enzymes topoisomerase IV and DNA gyrase, which are needed for the DNA replication, transcription, repair and recombination.

Levofloxacin is bactericidal *in vitro.* Cross-resistance exists between levofloxacin and other fluoroquinolones *in vitro.* Generally there is no cross-resistance between levofloxacin and other classes of antibacterial medicines, due to the mechanism of action of levofloxacin.

The antibacterial spectrum of levofloxacin covers many Gram-positive and Gram-negative bacteria.

Acquired resistance:

Resistant strains, particularly of methicillin-resistant *S. aureus* (MRSA), *P. aeruginosa, E. coli, K. pneumoniae, C. jejuni, N. gonorrhoeae* and *S. pneumoniae* have emerged during treatment with levofloxacin, although there are widely differing patterns of resistance geographically.

5.2 Pharmacokinetic properties:

Absorption:

After oral administration levofloxacin is well and almost completely absorbed with peak plasma concentrations being obtained within 1 hour. Food has little effect on the absorption of levofloxacin and the film coated tablets may be taken during or between meals. The absolute bioavailability is approximately 100 %.

Distribution:

Levofloxacin is approximately 30 – 40 % bound to serum protein. Steady-state is achieved within three days.

Levofloxacin penetrates well into lung tissue, bone tissue, bronchial mucosa, epithelial lining fluid and blister fluid.

Metabolism and excretion:

Levofloxacin is metabolised to a small degree to inactive metabolites being desmethyl-levofloxacin and levofloxacin-N-oxide. The elimination half-life of levofloxacin is six to eight hours after oral administration. Levofloxacin is excreted largely unchanged, primarily via the kidney.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Inactive ingredients: crospovidone, hypromellose, magnesium stearate, microcrystalline cellulose, Opadry pink (containing hypromellose, iron oxide red, iron oxide yellow, macrogol, talc, titanium dioxide), talc.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years.

6.4 Special precautions for storage

Store at or below 25 °C.

Protect from light and moisture.

Do not remove from the outer carton until required for use.

KEEP OUT OF THE REACH OF CHILDREN.

6.5 Nature and contents of container

LEVOFLOXACIN UNICORN 250: Blister pack comprising of a lidding foil made up of plain aluminium foil coated with heat sealable lacquer and base film made up of transparent PVC.

5 or 10 tablets per blister strip

LEVOFLOXACIN UNICORN 500: Blister pack comprising of a lidding foil made up of plain aluminium foil coated with heat sealable lacquer and base film made up of transparent PVC.

5 or 10 tablets per blister strip

6.6 Special precautions for disposal and other handling

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Unicorn Pharmaceuticals (Pty) Ltd

Corner of Searle & Pontac Streets

Woodstock

Cape Town

South Africa 8001

8. REGISTRATION NUMBER

LEVOFLOXACIN UNICORN 250: 46/20.1.1/0944

LEVOFLOXACIN UNICORN 500: 46/20.1.1/0945

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

02 March 2021.

10. DATE OF REVISION OF THE TEXT

Not applicable.