WHO-PQ RECOMMENDED PATIENT INFORMATION LEAFLET

This patient information leaflet focuses on uses of the medicine covered by WHO's Prequalification Team - Medicines. The recommendations for use are based on WHO guidelines and on information from stringent regulatory authorities.[*]

The medicine may be authorised for additional or different uses by national medicines regulatory authorities.

[*] https://extranet.who.int/pqweb/sites/default/files/documents/75%20SRA%20clarification_Feb2017_newtempl.pdf

Information for the patient

[TB381 trade name][†]
Levofloxacin (as hemihydrate)

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have questions about the medicine, ask your health care provider.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness seem to be the same as yours.
- If you are concerned about any side effects, talk to your health care provider. This includes unwanted effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What [TB381 trade name] is and what it is used for

[TB381 trade name] is a medicine used to treat tuberculosis (TB), an infection caused by bacteria called *Mycobacterium tuberculosis*. It is always given together with other medicines to treat tuberculosis. Your health care provider has chosen the combination that is right for your condition.

[TB381 trade name] is also used on its own for the prevention of tuberculosis if you are at high risk of infection.

[TB381 trade name] contains the active substance levofloxacin and belongs to a group of antibiotics called fluoroquinolones.

2. What you need to know before you take [TB381 trade name]

Do not take [TB381 trade name] if:

- you are allergic to levofloxacin, any other quinolone antibiotic such as moxifloxacin, ciprofloxacin or ofloxacin, or any of the other ingredients of [TB381 trade name] (listed in Section 6 below). Signs of an allergic reaction include: rash, swallowing or breathing problems, swelling of your lips, face, throat or tongue
- you have ever had epilepsy
- you have ever had a problem with your tendons such as tendinitis that was related to treatment with a fluoroquinolone antibiotic.

You must not take this medicine if any of the above applies to you. If you are not sure, talk to your health care provider before taking [TB381 trade name].

[†] Trade names are not prequalified by WHO. This is the national medicines regulatory agency's responsibility.

Warnings and precautions

Talk to your health care provider before taking [TB381 trade name]:

- If you are 60 years or older
- If you are using corticosteroids, sometimes called steroids (see "Other medicines and [TB381 trade name]" below)
- If you have received a transplant
- If you have ever had a fit (seizure)
- If you have had damage to your brain due to a stroke or other brain injury
- If you have kidney problems
- If you have something known as 'glucose-6-phosphate dehydrogenase deficiency' (a rare hereditary disease). If so, you are more likely to have serious problems with your blood when taking this medicine
- If you have ever had mental health problems
- If you have a peripheral nerve disorder (peripheral neuropathy)
- If you have ever had heart problems: caution should be taken when using [TB381 trade name], if you were born with or have family history of prolonged QT interval (seen on ECG, electrical recording of the heart), have salt imbalance in the blood (especially low level of potassium or magnesium in the blood), have a very slow heart rhythm (called 'bradycardia'), have a weak heart (heart failure), have a history of heart attack (myocardial infarction), you are female or elderly or you are taking other medicines that result in abnormal ECG changes or are taking vitamin K antagonists (e.g. warfarin), due to a possible increase in coagulation tests and/or bleeding (see section "Other medicines and [TB381 trade name]")
- If you have been diagnosed with heart valve failure (regurgitation of the heart valves)
- If you are diabetic
- If you have ever had liver problems
- If you suffer from myasthenia gravis (abnormal muscle fatigue leading to weakness and in serious cases paralysis), taking [TB381 trade name] may worsen the symptoms of your disease
- If you have experienced a previous episode of aortic dissection (a tear in the aorta wall).
- If you have a family history of aortic aneurysm or aortic dissection or other risk factors or predisposing conditions (e.g. connective tissue disorders such as Marfan syndrome, or vascular Ehlers-Danlos syndrome, Turner or Sjögren's syndrome (an inflammatory autoimmune disease), or vascular disorders such as Takayasu arteritis, giant cell arteritis, Behcet's disease, high blood pressure, or known atherosclerosis, rheumatoid arthritis (a disease of the joints), or endocarditis (a heart infection))
- If you have ever developed a severe or peeling skin rash, blisters and / or mouth sores after taking levofloxacin.

Talk to your health care provider if any of the above apply to you.

When taking [TB381 trade name]

- If you feel sudden, severe pain in your abdomen, chest or back, which can be symptoms of aortic aneurysm and dissection, go immediately to an emergency room. Your risk may be increased if you are being treated with systemic corticosteroids.
- If you start experiencing a rapid onset of shortness of breath, especially when you lie down flat in your bed, or you notice swelling of your ankles, feet or abdomen, or a new onset of heart palpitations (sensation of rapid or irregular heartbeat), you should inform a health care provider immediately.
- Serious skin reactions including Stevens-Johnson syndrome, toxic epidermal necrolysis, and drug reaction with eosinophilia and systemic symptoms (DRESS) have been reported with the use of levofloxacin. If you develop a skin reaction or blistering / peeling of the skin and/or mucosal reactions (see section 4, 'Possible side effects') contact your health care provider or seek medical

attention immediately before you continue treatment.

- Try to keep out of direct sunlight while taking this medicine and for 2 days after you stop taking it. Your skin may become much more sensitive to the sun and may burn, tingle or severely blister. Therefore it is recommended you take the following precautions:
  - Always wear a hat and clothes which cover your arms and legs
  - Make sure you use high factor sun cream
  - Avoid sun beds
- [TB381 trade name] may cause a rapid and severe inflammation of the liver which could lead to life-threatening liver failure (including fatal cases, see section 4, 'Possible side effects'). If you suddenly feel unwell and/or are being sick and also have yellowing of the whites of the eyes (jaundice), dark urine, itching of the skin, a tendency to bleed or confusion (symptoms of a reduced liver function or a rapid and severe inflammation of the liver), please contact your health care provider before taking any more tablets.
- The risk of heart problems may increase with higher doses, therefore, you should keep to the prescribed dose.
- There is a small risk that you may experience a severe, sudden allergic reaction (an anaphylactic reaction/shock) even with the first dose. Symptoms include tightness in the chest, feeling dizzy, feeling sick or faint, or dizziness when standing up. If so, stop taking [TB381 trade name] and seek medical help immediately.
- Quinolone antibiotics, including [TB381 trade name], may cause convulsions. If this happens, stop taking [TB381 trade name] and contact your health care provider immediately.
- You may experience symptoms of neuropathy such as pain, burning, tingling, numbness and/or weakness. If this happens, inform your health care provider immediately prior to continuing treatment with [TB381 trade name].
- You may experience mental health problems even when taking quinolone antibiotics, including [TB381 trade name], for the first time. In very rare cases depression or mental health problems have led to suicidal thoughts and self-endangering behaviour such as suicide attempts (see section 4, 'Possible side effects'). If you develop such reactions, stop taking [TB381 trade name] and inform your health care provider immediately.
- You may develop diarrhoea whilst or after taking antibiotics including [TB381 trade name]. If this becomes severe or persistent or you notice that your stool contains blood or mucus you should stop taking [TB381 trade name] immediately and consult your health care provider. You should not take medicines that stop or slow down bowel movement.
- [TB381 trade name] may occasionally cause pain and inflammation of your tendons, particularly if you are elderly or if you are also taking corticosteroids. At the first sign of any pain or inflammation you should stop taking [TB381 trade name], rest the affected limb and consult your health care provider immediately. Avoid any unnecessary exercise, as this might increase the risk of a tendon rupture. Inflammation and ruptures of tendons may occur even up to several months after discontinuing therapy with [TB381 trade name].
- If you have diabetes and are using medicines to control your blood sugar, you should monitor your blood sugar levels carefully, as [TB381 trade name] in such cases may lower blood sugar levels.

Other medicines and [TB381 trade name]

Please tell your health care provider if you are taking or have recently taken any other medicines. This includes medicines you buy without a prescription, including herbal medicines. This is because [TB381 trade name] can affect the way some other medicines work. Also some medicines can affect the way [TB381 trade name] work. In particular, tell your health care provider if you are taking any of the following medicines. This is because it can increase the risk of you getting side effects, when taken with [TB381 trade name]:

- Corticosteroids, sometimes called steroids – used for inflammation. You may be more likely to have inflammation and/or breakage of your tendons.
- Vitamin K antagonists such as warfarin - used to thin the blood. You may be more likely to have a bleed. Your health care provider may need to take regular blood tests to check how well your blood can clot.

- Theophylline - used for breathing problems. You may be more likely to have a fit (seizure) if you take theophylline with [TB381 trade name].
- Non-steroidal anti-inflammatory drugs (NSAIDS) - used for relief of pain and inflammation such as aspirin, ibuprofen, fenbufen, ketoprofen and indomethacin. You may be more likely to have a fit (seizure) if taken with [TB381 trade name].
- Ciclosporin - used after organ transplants. You may be more likely to get the side effects of ciclosporin
- Medicines known to affect the way your heart beats. This include medicines used for abnormal heart rhythm (antiarrhythmics such as quinidine, hydroquinidine, disopyramide, sotalol, dofetilide, ibutilide and amiodarone), for depression (tricyclic antidepressants such as amitriptyline and imipramine), for psychiatric disorders (antipsychotics), for bacterial infections ('macrolide' antibiotics such as erythromycin, azithromycin and clarithromycin) and for pain or treatment of drug addiction (methadone).
- Probenecid (used for gout), cimetidine (used for stomach ulcers and heartburn) and methotrexate (used for rheumatism or cancer). Special care should be taken when taking either of these medicines with [TB381 trade name]. If you have kidney problems, your health care provider may want to give you a lower dose.

Do not take [TB381 trade name] at the same time as the following medicines. This is because they can affect the way [TB381 trade name] works:

Iron tablets (for anaemia), zinc supplements, magnesium or aluminum-containing antacids (for heartburn), didanosine, or sulcralfate (for stomach ulcers). Take your dose of these medicines at least 2 hours before or after [TB381 trade name].

Urine tests for opiates

Urine tests may show 'false-positive' results for strong painkillers called 'opiates' in people taking [TB381 trade name]. If your health care provider has prescribed a urine test, tell your health care provider you are taking [TB381 trade name].

Tuberculosis test

This medicine can cause a "false negative" result in some laboratory tests that look for the bacteria causing tuberculosis.

Taking [TB381 trade name] with food and drink

There are no restrictions on taking [TB381 trade name] with food and drink.

Pregnancy

If you become pregnant, or are planning to become pregnant, you must contact your health care provider to discuss the potential benefits and risks of your tuberculosis therapy to you and your child.

Since the safety of taking levofloxacin during pregnancy has not been investigated in humans, you should avoid becoming pregnant during treatment. You or your partner need to use a reliable form of barrier contraception (for example, a condom), or oral (pill) or other hormonal contraceptives (for example, implants, injection).

Breastfeeding

Since levofloxacin may pass over into the mother's milk and might hurt the development of your child's skeleton, you must not breastfeed while taking [TB381 trade name].

Driving and using machines

You may get side effects after taking this medicine, including feeling dizzy, sleepy, a spinning feeling (vertigo) or changes to your eyesight. Some of these side effects can affect you being able to concentrate and your reaction speed. If this happens, do not drive or carry out any work that requires a high level of attention.

3. How to take [TB381 trade name]

Always take [TB381 trade name] exactly as your health care provider has told you. You should check with your health care provider if you are not sure.

Treatment of tuberculosis

Dosing recommendations for patients aged 15 years or older

Weight	**Dose**
30 – 35 kg	3 tablets once daily (750 mg)
36 – 45 kg	3 tablets once daily (750 mg)
46 – 55 kg	4 tablets once daily (1000 mg)
56 – 70 kg	4 tablets once daily (1000 mg)
> 70 kg	4 tablets once daily (1000 mg)
Usual upper daily dose	6 tablets once daily (1500 mg)

Dosing recommendations for patients less than 15 years of age

Weight	**Dose**
5 – 6 kg	½ tablet once daily (125 mg)
7 – 9 kg	½ tablet once daily (125 mg)
10 – 15 kg	1 or 1 ½ tablets once daily (250 mg or 375 mg)
16 – 23 kg	1 ½ or 2 tablets once daily (375 mg or 500 mg)
24 – 30 kg	2 tablets once daily (500 mg)
31 – 34 kg	3 tablets once daily (750 mg)
> 34 kg	See dosing in patients older than 14 years
Usual upper daily dose	6 tablets once daily (1500 mg)

Preventive treatment of tuberculosis

For prevention of tuberculosis, take the number of tablets given in the tables below once a day for 6 months.

Dosing recommendation for patients aged older than 14 years

Weight	**Dose**
< 46 kg	3 tablets once daily (750 mg)
> 45 kg	4 tablets once daily (1000 mg)

Dosing recommendation for patients less than 15 years

Weight	**Dose**
5 – 9 kg	½ tablet once daily (150 mg)
10 – 15 kg	1 tablet once daily (200 – 300 mg)
16 – 23 kg	1 ½ tablets once daily (300 – 400 mg)
24 – 34 kg	2 or 3 tablets once daily (500 – 750 mg)

If you have kidney problems

Your health care provider may need to give you a lower dose.

If you take more [TB381 trade name] than you should

If you accidentally take more tablets than you should, tell a health care provider or get other medical advice straight away. Take the medicine pack with you. This is so the health care provider knows what you have taken. The following effects may happen: convulsive fits (seizures), feeling confused, dizzy, less conscious, having tremor and heart problems leading to uneven heart beats as well as feeling sick (nausea) or having stomach burning.

If you forget to take [TB381 trade name]

If you forget to take your dose, you should take it as soon as you remember on the same day. If you do not remember on the same day, take your normal dose on the next day. Do not take a double dose to make up for a forgotten dose. If you are unsure about what to do, ask your health care provider.

If you stop taking [TB381 trade name]

It is important that you complete the course of treatment even if you begin to feel better. If you stop taking [TB381 trade name] too soon, your infection may not be completely cured and the infection may return or your condition may get worse. The bacteria causing your infection may become resistant to [TB381 trade name].

Taking this medicine

- Take this medicine by mouth
- Swallow the tablets whole with plenty of liquid
- The tablets may be taken during meals or at any time between meals
- Try to take the tablet(s) at approximately the same time each day.

If you have any further questions on the use of this medicine, ask your health care provider.

4. Possible side effects

Like all medicines, [TB381 trade name] can cause side effects, but not everybody gets them. When treating tuberculosis, it is not always possible to differentiate between unwanted effects from [TB381 trade name] and those caused by any other medicines you may be taking at the same time. For this reason, it is important that you inform the health care provider of any change in your health.

Common side effects (may affect up to 1 in 10 people):

- Feeling and being sick (nausea, vomiting) and diarrhoea
- Increase in the level of some liver enzymes in the blood
- Headache, feeling dizzy
- Sleeping problems

Uncommon side effects (may affect up to 1 in 100 people):

- Itching and skin rash, severe itching or hives (urticaria), sweating too much (hyperhidrosis)
- Changes in the way things taste, loss of appetite, stomach upset or indigestion (dyspepsia), pain in your stomach area, feeling bloated (flatulence) or constipation
- Blood tests may show abnormal results due to liver (bilirubin increased) or kidney (creatinine increased) problems
- Changes in the number of white blood cells shown up in the results of some blood tests
- General weakness
- Changes in the number of other bacteria or fungi that are normally found in the body, infection with a fungus called Candida, which may need to be treated
- Feeling stressed (anxiety), feeling confused, feeling nervous, feeling sleepy, trembling, a spinning feeling (vertigo)
- Shortness of breath (dyspnea)
- Joint pain or muscle pain

Rare side effects (may affect up to 1 in 1,000 people):

- Pain and inflammation in your tendons or ligaments, which could lead to rupture. The Achilles tendon is affected most often
- Widespread rash, high body temperature, liver enzyme elevations, blood abnormalities (eosinophilia), enlarged lymph nodes and other body organs involvement (Drug Reaction with Eosinophilia and Systemic Symptoms which is also known as DRESS or drug hypersensitivity syndrome). See also section 2.
- Red patches with or without blistering that develop within hours of intake of levofloxacin. After these haves healed darker patches of skin are located at the site of the original disease. This usually comes back at the same site of the skin or mucous membrane upon another exposure to levofloxacin (post infammatory residual hyperpigmentation)
- Syndrome associated with impaired water excretion and low levels of sodium (SIADH)
- Allergic reactions
- Painless swelling under the skin
- *Lowering* of your blood sugar levels (hypoglycaemia) or lowering of your blood sugar levels leading to coma (hypoglycaemic coma). This is important for people that have diabetes.
- Seeing or hearing things that are not there (hallucinations, paranoia), change in your opinion and

thoughts (psychotic reactions)

- Tingly feeling in the hands and feet (paraesthesia) or trembling, fits
- Feeling depressed, mental problems, feeling restless (agitation), abnormal dreams or nightmares
- State of mental confusion (delirium)
- Problems with hearing (tinnitus) or eyesight (blurred vision)
- Unusual fast beating of the heart (tachycardia), awareness of the heartbeat (palpitation) or low blood pressure (hypotension)
- Bruising and bleeding easily due to a lowering in the number of blood platelets (thrombocytopenia)
- Low number of white blood cells (called neutropenia)
- Muscle weakness. This is important in people with myasthenia gravis (a rare disease of the nervous system).
- Memory impairment
- Changes in the way your kidney works and occasional kidney failure which may be due to an allergic kidney reaction called interstitial nephritis
- Lowering of blood sugar levels leading to coma (hypoglycaemic coma).
- Fever

Other possible side effects, occurring at an unknown frequency, include:

- Serious skin rashes including Stevens-Johnson syndrome and toxic epidermal necrolysis. These can appear as reddish target-like macules or circular patches often with central blisters on the trunk, skin peeling, ulcers of mouth, throat, nose, genitals and eyes and can be preceded by fever and flu-like symptoms. See also section 2.
- Loss of appetite, yellowing of the skin and eyes, dark-colored urine, stinging, or tender stomach (abdomen). These may be the signs of liver problems which may include sudden liver failure.
- Lowering in red blood cells (anaemia): this can make the skin pale or yellow due to damage of the red blood cells; lowering in the number of all types of blood cells (pancytopenia)
- Fever, sore throat and a general feeling of being unwell that does not go away. This may be due to a lowering in the number of white blood cells (agranulocytosis).
- Loss of circulation (anaphylactic like shock)
- Watery diarrhoea which may have blood in it
- Increase of blood sugar levels (hyperglycaemia). This is important if you have diabetes.
- Changes in the way things smell, loss of smell or taste (parosmia, anosmia, ageusia)
- Problems moving and walking (dyskinesia, extrapyramidal disorders)
- Temporary loss of consciousness or posture (syncope)
- Temporary loss of vision
- Eye redness, pain and blurred vision (uveitis)
- Impairment or loss of hearing
- Life-threatening irregular heart rhythm including cardiac arrest, alteration of the heart rhythm (called ‘prolongation of QT interval’, seen on ECG, electrical activity of the heart)
- Enlargement and weakening of the aortic wall or a tear in the aortic wall (aneurysms and dissections), which may rupture and may be fatal, and of leaking heart valves. See also section 2.
- Difficulty breathing or wheezing (bronchospasm)

- Allergic lung reactions
- Pancreatitis
- Inflammation of the liver (hepatitis)
- Increased sensitivity of your child's skin to sun and ultraviolet light (photosensitivity)
- Inflammation of the vessels that carry blood around the body due to an allergic reaction (vasculitis)
- Inflammation of the tissue inside the mouth (stomatitis)
- Muscle rupture and muscle destruction (rhabdomyolysis)
- Joint redness and swelling (arthritis)
- Ligament and muscle rupture
- Pain, including pain in the back, chest and extremities
- Pain, numbness, tingling, burning, stabbing, muscle weakness in the feet or hands (peripheral sensory neuropathy)
- Decreased feeling in any area of the body, difficulty swallowing or breathing, difficulty using the arms or hands, legs or feet or difficulty walking. (peripheral sensory motor neuropathy)
- Attacks of porphyria in people who already have porphyria (a very rare metabolic disease)
- Persistent headache with or without blurred vision (benign intracranial hypertension)
- Risk of having suicidal thoughts or actions

Very rare cases of long lasting (up to months or years) or permanent adverse drug reactions, such as tendon inflammations, tendon rupture, joint pain, pain in the limbs, difficulty in walking, abnormal sensations such as pins and needles, tingling, tickling, burning, numbness or pain (neuropathy), depression, fatigue, sleep disorders, memory impairment, as well as impairment of hearing, vision, and taste and smell have been associated with administration of quinolone and fluoroquinolone antibiotics, in some cases irrespective of pre-existing risk factors.

Reporting of side effects

If you get any side effects,talk to your health care provider. This includes unwanted effects not listed in this leaflet. If available, you can also report side effects directly through the national reporting system. By reporting side effects, you can help improve understanding about the safety of this medicine.

5. How to store [TB381 trade name]

Keep this medicine out of the sight and reach of children.
Do not store above 30°C. Keep the tablets in the blister in the provided carton to protect from light and moisture.
Do not use this medicine after the expiry date stated on the blister or carton, after "EXP". The expiry date refers to the last day of that month.
Do not use this medicine if you notice visible signs of deterioration or that it is different from the description below.
Do not throw away any medicines in wastewater or household waste. Ask your health care provider how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What [TB381 trade name] contains

The active ingredient of [TB381 trade name] is levofloxacin (as hemihydrate) 250 mg.
The other ingredients are:
Core tablet: crospovidone, hypromellose, microcrystalline cellulose and sodium stearyl fumarate
Film coat: hypromellose, titanium dioxide, talc and macrogol

What [TB381 trade name] looks like and contents of the pack

[TB381 trade name] is a light pink coloured, oblong, film coated tablet with a bisect line on both sides. The tablet can be divided into 2 equal doses.

[TB381 trade name] is available in a clear PVC-aluminium blister card. 10 tablets are packed in a blister card. Pack sizes: 1 x 10 tablets; 10 x10 tablets

Supplier & Manufacturer
Remington Pharmaceutical Industries (Pvt) Ltd
18km Multan Road
Lahore 53800
Pakistan

For any information about this medicine, contact the local representative of the supplier.

This leaflet was last revised in November 2021.

Section 6 was updated in February 2024.

Detailed information on this medicine is available on the World Health Organization (WHO) website: https://extranet.who.int/pqweb/medicines