PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) - 1986

The medicine is dispensed with a doctor's prescription only

Tavanic Tablets 500 mg

Film-coated Tablets

Active ingredient: Levofloxacin (as hemihydrate) 500 mg

Inactive ingredients in the preparation, see section 6.

Read the leaflet carefully in its entirety before using the medicine.

This leaflet contains concise information about the medicine. If you have further questions, refer to the doctor or pharmacist.

This medicine has been prescribed for you. Do not pass it on to others. It may harm them even if it seems to you that their medical condition is similar.

The medicine is not intended for children or adolescents.

1. WHAT IS THE MEDICINE INTENDED FOR?

The medicine is intended to treat the following infections in adults:

- Acute inflammation of the kidney and renal pelvis and complicated urinary tract infections
- Prolonged bacterial prostatitis

Tavanic should be used only when it is considered inappropriate to use other antibacterial agents that are commonly recommended for the treatment of these infections:

- Acute bacterial sinusitis
- Acute exacerbations of chronic obstructive pulmonary disease, including bronchitis
- Community-acquired pneumonia
- Complicated skin and soft tissue infections.

Tavanic may also be used to complete a course of therapy in patients who have shown improvement during initial treatment with intravenous levofloxacin.

Therapeutic group: An antibiotic belonging to the 'fluoroquinolone' family.

2. BEFORE USING THE MEDICINE

Do not use the medicine if:

- You are sensitive (allergic) to levofloxacin, to any other 'quinolone' antibiotic, such as moxifloxacin, ciprofloxacin or ofloxacin or to any of the additional ingredients contained in the medicine (see section 6).
  Signs of an allergic reaction include: rash, problems swallowing or breathing, swelling of the lips, face, throat or tongue.
- You suffer, or have suffered in the past, from epilepsy.
- You suffer, or have suffered in the past, from tendon problems, e.g., tendinitis, that arose from treatment with a 'quinolone' antibiotic. The tendon connects the muscle and the bone.
- You are a child or teenager.
- You are pregnant, may become pregnant or think you are pregnant.
- You are breastfeeding.

Do not take the medicine if any of the above conditions applies to you. If you are uncertain, speak to the doctor or pharmacist before taking Tavanic.

Special warnings regarding use of the medicine

Before beginning treatment with Tavanic, tell the doctor if:

- You are 60 years of age or older.
- You are taking 'corticosteroid' medicines, which are sometimes called steroids (see "Drug interactions" section).
- You have received a transplant.
- You have ever had a fit (seizure).
- You have suffered from brain damage due to a stroke or other brain injury.
- You have kidney problems.
- You suffer from G6PD enzyme deficiency (glucose-6-phosphate dehydrogenase deficiency).
  There is a higher chance that you will suffer from severe blood problems when you take this medicine.
- You are suffering, or have suffered in the past, from mental health problems.
- You are suffering, or have suffered in the past, from heart problems: caution should be taken when taking this kind of medicine if you were born with or have a family history of prolonged QT interval (seen in an ECG test, recording of the electrical activity of the heart), if you are suffering from a salt imbalance in the blood (especially a low level of potassium or magnesium in the blood), if your heart rhythm is very slow (called 'bradycardia'), if you have heart failure, if you experienced a myocardial infarction (heart attack) in the past, if you are female or elderly or if you are taking other medicines that result in abnormal ECG changes (see "Drug interactions" section).
- You have diabetes.
- You are suffering, or have suffered in the past, from liver problems.
- You have a disease that causes severe muscle weakness (myasthenia gravis).
- You have nervous system problems (peripheral neuropathy).
- You have been diagnosed with an enlargement or bulge of a large blood vessel (aortic aneurysm or large vessel peripheral aneurysm).
- You have previously had an aortic dissection (a tear in the aorta wall).
- You have been diagnosed with heart valve regurgitation.
- You have a family history of aortic aneurysm or aortic dissection or a congenital heart valve disease or other risk factors or predisposing conditions (e.g., connective tissue disorders such as Marfan syndrome, Ehlers-Danlos syndrome, Turner syndrome, Sjogren'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, or rheumatoid arthritis [a joint disease], or endocarditis [an infection of the heart]).
- You have ever developed a severe skin rash or skin peeling, blistering and/or mouth sores after taking levofloxacin.

Serious skin reactions

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.

- SJS/TEN can appear initially as reddish target-like spots or circular patches, often with central blisters, on the trunk. Also, ulcers of the mouth, throat, nose, genitals and eyes (red and swollen eyes) can occur. These serious skin rashes are often preceded by fever and/or flu-like symptoms. The rashes may progress to widespread peeling of the skin and life-threatening complications or be fatal.
- DRESS appears initially as flu-like symptoms and a rash on the face and then an extended rash with a high body temperature, increased levels of liver enzymes seen in blood tests and an increase in a type of white blood cell (eosinophilia) and enlarged lymph nodes.

If you develop a serious rash or another of these skin symptoms, stop taking levofloxacin and contact your doctor or seek medical attention immediately.

You should not take fluoroquinolone/quinolone antibacterial medicines, including levofloxacin, if you have experienced any serious adverse reaction in the past when taking a quinolone or fluoroquinolone. In this situation, you should inform your doctor as soon as possible.

When you are taking the medicine:

- If you experience sudden and severe pains in your stomach, chest or back, which can be symptoms of aortic aneurysm and aortic dissection, proceed to a hospital emergency room immediately. Your risk may increase if you are being treated with systemic corticosteroids.
- If you start to experience a rapid onset of shortness of breath, especially when you lie flat on your bed, or if you notice swelling of the ankles, legs or stomach, or upon new onset of palpitations (a feeling of rapid or irregular heart rate), inform the doctor immediately.
- If you are having nausea, feeling generally unwell, have severe discomfort or on-going pain or worsening pain in the stomach area or vomiting – refer to a doctor immediately as this could be a sign of an inflamed pancreas (acute pancreatitis).

Pain and swelling in the joints and inflammation or rupture of tendons may occur rarely. Your risk is increased if you are elderly (above 60 years of age), have received an organ transplant, have kidney problems or if you are being treated with corticosteroids. Inflammation and tendon ruptures may occur within the first 48 hours of treatment and even up to several months after stopping of Tavanic therapy. At the first sign of pain or inflammation of a tendon (for example, in your ankle, wrist, elbow, shoulder or knee), stop taking Tavanic, contact your doctor and rest the painful area. Avoid any unnecessary exercise as this might increase the risk of a tendon rupture.

You may rarely experience symptoms of nerve damage (neuropathy) such as pain, burning, tingling, numbness and/or weakness especially in the feet and legs or hands and arms. If this happens, stop taking Tavanic and inform your doctor immediately in order to prevent the development of a potentially irreversible condition.

Prolonged, disabling and potentially irreversible serious side effects

Fluoroquinolone/quinolone antibacterial medicines, including Tavanic, have been associated with very rare but serious side effects, some of them being long-lasting (continuing months or years), disabling or potentially irreversible. This includes tendon, muscle and joint pain of the upper and lower limbs, difficulty in walking, abnormal sensations such as pins and needles, tingling, tickling, numbness or burning (paraesthesia), sensory disorders including impairment of vision, taste and smell, and hearing, depression, memory impairment, severe fatigue, and severe sleep disorders.

If you experience any of these side effects after taking Tavanic, contact your doctor immediately prior to continuing treatment. You and your doctor will decide on continuing the treatment, considering also the possibility of taking an antibiotic from another class.

Medicines from the 'fluoroquinolone' family, including Tavanic, may cause worsening of the symptoms of myasthenia gravis, such as worsening of muscle weakness or breathing problems – if you experience these effects, refer to the doctor immediately.

If you are not sure if any of the above warnings applies to you, refer to the doctor or pharmacist before taking Tavanic.

Children and adolescents

The medicine is not intended for children and adolescents.

Drug interactions

If you are taking, or have recently taken, other medicines, including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist. This is because Tavanic may affect the activity of other medicines and other medicines may affect the activity of Tavanic.

In particular, inform the doctor or pharmacist if you are taking the following medicines, and this is because the combination with Tavanic can increase the chance of side effects:

- Corticosteroids, sometimes called steroids – used to treat inflammations. You may be at a higher risk of tendon inflammation and/or rupture.
- Warfarin – used to thin the blood. You may be at a higher risk of bleeding. Your doctor may need to refer you to regular blood tests to check how well your blood can clot.
- Theophylline – used for breathing problems. You are more likely to have a seizure when taken with Tavanic.
- Non-steroidal anti-inflammatory drugs – used for pain and inflammation, such as aspirin, ibuprofen, fenbufen, ketoprofen and indomethacin. You are more likely to have a seizure when taken with Tavanic.
- Ciclosporin – used after organ transplants. You may be at a higher risk of suffering from the side effects of ciclosporin.
- Medicines that affect the way the heart beats. This includes medicines to treat abnormal heart rhythm (antiarrhythmics such as quinidine, hydroquinidine, disopyramide, sotalol, dofetilide, ibutilide and amiodarone), medicines to treat depression (tricyclic antidepressants such as amitriptyline and imipramine), medicines to treat psychiatric disorders (antipsychotics), medicines to treat bacterial infections ('macrolide' antibiotics such as erythromycin, azithromycin and clarithromycin).
- Probenecid – to treat gout. If you have kidney problems, your doctor may give you a lower dosage.
- Cimetidine – to treat ulcers in the digestive system and heartburn. If you have kidney problems, your doctor may give you a lower dosage.

Tell your doctor if any of the above conditions applies to you.

Do not take Tavanic tablets at the same time as the following medicines, as this may affect the way Tavanic works:

Iron tablets (for treatment of anemia), zinc supplements, magnesium- or aluminum-containing antacids (given for heartburn), didanosine or sucralfate (for stomach ulcers). (See section 3 "If you are already taking iron tablets, zinc supplements, antacids, didanosine or sucralfate" below).

Urine tests for opiates

While using Tavanic, urine tests may show false-positive results for strong painkillers called opiates. If your doctor has referred you for a urine test, tell the doctor that you are taking Tavanic.

Tuberculosis tests

While using Tavanic, certain laboratory tests that search for the bacteria that cause tuberculosis may show false-negative results.

Sugar tests

Diabetic patients being treated with oral anti-diabetes preparations or insulin must monitor their blood sugar levels.

Use of the medicine and food

The medicine can be taken with a meal or at any time between meals.

Pregnancy and breastfeeding

Do not use Tavanic if:

You are pregnant, may become pregnant or think you are pregnant.

You are breastfeeding or plan to breastfeed.

Driving and operating machinery

You may suffer from side effects after taking this medicine, including sensations of dizziness, sleepiness, a spinning sensation (vertigo) or vision changes. Some of these side effects may influence your ability to concentrate and your reaction speed. If this happens, do not drive or engage in any activity that requires a high level of attention.

Important information about some of the ingredients in the medicine

This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium-free'.

3. HOW SHOULD YOU USE THE MEDICINE?

Always use the preparation according to the doctor's instructions. Check with the doctor or pharmacist if you are uncertain about the dosage and treatment regimen of the preparation.

The dosage and the treatment regimen will be determined by the doctor only. The dosage depends on the type of infection that you have and on its location in the body. The duration of treatment will be determined by the severity of the infection.

If you feel that the effect of the medicine is too weak or too strong, do not change the dosage on your own, rather, ask your doctor about it.

Adults and elderly with kidney problems

The doctor may give you a lower dosage.

Do not exceed the recommended dose.

Do not give this medicine to children or adolescents.

Do not chew! Do not crush. Swallow the medicine with a glass of water.

The tablet can be halved on the score line that is on the surface of the tablet, in order to take half a dose when necessary.

If you are already taking iron tablets, zinc supplements, antacids, didanosine or sucralfate

- Do not take these medicines at the same time as Tavanic. Wait an interval of at least two hours before or after taking Tavanic.

Protect your skin from the sun

During treatment with this medicine and for two additional days after you stop taking it, avoid direct exposure to the sun. This is because your skin will become more sensitive to the sun and may burn, tingle or severely blister if you do not take the following precautions:

- Make sure you use a cream with a high protection factor
- Always wear a hat and clothes that cover your arms and legs
- Avoid using tanning beds

If you accidentally took a higher dosage

If you accidentally took a higher dosage, or if a child has accidentally swallowed the medicine, refer immediately to a doctor or proceed to a hospital emergency room and bring the package of the medicine with you. This is so the doctor will know what you have taken.

You may suffer from the following side effects: seizures, feeling confused, dizziness, reduced consciousness, tremor, and heart problems – leading to an irregular pulse, as well as nausea or burning sensation in the stomach.

If you forgot to take the medicine at the required time, take the medicine as soon as you remember, unless it is nearly time to take the next dose. Do not take a double dose to make up for the forgotten dose.

Adhere to the treatment regimen as recommended by the doctor. Even if there is an improvement in your health, do not stop treatment with the medicine without consulting the doctor or pharmacist.

If you stop taking the medicine

Do not stop taking the medicine just because you feel better. It is important that you complete the treatment as prescribed by the doctor. If you stop the treatment too soon, the infection may return, your condition may get worse or the bacteria may develop resistance to the medicine.

Do not take medicines in the dark! Check the label and the dose each time you take medicine. Wear glasses if you need them.

If you have further questions regarding use of the medicine, consult the doctor or pharmacist.

4. SIDE EFFECTS

As with any medicine, use of Tavanic may cause side effects in some users. Do not be alarmed by reading the list of side effects. You may not suffer from any of them.

These effects are generally mild or moderate and often disappear after a short time.

Discontinue use of Tavanic and refer immediately to a doctor or proceed to a hospital if you suffer from the following side effects:

Very rare (effects which can occur in up to 1 patient in 10,000)

- Allergic reaction. Signs may include: rash, breathing or swallowing problems, swelling of your lips, face, throat or tongue.

Discontinue use of Tavanic and refer immediately to a doctor if you notice any of the following severe side effects – you may need urgent medical attention:

Rare (effects which can occur in up to 1 patient in 1,000)

- Watery diarrhea that may also be bloody, possibly with stomach cramps and a high temperature; these may be signs of a severe bowel problem.
- Pain and inflammation in the tendons or ligaments, which may lead to their rupture. The Achilles tendon is affected most often.
- Convulsions.
- Seeing or hearing things that do not exist (hallucinations, paranoia).
- Feeling of depression, mental problems, feeling of restlessness, strange dreams or nightmares.
- Decreased blood sugar levels (hypoglycemia) or decreased blood sugar levels leading to coma (hypoglycemic coma). This information is important for people suffering from diabetes.

Very rare (effects which can occur in up to 1 patient in 10,000)

- Burning sensation, tingling, pain or numbness. These can be signs of 'neuropathy'.

Side effects of unknown frequency (effects whose frequency has not yet been determined)

- Severe skin rashes including Stevens-Johnson syndrome and toxic epidermal necrolysis (TEN). These can appear as reddish target-like macules, or circular patches, often with central blisters on the trunk, skin peeling, ulcer in the mouth, throat, nose, genitals and eyes and may be preceded by fever and flu-like symptoms. See section 2.
- Loss of appetite, yellowing of the skin and eyes, dark-colored urine, itching or tender stomach. These may be signs of liver problems, which may include fatal liver failure.
- Change in your opinion and thoughts (psychotic reactions) with risk of suicidal thoughts or actions.
- Nausea, feeling generally unwell, discomfort or pain in the stomach area or vomiting. These could be signs of an inflamed pancreas (acute pancreatitis). see section 2 "Before using the medicine".

If your eyesight has become impaired or if you suffer from any disturbances of the eyes during the course of treatment with Tavanic, consult an eye doctor immediately.

Very rare cases of long-lasting (even 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.

There have been reports of cases of enlargement and weakening of the wall of the aorta or perforation of the wall of the aorta (aneurysm and dissection), which may burst and may be fatal, and of leakage of heart valves in patients who received fluoroquinolone. Also see section 2.

Consult the doctor if any of the following side effects worsens or lasts longer than a few days:

Common (effects which can occur in up to 1 patient in 10)

- Sleeping problems.
- Headache, feeling dizzy.
- Nausea, vomiting, and diarrhea.
- Increase in the level of certain liver enzymes in the blood.

Uncommon (effects which can occur in up to 1 patient in 100)

- Changes in the number of other bacteria or fungi, infection by a fungus called *Candida*, which may require treatment.
- Changes in the number of white blood cells in blood test results (leukopenia, eosinophilia).
- Feeling stressed (anxiety), feeling confused, feeling nervous, feeling sleepy, trembling, a spinning feeling (vertigo).
- Shortness of breath (dyspnea).
- Changes in sense of taste, loss of appetite, stomach upset or indigestion, pain in the stomach area, feeling bloated (flatulence), or constipation.
- Itching and skin rash, severe itching or hives (urticaria), excessive sweating.
- Joint or muscle pain.
- Blood tests may show unusual results due to liver (increased bilirubin) or kidney (increased creatinine) problems.
- General weakness.

Rare (effects which can occur in up to 1 patient in 1,000)

- Bruising and bleeding easily due to a decrease in the number of blood platelets (thrombocytopenia).
- Low level of white blood cells (neutropenia).
- Exaggerated reaction of the immune system (hypersensitivity).
- Tingly feeling in the hands and feet (paresthesia).
- Problems with hearing (tinnitus) or eyesight (blurred vision).
- Unusually fast heartbeat (tachycardia) or low blood pressure.
- Muscle weakness. This is important in patients with myasthenia gravis (a rare disease of the nervous system).
- Changes in kidney function and sometimes kidney failure, which may be caused as a result of an allergic kidney reaction, called interstitial nephritis.
- Fever.
- Sharply demarcated, erythematous patches with/without blistering that develop within hours of administration of levofloxacin and heal with postinflammatory residual hyperpigmentation; this usually recurs at the same site of the skin or mucous membrane upon subsequent exposure to levofloxacin.
- Memory impairment.

Side effects of unknown frequency (effects whose frequency has not yet been determined)

- Decrease in red blood cells (anemia): can cause paleness or yellowing of the skin due to damage to red blood cells; decreased number of all blood cell types (pancytopenia).
- Fever, sore throat and a general feeling of being unwell that does not go away. This may be due to a decrease in the number of white blood cells (agranulocytosis).
- Loss of blood circulation (anaphylactic-like shock reaction).
- Increase of your blood sugar levels (hyperglycemia). This information is important for patients with diabetes.
- Changes in sense of smell, loss of smell or taste.
- Problems moving and walking (dyskinesia, extrapyramidal disorders).
- Temporary loss of consciousness or posture (syncope).
- Temporary loss of vision, eye inflammation.
- Impaired hearing or loss of hearing.
- Abnormally fast heart rhythm, life-threatening irregular heart rhythm, including cardiac arrest, alteration of the heart rhythm (called 'prolongation of the QT interval', seen in an ECG test, recording of the electrical activity of the heart).
- Breathing difficulties or wheezing (bronchospasm).
- Allergic lung reactions.
- Pancreatitis.
- Inflammation of the liver (hepatitis).
- Increased sensitivity of the skin to sunlight and to ultraviolet light.
- Inflammation of the blood vessels due to an allergic reaction (vasculitis).
- Inflammation of the oral mucosa (stomatitis).
- Muscle rupture and muscle destruction (rhabdomyolysis).
- Joint redness and swelling (arthritis).
- Pain, including pain in the back, chest and extremities.
- Attacks of porphyria in patients with porphyria (a very rare metabolic disease).
- Persistent headache, with or without blurred vision (benign intracranial hypertension).

If a side effect occurs, if one of the side effects worsens, or if you suffer from a side effect not mentioned in the leaflet, consult a doctor.

Reporting side effects

Side effects can be reported to the Ministry of Health by clicking on the link "Report Side Effects of Drug Treatment" found on the Ministry of Health homepage (www.health.gov.il), that directs you to the online form for reporting side effects, or by entering the link: https://sideeffects.health.gov.il

5. HOW SHOULD THE MEDICINE BE STORED?

Avoid poisoning! This medicine, and any other medicine, should be kept in a safe place out of the reach and sight of children and/or infants in order to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by the doctor.

Do not use the medicine after the expiry date (exp. date) that appears on the package. The expiry date refers to the last day of that month.

Store at a temperature below 30°C. Keep the tablets in the original package.

6. FURTHER INFORMATION

In addition to the active ingredient, the medicine also contains:

Microcrystalline cellulose, hypromellose, crospovidone, sodium stearyl fumarate, titanium dioxide (E171), talc, macrogol 8000, red & yellow ferric oxide (E172).

What the medicine looks like and the contents of the package:

Tavanic tablets are film-coated tablets intended for swallowing. The tablets are oblong, with a score line, with a pale yellowish-white to reddish-white color.

The tablets are packaged in trays of 1, 5, 7, 10 tablets.

Not all package sizes may be marketed.

License holder and importer and its address: sanofi-aventis Israel ltd., P.O.B. 8090, Netanya 4250499.

Revised in October 2022 according to MOH guidelines.

This leaflet does not contain all the information about your medicine. If you have any questions or are not sure about anything, please ask your doctor.

Registration number of the medicine in the National Drug Registry of the Ministry of Health: 119442996321