

PATIENT INFORMATION LEAFLET

WARNING: SERIOUS ADVERSE REACTIONS INCLUDING TENDINITIS AND TENDON RUPTURE (inflammation or tearing of tissues that connect muscles to the bones), PERIPHERAL NEUROPATHY (disorders seen in the nerves away from the center - loss of sensation), CENTRAL NERVOUS SYSTEM AFFECTS AND MYASTHENIA GRAVIS (a kind of muscle weakness disease).

- The antibiotics called fluoroquinolone, including levofloxacin, which is one of the active substances contained in RAVIVO, can cause disabling and irreversible adverse effects such as:
 - o Tissue inflammation that connects muscles to bones (tendinitis; symptoms can be severe pain in the joints, swelling and redness) and laceration of tissue connecting the muscles to the bones (tendon) (Symptoms are severe pain in the muscles, sudden and rapid bruising, weakness, inability to move)
 - o Disorders seen in the distant nerves for any reason - loss of sensation (peripheral neuropathy; symptoms, pain in the nerves, tenderness with numbness in the feet and hands, weakness in the muscles, tremors in the hands)
 - o The effects of the central nervous system (symptoms may be imagination, anxiety, mental breakdown, suicidal tendency, insomnia, severe headache and confusion)

If any of these undesirable effects occur during the use of RAVIVO, stop using RAVIVO immediately and talk to your doctor or pharmacist.

The antibiotics called fluoroquinolone, including levofloxacin, which is one of the active substances contained in RAVIVO, may exacerbate muscle weakness in patients with myasthenia gravis (a kind of muscle weakness disease). If you have a known muscle weakness talk to your doctor or pharmacist before using RAVIVO.

- Since the fluoroquinolone group medicines, including RAVIVO, are known to be associated with serious adverse reactions, RAVIVO may be used if there are no other alternatives in the following indications:
 - o Acute inflammation of the air spaces inside the facial bones caused by bacteria (Acute bacterial sinusitis)
 - o Acute bacterial exacerbation of chronic bronchitis (re-aggravation of persistent inflammation of bronchial tubes-membranes in the lung)

RAVIVO 500 mg Film-coated Tablet

It is taken orally.

- **Active pharmaceutical ingredient:** Each film-coated tablet contains 512.46 mg of levofloxacin hemihydrate that is equivalent to 500 mg levofloxacin.
- **Excipients:** Microcrystalline cellulose (Avicel PH102), Crospovidone, Hydroxypropyl methyl cellulose, Sodium stearyl fumarate, Opadry White (Polyvinyl alcohol, Titanium Dioxide, Polyethylene Glycol, Talc).

Please read the LEAFLET carefully before you start using this drug as it involves important information for you.

- *Keep this leaflet. You may need to read it again later.*
- *If you have further questions, please consult your doctor or pharmacist.*
- *This medication is prescribed specifically for you; please do not give it to others.*
- *Tell your doctor that you are on this medication when you go to the doctor or hospital while using this medication.*
- *Please follow what is written in this leaflet. Do not use **over or below** the dose recommended for you.*

This patient information leaflet includes the following headings:

- 1. What is RAVIVO and what is it used for?***
- 2. Precautions before the use of RAVIVO***
- 3. How to take RAVIVO?***
- 4. What are the possible side effects?***
- 5. How to store RAVIVO***

1. What is RAVIVO and what is it used for?

It should not be used because of the risk of serious side effects in the presence of alternative treatment options for acute exacerbation of airways in the facial bones caused by bacteria (acute bacterial sinusitis) and acute exacerbation of chronic bronchitis. In addition, urinary tract infections need to be proven by antibiogram.

RAVIVO tablet is taken orally. RAVIVO is a white film coated, notched, oblong (oval shaped) tablet. A box of your medicine contains 7 film coated tablets each containing 500 mg of levofloxacin. The tablet is notched to facilitate dosage adjustment.

RAVIVO is an effective antibiotic against bactericides. It belongs to the group of antibiotics called fluoroquinolones. It prevents the growth of the bacteria, their multiplication and it provides the destruction of the bacteria.

RAVIVO is used to treat infections caused by bacteria that are sensitive to levofloxacin the active substance.

Your doctor may have prescribed RAVIVO because you have one of the following conditions:

- The acute inflammation of the air spaces in the facial bones caused by the bacteria (sinusitis)
- Acute exacerbation of chronic bronchitis
- Community-acquired pneumonia (pneumonia)
- Complicated kidney and urinary tract infections, including inflammation of the urinary tract and kidney (pyelonephritis)
- Prostate inflammation
- Skin and soft tissue infections: uncomplicated skin and skin patch infections caused by Abscess (pustule), cellulitis, furuncles, impetigo (deep infectious, superficial, microbial infection), pyoderma (pus skin infections), wound infections.
- Exposure to airborne anthrax microbes

2. Precautions before the use of RAVIVO

DO NOT USE RAVIVO in the following situations.

If,

- You are allergic to levofloxacin or to any of the components in this medication or to something else from the group of fluoroquinolones antibiotics (moxifloxacin, ciprofloxacin, ofloxacin)

Allergy symptoms: itching, swallowing or breathing problems, swelling of the lips, face, throat or tongue.

- You have Sara (epilepsy) disease,
- You experienced tendonit disorder (tendonitis) due to the quinolone group antibiotic use (The tendon is a bond that connects the muscle and the skeleton)
- You are pregnant,
- You are breastfeeding,
- In children and adolescent who continue to grow up

Please do not use RAVIVO.

It should not be used in children, growing adolescents, during pregnancy and lactating women because it damages the developing cartilage tissue.

USE RAVIVO in the following situations CAREFULLY.

If,

- Any of the following situations occurs during use of RAVIVO, stop using RAVIVO immediately and talk to your doctor or pharmacist:
 - Tissue inflammation that connects muscles to bones (tendinite; symptoms can be severe pain in the joints, swelling and redness) and laceration of tissue connecting the muscles to the bones (tendon) (Symptoms are severe pain in the muscles, sudden and rapid bruising, weakness, inability to move)
 - Disorders seen in the distant nerves for any reason – loss of sensation (peripheral neuropathy; symptoms may include pain in the nerves, tenderness, numbness in the feet and hands, weakness in the muscles, trembling in the hands.)
 - The effects of the central nervous system (symptoms may be imagination, anxiety, mental breakdown, suicidal tendency, insomnia, severe headache and confusion)
 - These reactions can be seen within hours or weeks after starting use of RAVIVO.

Patients, in any age group or without pre-existing risk factors, experienced these adverse reactions. RAVIVO should be discontinued immediately if any first signs or symptoms of any serious adverse reaction occur. In addition, the use of fluoroquinolones including RAVIVO should be avoided in patients experiencing any of these serious adverse reactions in connection with fluoroquinolones.

- If you have had muscle weakness (myasthenia gravis) before,
- If you have a very severe lung infection or serious nonsocial infection (use of another antibiotic may be more appropriate)
- If you have a discomfort related to your central nervous system and you have experienced involuntary contractions,
- If you have brain damage due to stroke or other brain injuries
- In cases of intestinal inflammation with bloody, irregular diarrhea due to prolonged use of antibiotics: If severe, persistent and / or bloody diarrhea occurs during or after treatment of RAVIVO, treatment of RAVIVO should be terminated immediately and appropriate supportive and / or specific treatment should be initiated without delay. Inform your doctor immediately. Your doctor will determine the appropriate treatment for you.
- If there is pain that may suggest an inflammation or rupture, redness, limitation of motion in muscular beams (tendons), the risk of tendon rupture increases in the elderly and in patients receiving corticosteroids. Your doctor may want to monitor this situation closely.
- If you have kidney failure: your doctor will give you a specific dose adjustment.
- It has been reported that sensitivity to light occurs rarely in patients receiving RAVIVO. Avoid exposure to sunlight or artificial ultraviolet radiation, such as a solarium, during the use of RAVIVO and 48 hours after the end of treatment.
- Superinfection (onset of a second infection in the weak body with any infection): As with other antibiotics, long-term use can result in excessive proliferation of non-resistant organisms. Your doctor may want to follow you closely with the aim of preventing this. If superinfection occurs, it will apply appropriate treatment methods.
- If prolongation of QT interval is present in you (a condition that can lead to severe arrhythmias in the heart and sudden deaths): Very rarely, prolongation of QT interval has been reported in patients receiving fluoroquinolone, including levofloxacin. The following risk groups should be cautious:
 - If you are advanced age (over 65 years) or female,
 - If you have a liver problem,
 - If you are using corticosteroids,
 - Uncorrected electrolyte imbalance (e.g. low levels of potassium and magnesium in the blood)

- Congenital QT syndrome (a condition that can lead to serious arrhythmias in the heart and sudden deaths)
- Heart disease (heart failure, heart attack history, slowing of heart beat)
- Concomitant use of drugs known to prolong QT interval (e.g. Class IA and III rhythm regulating drugs, some depression drugs, macrolide antibiotics and antipsychotics)
- If you have an innate deficiency of an enzyme called glucose-6-phosphate dehydrogenase,
- Hypoglycemia (decrease in blood sugar level) and hyperglycemia (increase in blood sugar level): If you have diabetes (diabetes) and you are using insulin or oral medications for this, your blood sugar may fall or the resulting coma may develop or your blood sugar may rise (your doctor may ask you to check your blood sugar on a regular basis).
- If you have peripheral neuropathy (disorders that occur for any reason in the nerves- loss of sensations)
- Exacerbation of Myasthenia Gravis (a kind of muscle weakness disease): Fluoroquinolones have an activity that inhibits muscle-nerve conduction and may exacerbate muscle weakness in patients with myasthenia gravis. In patients with myasthenia gravis using fluoroquinolone respiratory failure that required respiratory support and post-marketing severe side effects, including death, have been associated with fluoroquinolone. Patients with myasthenia gravis history should avoid fluoroquinolone use.
- Hypersensitivity reactions: Following the first dose, severe hypersensitivity reactions (face and throat swelling as a result of allergies) that have a seldom lethal potential can be seen. You should interrupt your treatment and apply to your doctor for emergency measures.
- Severe diseases in the skin with bubbles filled with water: RAVIVO can cause severe skin reactions such as Stevens-Johnson syndrome (inflammation with blood blister around the skin and eyes, swelling and redness) and toxic epidermal necrolysis (a severe illness with fluid-filled bubbles in the deep). In this case, please apply to your doctor immediately before continuing treatment.
- Very rarely, a single dose of levofloxacin can lead to suicidal thoughts and dangerous behavior. In this case, your doctor may terminate your treatment and determine the appropriate treatment for you.
- If you have a psychological discomfort or a psychiatric illness, use RAVIVO with caution.

- If you have anorexia, jaundice, dark urine, itching or abdominal tenderness during your treatment, contact your doctor immediately. Your doctor may terminate the treatment and determine the appropriate treatment for you.

Please consult your doctor if these warnings apply to you, even at any time in the past.

Use of RAVIVO with food and drink

The absorption of RAVIVO is not affected by the foods, you can get the tablet before or after meals as your doctor recommends.

If you need to use drugs contain magnesium or aluminium or iron or zinc, drugs called antacids that neutralize stomach acid or sucralfate for stomach ulcer or reflux disease, as these products may affect the absorption of RAVIVO, we recommend taking RAVIVO at least two hours before or after the administration of these drugs.

Pregnancy

Please consult your doctor or pharmacist before using this medication..

There is insufficient data on the use of levofloxacin in pregnant women.

The potential risk for humans is unknown. RAVIVO should not be used during pregnancy due to the lack of adequate data on humans and the demonstration of the risk of damaging weight bearing cartilage in growing organisms during experimental studies with fluoroquinolones,

If you notice that you are pregnant during your treatment, please consult your doctor or pharmacist immediately

Breast-feeding

Consult your doctor or pharmacist before using this medication.

There is insufficient / limited information about levofloxacin being excreted in human or animal milk. It can not be ignored that there is a risk for the breast-feeding child because of physicochemical and direct pharmacodynamic / toxicological data for the excretion of levofloxacin by milk. RAVIVO should not be used during breast-feeding because of the risk of damaging weight bearing cartilage in growing organisms in experimental studies with fluoroquinolones.

Vehicle and machine use

The use of RAVIVO can lead to some undesirable side effects like dizziness, visual disturbances, drowsiness that may impair the patient's ability to concentrate and react. In situations that require special attention, such as vehicle and machine use, the reduction in these abilities may constitute a risk.

If you experience such side effects while using RAVIVO, do not use vehicle and machinery.

Important information about some of the excipients in the content of RAVIVO

Contains no excipients that require warning.

Use with other drugs:

- Theophylline, a drug that expands the bronchi and facilitates breathing when used in conjunction with RAVIVO, the brain contraction threshold falls
- Similar non-steroidal anti-inflammatory drugs such as fenbufen, ketoprofen, ibuprofen, aspirin, and indomethacin (when used in combination with RAVIVO, brain contraction threshold falls)
- Probenesid used in gout disease or cymetidine used in stomach ulcer :Reduces body excretion of RAVIVO
- Sucralfate (used to treat stomach ulcers) reduces the absorption of RAVIVO.
- Cyclosporine, a drug that suppresses the immune system (prolonged half-life)
- Vitamin K antagonists used to prevent blood clotting (e.g., warfarin). (The effect may increase, the risk of bleeding may occur.) Your doctor may ask you for blood clotting tests.
- Medications known to prolong the QT interval in the heart (which can lead to severe arrhythmia in the heart)
 - o Class Ia antiarrhythmics (drugs used against heart arrhythmia) (quinidine) and class III antiarrhythmics (amiodarone)
 - o Some depression medications (tricyclic antidepressants, e.g., amitriptyline, imipramine)
 - o Macrolides (an antibiotic group) (erythromycin, azithromycin, clarithromycin)
 - o Antipsychotics (used in the treatment of some mental illnesses)
- Corticosteroid (used in the treatment of asthma and inflammation)

- A urine test making for opiates which is strong painkillers may give false positive results when using this drug

Other medicines: Digoxin, glibenclamide and ranitidine are not expected to change the RAVIVO's effect.

Please inform your doctor or pharmacist if you are using or have recently used any medicine with or without a prescription.

3. How to take RAVIVO?

Instructions for proper use and dose / application frequency:

Your doctor will determine the amount of dose and the duration of treatment with RAVIVO.

RAVIVO is used in adults.

RAVIVO film coated tablet is applied once or twice a day. The dosage depends on the type and severity of the infection as well as on the susceptibility of the infecting bacteria.

It is recommended that RAVIVO be administered at the following doses:

Type of Infection	Dose Every 24 hours (according to the severity of infection)	The Duration of Treatment
Acute sinusitis (inflammation of the air cavities in the facial bones)	500 mg once daily	10-14 days
Acute exacerbations of chronic bronchitis(bronchial inflammation)	250 to 500 mg once daily	7-10 days
Community-acquired pneumonia	500 mg once or twice daily	7-14 days
Pyelonephritis (urinary tract and kidney inflammation)	500 mg once daily	7-10 days
Complicated urinary tract infections	500 mg once daily	7-14 days
Skin and soft tissue infections	250 mg once daily or 500 mg once or twice daily	7-14 days
Chronic bacterial prostatitis (inflammation of the prostate)	500 mg once daily	28 days
Exposure to airborne anthrax microbes	500 mg once daily	8 weeks

The duration of treatment depends on the course of your disease (see table above). As with all antibiotic treatments in general, the use of RAVIVO should be continued for at least 48-72 hours after the patient has received evidence that the infection has ceased and the fever has dropped.

Administration way and method

RAVIVO is taken orally. Film tablet should be taken with sufficient amount liquid without chewing. You can divide from the notch line to fit the dosage. The tablets may be taken during meals or at any time between meals.

We recommend that you take RAVIVO at least two hours before or after administration of iron salts, antacids or sucralfate, as absorption may be reduced.

Sunlight protection

Do not expose to direct sunlight when using this medicine. Your skin may become more sensitive to the sun, causing burning, tingling, or severe get blister. For this reason, use sun protection with high protection factor. Wearing a hat and sunglasses that will not leave your arms and legs open to the sun. Avoid sunbathing.

Different age groups**Use in children:**

RAVIVO is not used in children and adolescents who are growing up.

Use in the elderly:

If there is no abnormality in renal function in the elderly, there is no need to adjust the dose of RAVIVO.

Special use cases**Renal failure:**

If your kidney function is impaired, your doctor will reduce the dose of RAVIVO and will monitor you more closely..

In patients with creatinine clearance ≤ 50 ml / min (the rate of clearance of the substance used in kidney function tests), the dosage (according to the severity of infection) will be determined by your doctor.

Liver failure:

In liver dysfunction, adjustment in the dose of RAVIVO is not necessary..

Your doctor will tell you how long your treatment of RAVIVO will continue. Do not interrupt your treatment without consulting your doctor.

If you have an impression that the effect of RAVIVO is too strong or weak, consult to your doctor or pharmacist.

If you use more RAVIVO than you should:

If you use RAVIVO than you should, you should speak to a doctor or pharmacist.

Overdose indication; mental confusion, dizziness and involuntary contractions in the muscles are related to the central nervous system, the prolongation of QT interval and nausea in the ECG.

If you forget to use RAVIVO:

If you miss a dose, take the missed dose soon as you remember it.

Do not take double doses to compensate for forgotten doses.

Possible side effect after termination of usage RAVIVO:

Do not terminate your RAVIVO treatment without consulting your doctor, the symptoms of your disease may reappear and resistance to bacteria may develop.

4. What are the possible side effects?

As with all medications, side effects may occur in people who are sensitive to the substances found in the content of RAVIVO.

The side-effects in this section are given with an estimation of the frequency:

Very common	: It can be seen in at least one of the 10 patients
Common	: It can be seen in less than one in 10 patients but one or more than one in 100 patients
Uncommon	: It can be seen in less than one in 100 patients but one or more than one in 1000 patients
Rare	: It can be seen in less than one in 1000 patients but more than one or more than one in 10 000 patients
Very rare	: It can be seen in less than one in 10 000 patients
Unknown	: It is unpredictable according to the available data

If any of the following conditions occur, stop using RAVIVO and tell your doctor IMMEDIATELY or contact the emergency department of the hospital nearest to you:

Rare:

- Along with common itching and rashes on the skin, swelling of the lips and face and throat and tongue, difficulty swallowing or breathing (hypersensitivity-anaphylaxis),

- Tendinitis, tendon rupture (inflammation or rupture of the tissues that bind the muscles to the bones),
- Muscle weakness
- Peripheral neuropathy (disorders caused by any reason in the distant nerves - loss of sensation)

Unknown:

- Stevens-Johnson syndrome, erythema multiforme (inflammation with blood blister around the skin and eyes, swelling and redness), toxic epidermal necrolysis (a serious disease with deep fluid-filled bubbles on the skin)

These are all very serious side effects.

If you have one of them, you may need urgent medical attention or hospitalization.

If you notice any of the following conditions, tell your doctor IMMEDIATELY or contact the emergency department of the hospital nearest to you:

Rare:

- Pain and inflammation in your tendons (muscle ligaments). The Achilles tendon is the most frequently affected tendon and in some cases the tendon may break
- Involuntary seizures of the muscles (convulsions)

Unknown:

- Loss of appetite, the white part of the eye and skin turn the yellow colour, darkening of the urine, itching, tenderness in the abdominal region. These can be indicative of liver problems that can be sometimes fatal
- Exacerbation of Myasthenia gravis (a kind of muscle weakness disease)
- Distortion in heart rhythm, palpitation
- Fever, tingling, pain or numbness. These may be signs of neuropathy
- Severe, persistent, bloody diarrhea combined with severe abdominal pain like cramp and high fever
- Rupture of joint ligaments and muscles, joint inflammation

These may be signs of serious bowel problems.

All these are serious side effects. Immediate medical attention may be required.

If you notice any of the following situations, tell your doctor:

Common:

- Nausea, vomiting, diarrhea
- Increase in levels of some liver enzymes in blood
- Headache, dizziness
- Insomnia

Uncommon:

- Fungal infections, consist of resistance to other micro-organisms
- Itching and skin eruption, rash, excessive sweating
- Abdominal pain, indigestion, loss of appetite, gas in your stomach, constipation
- Vertigo
- Anxiety, mental confusion, irritability
- Sleepiness, shaking, disorder of taste sensation
- Shortness of breath (dyspnea)
- Joint or muscle pain
- Blood tests may show unexpected results due to liver or kidney problems (bilirubin, increase in creatinine)
- Decrease in the number of white blood cells (leukopenia)
- Fatigue

Rare:

- Decrease in blood sugar. This is important for diabetic patients and may cause coma.
- Visual and auditory hallucinations and excessive skepticism (paranoia) may accompany psychiatric disorders and unrest and depression
- Abnormal dreams, nightmares
- Visual disturbances including blurred vision
- Tinnitus
- Muscle weakness. This is an important condition for myasthenia gravis (a rare disease of the nervous system) patients.

- Low blood pressure
- Acceleration of the heart beat, pulsation
- Bleeding and bruising can easily occur due to decreased count of blood platelet (thrombocytopenia)
- Decrease in the number of white blood cells (neutropenia)
- Fever
- Changes in renal function, kidney failure caused by allergic kidney reactions called interstitial nephritis

Very rare:

- Attacks in patients with porphyria (a metabolic disease that can be seen rarely)

Unknown:

- Coma due to decrease in blood sugar
- Increase in blood sugar
- Self-injurious behavior, including suicidal ideation and suicide attempts
- Loss of taste sensation
- Odor disorders including loss of sense of smell
- Fainting (syncope), benign intracranial hypertension (increase benign internal pressure of the head)
- Deterioration of hearing ability, hearing loss
- Temporary visual loss
- Increased skin sensitivity to sun and ultraviolet light (sensitivity to light)
- Decrease in count of all blood cells (pancytopenia) or red blood cells (anemia). The skin may be pale and yellow due to damage to red blood cells and a decrease in the number of all type of blood cells. Fever, sore throat and a general feeling of illness may occur
- Inflammation in the mouth (stomatitis)
- Excessive immune responses may occur (hypersensitivity)
- Movement and gait problems (dyskinesia, extrapyramidal disorder)
- Allergically-induced pneumonia
- Inflammation of blood vessels arising from allergic reaction
- Inflammation of the pancreas (pancreatitis)

- Pain (back, chest, arms and legs)

These are the minor side effects of RAVIVO.

If you encounter any side effects not mentioned in these instructions for use inform your doctor or pharmacist.

5. How To Store RAVIVO?

Keep RAVIVO in places where children can not see, can not reach and in its packaging

Store at room temperature below 30°C and in its packaging.

Use in accordance with the expiration date.

Do not use RAVIVO after the expiration date on the packaging.

If you notice any signs of deterioration on the tablets do not use RAVIVO.

Do not throw away any expired or unused medicines! Give to the collection system determined by the Ministry of Environment and Urbanization.

Marketing Authorization Holder

Drogsan İlaçları San. ve Tic. A.Ş.

Oğuzlar Mah. 1370. Sok No: 7/3

06520 Balgat- ANKARA / TURKEY

Manufacturer:

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06760 Çubuk/ANKARA / TURKEY

Date of Revision of the Text

03/08/2022

