PATIENT INFORMATION LEAFLET

WARNING: TENDINITIS AND TENDON TEAR (inflammation and tear in the tissues that connect the muscles to the bones), PERIPHERAL NEUROPATHY (Disorders of the central nerves for any reason - loss of sensation), CENTRAL NERVOUS SYSTEM (central nervous system) EFFECTS AND UNDESIRABLE EFFECTS INVOLVING THE VIOLATION OF MYASTENIA GRAVIS (a type of muscle weakness disease)

- Fluoroquinolones, including LEVOXIPOLIN, can cause undesirable and irreversible adverse effects such as:
  - Tissue inflammation that connects the muscles to the bones (tendinitis; there may be severe pain, swelling and redness in the joints) and tissue (tendon) tearing that connects the muscles to the bones (symptoms may be severe pain in the muscles, sudden and rapid bruising, weakness, inability to move)
  - Disorders seen in the nerves far from the center for any reason - loss of sensation (peripheral neuropathy; symptoms of pain in the nerves, tenderness, tingling with feet and hands, weakness in the muscles, tremors in the hands may be)
  - Central nervous system (central nervous system) effects (symptoms can be imagination (hallucination), anxiety (anxiety), mental breakdown (depression), suicidal tendency, insomnia, severe headache and confusion.

If you experience any of these undesirable effects during the use of LEVOXIPOLIN, stop using LEVOXIPOLIN immediately and see your doctor or pharmacist.

- Antibiotics called fluoroquinolone, including levofloxacin, the active ingredient contained in LEVOXIPOLIN, may exacerbate muscle weakness in patients with myasthenia gravis (a type of muscle weakness disease). If you have a known muscle weakness disease, talk to your doctor or pharmacist before using LEVOXIPOLIN.

LEVOXIPOLIN 500 mg/100 ml solution for i.v. infusion
For intravenous administration.
Sterile.

- ***Active Substance:*** 100 ml solution for infusion contains 512.48 mg levofloxacin hemihydrate equivalent to 500 mg levofloxacin.

- ***Excipients:*** Sodium chloride, sodium hydroxide, hydrochloric acid, water for injection.

Before using this medicine, read all of this PATIENT INFORMATION LEAFLET carefully. Because, this leaflet includes important information for you.

- *Keep this PATIENT INFORMATION LEAFLET. You may need to read it again.*
- *If you have any further questions, ask your doctor or pharmacist.*
- *This medicine has been prescribed for you. Do not pass it on to others.*
- *During the use of this medicine, tell that you are using this medicine when you go to a doctor or hospital.*
- *Follow the written instructions exactly. Do not use **higher or lower** dose than the recommended dose.*

The following subjects are covered herein:

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

LEVOXIPOLIN is a greenish yellow solution administered to the vein. LEVOXIPOLIN is presented in polypropylene (non-PVC) bags containing a total of 100 mL of solution containing 1 mg of levofloxacin per 1 mL.

LEVOXIPOLIN is an antibiotic active against bacteria. This belongs to a group of antibiotics called fluoroquinolones. It prevents the growth, proliferation of bacteria, and eliminates them.

It is used in the treatment of infections caused by bacteria that are susceptible to levofloxacin, the active substance of LEVOXIPOLIN.

Your doctor may prescribe this intravenous LEVOXIPOLIN form because you are unable to take oral antibiotic treatment for one of the following conditions:

- Community-acquired pneumonia (pneumonia)
- Complicated renal and urinary tract infections, including inflammation of the urinary tract and kidney (pyelonephritis)
- Prostate inflammation
- Skin and soft tissue infections: abscess, cellulitis, froncles, impetigo (deep infectious superficial microbial infection), pyoderma (purulent skin infection), uncomplicated skin and skin structure infections caused by wound infections.
- Hospital acquired pneumonia (pneumonia)
- Exposure to airborne anthrax microbes

2. What you need to know before you are given LEVOXIPOLIN 500 mg/100 ml solution for IV infusion

DO NOT USE LEVOXIPOLIN under the following circumstances

If,

- You are allergic to levofloxacin or any of the ingredients of this medicine or any other antibiotic of the fluoroquinolone group,
- You suffer from epilepsy,
- You have ever had tendon problems (e.g. tendinitis) related to treatment with a quinolone antibiotic (tendon is a cord that joins your muscle to your skeleton),
- You are pregnant,
- You are breastfeeding,
- In children and growing adolescents

- It should not be used in children, in growing adolescents, during pregnancy and in breastfeeding women because of the risk of damage to the developing cartilage tissue.

USE LEVOXIPOLIN 500 mg/100 ml solution for IV infusion with CAUTION

If,

- You have a very severe lung infection or serious hospital-acquired infection (use of another antibiotic may be more appropriate)

- You have a disorder related to your central nervous system and you have experienced associated involuntary contractions
- You have brain damage due to stroke or other brain injuries
- You suffer from enteritis with bloody, watery diarrhea due to prolonged use of antibiotics: Severe, persistent and/or bloody diarrhea occurs during or after LEVOXIPOLIN treatment, LEVOXIPOLIN treatment should be terminated immediately and appropriate supportive and/or specific treatment should be initiated without delay. Contact you doctor immediately. Your doctor will prescribe the appropriate treatment for you.
- Risk of tendon rupture increase in elderly and in patients who use corticosteroids and when pain, redness, limitation of movement occurs in the tendons that may suggest inflammation or rupture. Your doctor may want to monitor this situation closely.
- You have renal failure: Your doctor will adjust the dose for you.
- It has been reported that patients who use LEVOXIPOLIN rarely develop sensitivity to light. Do not be exposed to strong sunlight or artificial ultraviolet rays such as solarium during the use of LEVOXIPOLIN and for 48 hours after the treatment.
- Superinfection (the beginning of a second infection in the structure weakened by any infection): As with other antibiotics, long-term use can result in excessive proliferation of non-resistant organisms. Your doctor may want to monitor you closely to prevent this condition. Superinfection occurs, appropriate treatment methods will be applied.
- If you are 60 years or older
- If you have had an organ transplant
- You are using anti-inflammatory drugs called corticosteroids.
- If you have had liver problems
- If you have a heart problem
- If any of the following applies to you, you should be careful while using this medicine:
  - If you are taking medications that may affect your heart (see section " Use in combination with other drugs"),
  - If you have a congenital heart disease called “long QT syndrome” or individuals in your family who have this disease (this is a defect in the heart electron (ECG)),
  - If you have salt imbalance in your blood (especially if your blood potassium and magnesium levels are low),
  - If your heart rhythm is too slow (this condition is called "bradycardia"),

  - If you have heart failure,
  - If you have ever had a heart attack (myocardial infarction),
  - If you are a woman or an elderly person or if you are using other medicines that cause changes in the ECG (see section " Use in combination with other drugs").
- 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 and you are using insulin or oral medication, your blood sugar may decrease or an associated coma may occur or your blood sugar may rise (your doctor may ask you to check your blood sugar regularly).
- You have peripheral neuropathy (disorders that occur for any reason in the nerves-sensory loss).
- 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. Post-marketing serious side effects, including respiratory failure requiring respiratory support and death have been associated with fluoroquinolone in patients with myasthenia gravis using fluoroquinolone. Patients with a history of myasthenia gravis should avoid fluoroquinolone use.
- Hypersensitivity reactions: Following the first dose, severe hypersensitivity reactions (swelling of the face and throat due to allergy), which are seldom lethal, can be seen. You should stop your treatment and ask your doctor for urgent medical care.
- Severe diseases with blisters on the skin: LEVOXIPOLIN can lead to severe skin reactions such as Stevens-Johnson syndrome (inflammation with infiltration of blood, swelling and redness on the skin and around the eyes), and toxic epidermal necrolysis (a serious disease with blisters on the skin). In this case, please contact 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 stop your treatment and prescribe an appropriate treatment for you.
- If you have a history of psychological or psychiatric disorder, use LEVOXIPOLIN with caution.
- If you experience loss of appetite, jaundice, dark urine, itching or tenderness during your treatment, contact your doctor immediately. Your doctor may stop your treatment and prescribe an appropriate treatment for you.
- Serious and irreversible adverse reactions that cause disability, including tendonitis (swelling around the joint, pain) and tendon rupture, peripheral neuropathy (pain at the ends of the body, numbness, needling, and muscle weakness) and effects of the central nervous system.
- Fluoroquinolones, including LEVOXIPOLIN, have been associated with potentially irreversible serious adverse reactions that can cause disability. Common adverse reactions musculoskeletal and peripheral nervous system (tendinitis (swelling around

the joint, pain), tendon rupture, swelling or inflammation in tendons, tingling or numbness, numbness in arms and legs, muscle pain, muscle weakness, joint pain, swelling in joints such as arthralgia (joint pain), myalgia (muscle rheumatism, muscle pain), peripheral neuropathy (pain in the extremities of the body, numbness, needling, and muscle weakness) and central nervous system effects (hallucination, anxiety, depression, tendency to suicide, insomnia (insomnia), severe headache and confusion (confusion) (See 4. Possible side effects).

If you feel sudden and severe pain in your stomach, chest or back, contact an emergency room immediately.

If these warnings are valid for you, even at any time in the past, please consult your doctor.

Using LEVOXIPOLIN 500 mg/100 ml solution for IV infusion with food and beverages
No interaction with food and drinks because of the method of administration.

Pregnancy
Before using this medicine consult your doctor or pharmacist.

No adequate data is available on the use of levofloxacin in pregnant women.
Potential risk for human is unknown. LEVOXIPOLIN should not be used during pregnancy in the absence of human data and since experimental data suggest a risk of damage by fluoroquinolones to the weight-bearing cartilage of the growing organism.

If you realize that you are pregnant during your treatment, immediately consult your physician or pharmacist.

Breastfeeding
Before using this medicine consult your doctor or pharmacist.

There are no or insufficient information on the excretion of levofloxacin into human or animal milk. The risk for the breastfed child cannot be ruled due to physicochemical and available pharmacodynamic/toxicological data for the excretion of levofloxacin by milk. LEVOXIPOLIN should not be used during breastfeeding since experimental data suggest a risk of damage by fluoroquinolones to the weight-bearing cartilage of the growing organism.

Ability to drive and use machines
Use of LEVOXIPOLIN may cause some undesirable effects such as dizziness/vertigo, visual disturbances, drowsiness that may impair the patient's ability to concentrate and react. Reduced ability may constitute a risk in situations where these abilities are of special importance e.g. driving a car or operating machinery.
Do not drive or use machinery if you experience such side effects when using LEVOXIPOLIN.

Vital information regarding some of the excipients contained in LEVOXIPOLIN 500 mg/100 ml solution for IV infusion
If you do not have hypersensitivity to the excipients of LEVOXIPOLINE, no adverse effect due to these substances is expected.

This medicinal product contains 15.4 mmol (354 mg) sodium per 100 ml. The sodium content should be taken into account in patients on a controlled sodium diet.

Use in combination with other drugs

- Theophylline, a drug that expands the bronchi and facilitate breathing (when used in combination with LEVOXIPOLIN, the cerebral seizure threshold is reduced)
- Similar non-steroidal anti-inflammatory drugs such as fenbufen, ketoprofen, ibuprofen, aspirin and indomethacin (when used in combination with LEVOXIPOLIN, cerebral seizure threshold is reduced)
- Probenecid used in gout disease or cimetidine used in stomach ulcer (reduces the elimination of LEVOXIPOLIN from the body)
- Cyclosporine, a drug that suppresses the immune system (may increase the likelihood of side effects from cyclosporine)
- Vitamin K antagonists used to prevent blood clotting (e.g. warfarin). The effect may increase, the risk of bleeding may occur. Your doctor may request blood clotting tests.
- Medications known to prolong the QT interval in the heart (which can lead to severe arrhythmia in the heart)

– Class Ia antiarrhythmic (quinidine) and class III antiarrhythmic (amiodarone)
– Some depression medications (tricyclic antidepressants, e.g. amitriptyline, imipramine)
– Macrolides (an antibiotic group)
– Antipsychotics (used in the treatment of some mental illnesses)
– Corticosteroid (used in the treatment of asthma and inflammation)
– Urine tests may show ‘false positive’ results for strong painkillers called ‘opiates’ in people taking this medicine.

Other medicines: Digoxin, glibenclamide and ranitidine are not expected to change the effect of LEVOXIPOLIN.

If you are currently taking or recently took any prescribed or over-the-counter drugs, please inform your physician or pharmacist.

3. How you will be given LEVOXIPOLIN?
Instructions for proper use and dosage/administration frequency:
LEVOXIPOLIN 500 mg/100 ml solution for IV infusion will be administered by a specialized health staff by slow injection through a vein for at least 60 minutes.
LEVOXIPOLIN is used in adults.
The dosage will depend on the type and severity of the infection and to the susceptibility of the bacteria causing the infection.

Depending on your condition, your doctor may switch to oral use several days after the initial intravenous administration.

LEVOXIPOLIN is recommended in the following doses:

Usage	**Daily dosage** *(Based on the severity of infection)*	**Treatment duration**
Community-acquired pneumonia	500 mg once or twice daily	7-14 days
Inflammation of urinary tract and kidney (pyelonephritis)	500 mg once daily	7-10 days
Complicated renal and 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
Prostate inflammation	500 mg once daily	28 days
Pneumonia acquired in the hospital	750 mg once daily	7-14 days
Exposure to airborne anthrax microbes	500 mg once daily	8 weeks

Treatment duration depends on the course of your disease (see above table). As with all antibiotic treatments in general, the use of LEVOXIPOLIN should be continued for at least 48-72 hours after the patient fever has dropped and evidence of bacterial eradication has been obtained.

- **Method of administration:**

LEVOXIPOLIN 500 mg/100 ml solution for I.V. infusion is administered by a specialized health staff by slow intravenous infusion. The infusion time must be 60 minutes for 500 mg LEVOXIPOLIN solution.

The solution must be visually inspected before use. Only clear, particle-free solutions should be used.

Once the rubber plug is punctured, the infusion solution must be used immediately to protect from contamination.

Sunlight protection

Do not expose yourself to direct sunlight while using this medicine. Your skin may become more sensitive to the sun and may cause burning, tingling or severe blisters. For this reason, use sunscreen with a high protection factor. When you go to the sun, wear a hat and clothes that will not leave your arms and legs exposed. Avoid sunbathing.

Different age groups:

Use in children:
LEVOXIPOLIN must not be given to children and growing adolescents.

Use in elderly:
No adjustment of LEVOXIPOLIN dose is required in the elderly, in the absence of renal dysfunction.

- **Special conditions of use:**

Renal failure:
If you have impaired renal functions, your doctor will lower the dose of LEVOXIPOLIN and monitor closely.
Dosage in patients with a creatinine clearance ≤ 50 ml/min (based on the severity of infection)

Hepatic failure:
No adjustment of dose is required in hepatic failure.
Your doctor will inform you on the duration of your treatment with LEVOXIPOLIN. Do not stop your treatment without consulting your doctor.

If you are under the impression that the effect LEVOXIPOLIN is too strong or weak, consult your physician or pharmacist..

If you have taken more LEVOXIPOLIN than you should have:
If you have used LEVOXIPOLIN more than you should have or more than prescribed, consult a physician or a pharmacist.
LEVOXIPOLIN 500 mg/100 ml solution for I.V. infusion will be administered by a specialized health staff as directed by your doctor.

If you forget to take LEVOXIPOLIN:
Your doctor will decide when to give you the missed dose. Follow the instructions of your doctor for the time of the next dose.

Do not double-dose to make up for forgotten doses.

Possible effects once LEVOXIPOLIN treatment is concluded
Do not stop treatment with LEVOXIPOLIN before consulting your doctor, your condition may get worse and the bacteria may become resistant to the medicine.

4. Possible side effects
Like all medicines, LEVOXIPOLIN may cause side effects in patients sensitive to its ingredients.
Side effects are listed as shown in the categories below.
Very common: It can be seen in at least 1 of 10 patients.
Common: Less than one in 10 patients, but more than one in 100 patients.
Uncommon: Less than one in 100 patients, but more than one in 1000 patients.

Rare: Less than one in 1,000 patients, but more than one in 10,000 patients.
Very rare: Less than one in 10,000 patients can be seen.
Unknown: It cannot be estimated from the available data.

If any of the following reactions happen, stop taking LEVOXIPOLIN 500 mg/100 ml solution for IV infusion and tell your doctor immediately or contact the casualty department at your nearest hospital:

- Fluoroquinolones, including LEVOXIPOLIN, can cause irreversible adverse reactions leading to disability such as:
  - Tendinitis and tendon rupture
  - Peripheral neuropathy
  - Central nervous system effects

In patients with any of these reactions, LEVOXIPOLIN should be discontinued immediately and fluoroquinolones should be avoided.

Rare (may be seen in less than one of 10,000 patients):

- Swelling of the face, lips, mouth or throat, difficulty in swallowing or breathing with generalized itching and rash on the skin (hypersensitivity-anaphylaxis)

Unknown:

- Stevens-Johnson Syndrome, erythema multiform (inflammation with infiltration of blood, swelling and redness on the skin and around the eyes), toxic epidermal necrolysis (a serious disease with blisters on the skin)
- Severe circulatory disturbance (anaphylactic shock, anaphylactoid) caused by hypersensitivity, manifested by rashes on the skin, itching or hives, swelling of the face, lips, tongue or other parts of the body, shortness of breath, wheezing or difficulty breathing.

These are all very serious side effects.

If you experience one of these side effects, it means that you are severely allergic to LEVOXIPOLIN. You may need urgent medical attention or to be hospitalized.

If you notice any of the following side effects, tell your doctor immediately or contact the casualty department at your nearest hospital

Rare (may be seen in less than one of 1,000 patients):

- Pain and inflammation in your tendons (muscle beams). Achilles tendon is the most commonly affected tendon, and in some cases, the tendon may break.
- Myastenia gravis (a type of muscle weakness disease) aggravation
- Involuntary seizures in the muscle (convulsions)

Not known:

- Loss of appetite, yellowing of your skin or white of your eyes (jaundice), dark colored urine, itching or abdominal pain or tenderness. These may be signs of liver problems that may be sometimes fatal.
- Changes in the rhythm of the heart ("QT interval prolongation" that can be seen on the electrocardiogram where the electrical activity of the heart is recorded)
- Abnormal very fast heart rhythm (ventricular tachycardia), life-threatening irregular heart rhythm (ventricular arrhythmia)
- Torsade de pointes (life-threatening irregular heart rhythm) that can result in cardiac arrest
- Fever, tingling, pain, or numbness. These may be symptoms of neuropathy.
- Severe, stubborn, bloody diarrhea with severe abdominal pain and high fever in the form of cramps. These may be symptoms of serious bowel problem.
- Breaking connective tissue that holds the bones together (ligament rupture)
- Break in muscles,
- Tendon rupture (eg Achilles tendon)
- Joint inflammation
- Skeletal muscle destruction (rhabdomialysis)

These are all serious side effects. You may need urgent medical attention.

If you notice any of the following side effects, tell your doctor:
Common (may be seen in less than one of 10 patients but more than one of 100 patients):

- Nausea, vomiting, diarrhea
- Increase in blood levels of liver enzymes
- Reddening, pain and tenderness at the injection site
- Inflammation of blood vessels (phlebitis)
- Headache, dizziness
- Insomnia

Uncommon (may be seen in less than one of 100 patients but more than one of 1,000 patients):

- Fungal infections (including fungal infection called candida), and growth of other resistant bacteria
- Itching and rash, hives, increased sweating
- Abdominal pain, indigestion, loss of appetite (anorexia), gas in the abdomen, constipation
- Dizziness (vertigo)
- Anxiety, confusion, irritability
- Sleepiness, shivering, impaired sense of taste
- Shortness of breath (dyspnea)
- Joint or muscle pain
- Abnormal blood tests due to liver or kidney problems (increased bilirubin, creatinine)
- Decrease in the number of white blood cells (leukopenia)
- Increased number of some white blood cells (eosinophilia)

- Fatigue, debilitation (asthenia).

Rare (may be seen in less than one of 1,000 patients but more than one of 10,000 patients):

- Reduced blood sugar. This is important for diabetic patients and may cause to coma.
- Psychiatric disorders that can accompany visual and auditory hallucinations (hallucinations) and excessive skepticism (paranoia), restlessness, depression,
- Abnormal dreams, nightmares
- Numbness and tingling sensation (paresthesia)
- Visual impairments including blurred vision
- Tinnitus
- Muscle weakness. This is an important condition for patient with myasthenia gravis (a rare disorder of the nervous system)
- Low blood pressure (hypotension)
- Increased heartbeat, palpitations
- decrease in the number of blood platelets (thrombocytopenia) leading to a tendency to bruise and bleed easily
- Decrease in the number of white blood cells (neutropenia)
- Fever
- Alterations in kidney function and kidney failure which may be due to allergic kidney reactions called interstitial nephritis.

Very rare (may be seen in less than one of 10,000 patients):

- Attacks in patients with porphyria (a very rare metabolic disease)

Not known:

- Coma associated with reduced blood sugar
- Increased blood sugar
- Self-destructive behavior, including suicidal thoughts and suicide attempts
- Loss of sense of taste
- Impaired sense of smell including loss of sense of smell
- Fainting (syncope), benign intracranial hypertension (benign pressure increase in the head)
- Impaired hearing ability, hearing loss
- Transient visual loss, eye inflammation
- Increased skin sensitivity to sun and ultraviolet light (light sensitivity)
- Decrease in number of all blood cells (pancytopenia), decreased number of white blood cells (agranulocytosis) or red blood cells (haemolytic anemia).
- Pale and yellow skin due to the damage in red blood cells and the decrease in the number of all kinds of blood cells. Fever, sore throat and a general feeling of illness may occur.
- Inflammation in the mouth (stomatitis)

- Excessive immune responses may develop (hypersensitivity).
- Movement and gait problems (dyskinesia, extrapyramidal disorder)
- Breathing difficulty and wheezing (bronchospasm)
- Allergy-induced pneumonia
- Inflammation of blood vessels caused by allergic reaction
- Inflammation of pancreas (pancreatitis)
- Pain (back, chest, arms and legs)

These are mild side effects of LEVOXIPOLIN.

If such symptoms become uncomfortable or continue for a long time, contact your doctor.

If you notice any side effect not mentioned in this leaflet, please inform your doctor or pharmacist.

5. How to store LEVOXIPOLIN

Keep LEVOXIPOLIN out of the sight and reach of children, and in its original packaging.
Store at room temperature below 25°C and in its packaging. Protect from light.

LEVOXIPOLIN is compatible with the following infusion solutions:

0.9% sodium chloride solution
5% Dextrose Solution
2.5% Dextrose Solution
Ringer solution
Isolated balanced electrolyte solution
10% amino acid solution

LEVOXIPOLIN must not be mixed with heparin or alkaline solutions (e.g. sodium bicarbonate).

Once removed from the package, the shelf life in the room is 3 days.

Use in compliance with the expiry date.
Do not use LEVOXIPOLIN after the expiry date which is stated on the packaging.
Do not use LEVOXIPOLIN if you notice defects on the product and/or its packaging.
Do not throw away drugs that have expired or are not used! Deliver to the collection system determined by the Ministry of Environment and Urbanism.

Marketing Authorization holder:
POLİFARMA İLAÇ SANAYİ VE TİC. A.Ş.
Vakıflar OSB Mahallesi,
Sanayi Caddesi, No:22/1

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