PATIENT INFORMATION LEAFLET

WARNING: TENDINITIS AND TENDON TEAR (inflammation or rupture in the tissues connecting the muscles to the bones), **PERIPHERAL NEUROPATHY** (Disorders of the central nerves for any reason - loss of sensation), **CENTRAL NERVOUS SYSTEM EFFECTS AND SERIOUS SIDE EFFECTS INCLUDING VIOLENCE OF MYASTENIA GRAVIS** (a kind of mucluar weakness disease)

- Fluoroquinolones, including CİPROPOL, have been associated with potentially irreversible serious Adverse reactions that can cause disability such as:
  - o Tissue inflammation that connects the muscles to the bones (tendinitis symptoms 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.)
  - o Disorders 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)
  - o Central nervous system effects (symptoms can be imagination (hallucination), anxiety, mental breakdown (depression), suicidal tendency, insomnia, severe headache and confusion

If you experience any of these undesirable effects during the use of CİPROPOL, stop using CİPROPOL and talk to your doctor or pharmacist.

- Antibiotics called fluoroquinolone, including ciprofloxacin, the active ingredient of CIPROPOL, can cause an exacerbation of muscle weakness in patients with myasthenia gravis (a form of muscular weakness). If you have a known muscle weakness disease, talk to your doctor or pharmacist before using CİPROPOL.

- Since it is known that fluoroquinolone drugs, including CİPROPOL, are associated with serious side effects, no other alternative can be used in the following indications.
  - o Acute bacterial sinusitis (an infection in the nasal cavity and sinuses)
  - oUncomplicated urinary infection (urinary tract infection in healthy people without structural and physical disorders)

CİPROPOL 2 mg /ml Solution For I.V. Infusion
Used intravenously
Sterile

- ***Active ingredient:*** Each ml contains 2.54 mg ciprofloxacin lactate equivalent to 2 mg ciprofloxacin. 100 ml solution contains 200 mg ciprofloxacin.

- ***Excipients:*** Sodium chloride, lactic acid, hydrochloric acid, water for injection

Please read this PATIENT INFORMATION LEAFLET carefully before starting to use the drug; because important information is included here.

- *Keep this PATIENT INFORMATION LEAFLET. You may need to re-read it later.*
- *In case you have additional questions, please consult your doctor or pharmacist.*
- *This drug is prescribed personally for you, do not give to others.*
- *During the use of this drug, please tell your doctor that you are using this drug when you visit your doctor or a hospital.*
- *Please follow these instructions strictly. Do not use dosages* ***higher or lower*** *than the dosage recommended to you.*

The following topics are included in this Patient Information Leaflet:

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

•CİPROPOL is available in bag. Each 100 ml bag contains ciprofloxacin lactate equivalent to 200 mg, 200 ml bag contains ciprofloxacin lactate equivalent to 400 mg ciprofloxacin.
• CİPROPOL contains ciprofloxacin is an antibiotic belonging to the fluoroquinolone family. Ciprofloxacin works by killing bacteria that cause infections.
• CİPROPOL located in 100 ml and 200 ml bags. Solution in bag is colorless and clear.

In the presence of acute bacterial sinusitis, uncomplicated urinary infection and alternative treatment options, it should not be used due to the risk of serious side effects. In these indications, it can only be used with the approval of an infectious diseases specialist if it is proven with an antibiogram and other alternative treatments cannot be applied.

• CİPROPOL is used in adults for the treatment of respiratory tract infections, long lasting or recurring ear or sinus infections, urinary tract infections, genital organ infections, gastro-intestinal tract infections and intra-abdominal infections, skin and soft tissue infections, bone and joint infections, infections occur in blood, to treat infections in patients with a very low

white blood cell count, intestinal infections in immunocompromised patients. CİPROPOL, used in children between the age of 1-17 for the treatment of complicated urinary tract infections, including infections that have reached the kidneys in 2. and 3. stages, lung and bronchial infections suffering from *P.aeruginosa* bacteria in cystic fibrosis.

Ciprofloxacin is also used for to reduce the emergence of anthrax transmitted by inhalation and slow the progression in the adults and children.

2. Before you are given CİPROPOL
DO NOT USE CİPROPOL UNDER THE FOLLOWING CONDITIONS
If:
• you are allergic to the active substance, to other quinolone drugs or to any of the other ingredients,
• you are taking tizanidine.

USE CİPROPOL CAREFULLY UNDER THE FOLLOWING CONDITIONS
Tell your doctor immediately if any of the following occurs before or during treatment of CİPROPOL.

Fluoroquinolones, including CİPROPOL, have been associated with potentially irreversible serious Adverse reactions that can cause disability. Common adverse reactions include musculoskeletal and peripheral nervous system (tendinitis, tendon rupture, swelling or inflammation in tendons, tingling or numbness, numbness in arms and legs, muscle pain, muscle weakness, joint pain, swelling in joints) atralgia, myalgia, peripheral neuropathy and central nervous system effects (hallucination, anxiety, depression, suicidal tendency, insomnia, severe headache and confusion) (See Chapter 4).

These reactions can be seen within hours or weeks after starting CİPROPOL. Patients of any age group or without pre-existing risk factors experienced these adverse reactions.

CİPROPOL should be discontinued immediately if the first signs or symptoms of any serious adverse reaction occur. In addition, the use of fluoroquinolones, including CİPROPOL, should be avoided in patients experiencing any of these serious adverse reactions associated with fluoroquinolones.

Considerations before using CİPROPOL:
If you,
• have ever had kidney problems because dose adjustment may be needed,
• suffer from epilepsy or other neurological,
• have a history of tendon problems during previous treatment with antibiotics such as CİPROPOL,
• have myasthenia gravis (a type of muscle weakness),
• have had heart problems (arythmia).

• are diabetic because you may experience a risk of low-blood sugar levels (hypoglycaemia) with CİPROPOL.
• if you have been diagnosed with an enlargement or “bulge” of a large blood vessel (aortic aneurysm or large vessel peripheral aneurysm).
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, or vascular disorders such as Takayasu arteritis, giant cell arteritis, Behcet’s disease, high blood pressure, or known atherosclerosis). If you feel sudden, severe pain in your abdomen, chest or back, go immediately to an emergency room.
Considerations while under treatment with CİPROPOL
If,
• Severe, sudden allergic reaction (an anaphylactic reaction/shock, angio-oedema) with the following symptoms: tightness in the chest, feeling dizzy, feeling sick or faint, or experience dizziness on standing. (If this happens, tell your doctor immediately since the administration will have to be stopped.)

• Pain and swelling in the joints, and tendinitis may occur occasionally, particularly if you are elderly and are also being treated with corticosteroids. At the first sign of any pain or inflammation CİPROPOL will have to be stopped, rest the painful area. Avoid any unnecessary exercise as this might increase the risk of a tendon rupture.

• Diarrhoea may develop while you are on antibiotics, including CİPROPOL, or even several weeks after you have stopped using them. If it becomes severe or persistent or you notice that your stool contains blood or mucus tell your doctor immediately. CİPROPOL treatment will have to be stopped immediately, as this can be life-threatening. Do not take medicines that stop or slow down bowel movements.

• If you suffer from epilepsy or other neurological conditions such as cerebral ischemia or stroke, you may experience side effects associated with the central nervous system. If this happens, stop taking CİPROPOL and contact your doctor immediately.

• You may experience symptoms of neuropathy such as pain, burning, tingling, numbness and/or weakness. If this happens, stop taking CİPROPOL and contact your doctor immediately.

• CİPROPOL may cause liver damage. If you notice any symptoms such as loss of appetite, jaundice (yellowing of the skin), dark urine, itching, or tenderness of the stomach, CİPROPOL must be stopped immediately.

• CİPROPOL may cause a reduction in the number of white blood cells and your resistance to infection may be decreased. If you experience an infection with symptoms such as fever and serious deterioration of your general condition, or fever with local infection symptoms such as sore throat/pharynx/mouth or urinary problems you should see your doctor immediately. A

blood test will be taken to check possible reduction of white blood cells (agranulocytosis). It is important to inform your doctor about your medicine.

• You have heart problems. Caution should be taken when using CİPROPOL, 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.

• Tell your doctor if you or a member of your family is known to have a deficiency in glucose-6- phosphate dehydrogenase (G6PD), since you may experience a risk of anemia with CİPROPOL.

• You may experience psychiatric reactions after first administration of CİPROPOL. If you suffer from depression or psychosis, your symptoms may become worse under treatment with CİPROPOL. If this happens, stop taking CİPROPOL and contact your doctor immediately.

• You have healing reactions at the application site,

• You use medicines like cortisone,

• Your skin becomes more sensitive to sunlight or ultraviolet (UV) light under treatment with CİPROPOL. Avoid exposure to strong sunlight or artificial UV light such as sunbeds. Myastenia Gravis may increase the symptoms of the disease in patients.

• If there is no improvement in symptoms after 3 days of treatment, please consult your doctor.

Consult your doctor about microorganisms that are resistant or susceptible to CİPROPOL.
Tell the doctor or laboratory staff that you are taking CİPROPOL if you have to provide a blood or urine sample.

Please consult your doctor if any of these alerts even applies to you at any time in the past.

Use of CİPROPOL with food and drink
Food and drink does not affect your treatment with CİPROPOL.

Pregnancy
Consult your doctor or pharmacist before using this drug.

You should not take CİPROPOL during pregnancy.

In case you become aware that you are pregnant during treatment, immediately consult your doctor or pharmacist.

Lactation
Consult your doctor or pharmacist before using this drug.

Do not take CİPROPOL during breast feeding because ciprofloxacin is excreted in breast milk and can be harmful for your child.

Driving and using machines
Ciprofloxacin may make you feel less alert. This situation especially occurs when taken in combination with alcohol.

Important information about some of the ingredients of CİPROPOL solution for infusion
This medicinal product' each 100 ml contains a dose of 15.4 mmol of sodium. This situation should be considered for patients with controlled sodium diet.

Taking other medicines
CİPROPOL or used other drug's effect may vary when used in combination with some drugs. Please tell your doctor if you are taking following drugs:

• Medicines that can alter your heart rhythm: medicines that belong to the group of anti-arrhythmics (e.g. quinidine, hydroquinidine, disopyramide, amiodarone, sotalol, dofetilide ibutilide), tricyclic antidepressants, some antipsychotics,
• Probenecid that ensure excretion uric acid from the body (an active substance for the treatment of gout),
•Omeprazole used in stomach diseases,
• Theophylline used in the treatment of asthma,
• Xanthine derivatives in the group of medicines such as caffeine and pentoxifylline,
• Methotrexate for the treatment of rheumatic diseases and cancer,
• Cortisone drugs used as a pain reliever and fever reducer (NSAIDs),
• An immunosuppressive agent, cyclosporine,
• Vitamin K antagonist medicines used as a blood thinner (e.g. warfarin, acenocoumarol, phenprocoumon or fluindion),
• Glibenclamide and glimepiride used in diabetes,
• Duloxetine used for the treatment of depression,
• Ropinirole used in Parkinson's disease,
• Lidocaine used as anesthesia,
• Clozapine and olanzapine used for the treatment of psychiatric disorders,
• Sildenafil used for erectile dysfunction in men,
• Some antimicrobials that belong to the group of macrolides
• Phenytoin used in the treatment of epilepsy.

CİPROPOL should not be used with tizanidine which is muscle relaxant may cause to decrease blood pressure and sleepiness.

If you are currently using any prescribed drug or OTC, or if you have used them recently, please inform your doctor or pharmacist about these.

3. How CİPROPOL will be given?
Instructions for use and dose/ frequency of administration:
Unless your doctor gives a separate advice, the following doses per day is recommended for adults:

Indication	Daily and single dose in adults (mg ciprofloxacin intravenously)	Treatment duration (including the transition to oral therapy as soon as possible)
Respiratory tract infections	2x400 mg – 3x400 mg	7-14 days
Urinary tract infections - Simple acute inflammation in the kidneys - Complicated	 2x200 mg – 2x400 mg 2x400 mg – 3x400 mg	 7-21 days 7-21 days
Genital infections - Adnexitis, prostatitis, epididymoorchitis	2x400 mg – 3x400 mg	14-28 days
Diarrhea	2x400 mg	1-5 days
Other infections	2x400 mg	7-14 days
Severe and life-threatening infections	3x400 mg	7-14 days
Bone and joint infections (ex. Bone infection)	2 x 400 mg – 3x 400 mg	Maximum 3 months (maximum 2 months in bone infection)
Immunocompromised patients	2x400 mg – 3x400 mg	During the period of white blood cells are low
Intra-abdominal infections	2 x 400 mg – 3x 400 mg	5-14 days
Transmitted by the respiratory route (seen after exposure to *Bacillus anthracis*) anthrax	2x400 mg	60 days

After intravenous treatment with CİPROPOL, treatment is continued used oral forms.

Treatment should be continued for 3 more days after decrease or disappearance of the symptoms of fever.

Infections caused by bacteria called *Streptococcus* and *Chlamydia*, treatment should last for at least 10 days. Intravenous started treatment then can be continued oral.

Your doctor will decide and give you the medicine depend on your situation and inform you about treatment period.

Route of administration and method:
CİPROPOL should be administered intravenously for 60 minutes.

Different age groups:
Usage in children

Infection	**Recommended dose**	**Recommended treatment duration** (including the transition to oral therapy as soon as possible)
Family pass for children between the ages of 5-17, especially cystic fibrosis a disease that keeps glands infection due to *P. aeruginosa* lung infection	CİPROPOL used intravenously, 3 times a day, 10 mg per kilogram (maximum daily dose is 1200 mg)	10-14 days
Simple non-urinary tract infections and kidney infection	6-10 mg per kilogram intravenously every 8 hours (maximum 400 mg/dose)	10-21 days
Anthrax transmitted by inhalation	2 times a day 10 mg/kg (maximum dose must not exceed 400 mg at a time. The maximum daily dose is 800 mg)	60 days

If you are exposed to anthrax or suspected to be exposure to anthrax, should be initiated to treatment as soon as possible.

Dose study has not been done for children with renal and hepatic impairment.

Usage in elderly:
Doses should be as low as possible in elderly patients.

Conditions of special use:
Renal failure:
Maximum daily dose in patients with moderate renal impairment is 800 mg administered intravenously. Maximum daily dose in patients with severe renal impairment is 400 mg administered intravenously. In patients with renal failure and dialysis, renal failure dose is administered, but drugs should be given after dialysis in dialysis days. In patients with renal

insufficiency and receiving continuous ambulatory peritoneal dialysis, 50 mg CİPROPOL is added every 6 hours to per liter of dialysis fluid or 500 mg ciprofloxacin given orally.

Liver failure:
Dose adjustment is not required in patients with liver failure.

In the case combination of kidney and liver failure, the above-mentioned doses are administered.

If you have an impression that the effect of CİPROPOL is very strong or weak, please tell your doctor or pharmacist.

If you use more CİPROPOL than you should:
If you use more CİPROPOL than you should, talk to a doctor or pharmacist.

It is recommended to monitorize renal functions except emergency measures.

If you forget to use CİPROPOL:
Do not take a double dose to compensate forgotten dose.

If CİPROPOL treatment stopped, effects may occur:
None

4. Possible side effects

Like all other medicines, CİPROPOL may cause side effects in patients with hypersensitivity to any component content.

If one of following occurs, stop using CİPROPOL and tell your doctor immediately or consult nearest emergency department of hospital

- feel pain in your chest
- feeling dizzy
- feeling sick or faint
- experience dizziness on standing
- tightness in the chest and difficulty in breathe
- swelling on eyelid, face and lips
- nodule on skin, itchy red macula on body and itching

All of adverse effects are serious.

If you have one of these, you are allergic to CİPROPOL.
You may need urgent medical attention or admitted to hospital.

The frequency of side effects is classified into the following categories:
Very common in more than 1 in 10 patients

Common in more than 1 in 100 patients, but less than 1 in 10 patients
Uncommon in more than 1 in 1,000 patients, but less than 1 in 100 patients
Rare in more than 1 in 10,000 patients, but less than 1 in 1,000 patients
Very rare in less than 1 in 10,000 patients, including isolated reports

Common:

- Nausea, diarrhoea,
- Local reaction at the injection site.

Uncommon:

- Fungal superinfections,
- High concentration of eosinophils, a type of white blood cell,
- Loss of appetite (anorexia),
- Hyperactivity, trouble,
- Headache, dizziness, sleeping problems, taste disorders,
- Vomiting,
- Abdominal or stomach pain, indigestion, gas, bloating,
- Increased amounts of one substance in the blood (bilirubin)
- Itching, hives, rash,
- Joint pain,
- Pain, discomfort, fever,
- Increase in alkaline phosphatase and transaminases as liver enzymes,
- Kidney failure.

Rare:

- Inflammation of the bowel (colitis) linked to antibiotic use (can be fatal in rare cases),
- Increased or decreased numbers of white blood cells in the blood (life-threatening),
- Reduction or increase in the number of cells in the blood clotting,
- Anemia,
- Allergic reaction,
- Allergic swelling (oedema), mouth, tongue and throat swelling,
- Increase or decrease in blood glucose,
- Not knowing where and at what time (loss of consciousness),
- To see things that are not real (hallucinations),
- Abnormal dreams (nightmares),
- Depression
- Tension,
- Abnormal feeling such as numbness, tingling, burning and stinging,
- Feeling decline,
- Flicker,
- Seizures
- Balance disorder,
- Visual disturbances,
- Tinnitus,

- Hearing loss,
- An increase in heart rate,
- The expansion of blood vessels,
- Low blood pressure,
- Fainting,
- Difficulty in breathing (including conditions related to asthma),
- Liver failure,
- Jaundice,
- Liver inflammation (non-infectious),
- Light sensitivity reactions,
- Skin blisters,
- Muscle pain,
- Articular rheumatism,
- Increase in muscle tension, cramps,
- Renal disfunction,
- Crystals in urine or blood,
- Kidney infection,
- Edema,
- Sweating,
- Blood clotting abnormalities,
- Digestive enzyme amylase increase.
- Hearing loss

Very rare:

- Special type of reduced red blood cell count (haemolytic anaemia),
- Dangerous drop in a type of white blood cells (agranulocytosis),
- Reduction in the number of all blood cells,
- Bone marrow depression (life threatening),
- Fatal allergic reaction,
- Allergic shock (life-threatening),
- Serum sickness-like reactions,
- Psychological reactions
- Migraine,
- Odor disorders,
- Sensory disturbances,
- Feeling rise,
- Dizziness,
- Increased intracranical pressure,
- Visual color disorders,
- Reduction of hearing,
- Vascular inflammation,
- Pancreas inflammation,
- Liver damage (very rarely progress to life-threatening liver failure),
- Severe blisters and bleeding in lips, eyes, mouth, nose and genitals (life-threatening),

- Skin diseases associated erythema (erythema multiforme, erythema nodosum and Stevens-Johnson syndrome (life-threatening)),
- Muscle weakness,
- Aggravation of Myasthenia gravis
- Inflammation or rupture in the tendons that connect muscles to bones,
- Walking disorders.

Not known:
- Outside of the brain and spinal cord and peripheral nerve injuries, numerous environmental nerve damage (polyneuropathy),
- Abnormal fast heart rhythm (QT prolongation, ventricular arrhythmia, torsades de pointes),
- Acute general exanthematous pustulosis (AGEP – widespread redness on the ground, full of internal inflammation, characterized by ridges the size of a pinhead, accompanied by high fever, often occurring after the use of clinical medicine),
- INR increase (International normalized ratio) (metering parameters used in blood clotting time)

The following undesirable side effects have higher frequency category in patient sub groups to which treatment is applied either intravenously or sequentially. (intravenous and oral)

Common	Temporary increase in transaminases, vomiting, rash
Uncommon	Thrombocytopenia, thrombocythemia, confusion and disorientation, hallucinations, paresthesia and dysesthesia, hypoesthesia, seizures, vertigo, vision disorders, hearing loss, tachycardia, vasodilation, hypotension, temporary hepatic failure, jaundice, renal failure, edema
Rare	Pancytopenia, bone marrow depression, anaphylactic shock, psychotic reactions, migraines, decreased hearing, olfactory disorders, Vasculitis, pancreatitis, liver necrosis, petechiae, tendon rupture

If you encounter with any side effects that are not mentioned in this leaflet, please inform your doctor or pharmacist.

5. How to store CİPROPOL
Keep CİPROPOL out of the reach and sight of children and store in the original container.

Storage below 25 °C. Protect from light. Do not refrigerate or freze.

Use in accordance with the expiration date.
Do not use CİPROPOL after the expiration date which is stated on the package.

If you notice any disorders in product and/or package, do not use CİPROPOL.

Unused products or waste materials must be disposaled according to “Medical Waste Control Regulation” and “Packaging and Packaging Waste Control Regulation”.

Marketing Authorisation Holder and Manufacturer:

POLİFARMA İLAÇ SAN. VE TİC. A.Ş.
Vakıflar OSB Mahallesi,
Sanayi Caddesi, No:22/1
Ergene/TEKİRDAĞ/TURKEY
Phone: +90 282 675 14 04
Fax: +90 282 675 14 05
e-mail: info@polifarma.com.tr

This patient information leaflet was last approved on 30/11/2019.

THE FOLLOWING INFORMATION IS INTENDED FOR HEALTHCARE PROFESSIONALS.
No special requirements for disposal.

Preparing for use
CİPROPOL must be administered with i.v. infusion for 60 minutes.
Slow infusion of a large vein, minimizes patient discomfort and reduces the risk of venous irritation.

Infusion solution can be given directly or mixed with other compatible infusion solutions. 0,9% NaCI-containing ciprofloxacin infusion solution is compatible with serum physiological, Ringer solution, Ringer lactate solution, 5% and 10 % glucose solution, 10 % fructose solution, 5 % glucose solution containing 0.45 % NaCl. When compared with specified infusion solutions, it should be administered within a short time after being compared in terms of microbiological aspect and light sensitivity. Unless it is specified as compatible for other infusion solutions and therapeutic products, it should be administered separately at all times.

It can be seen not physically or chemically stable penicillins, all infusions solutions such as heparin solution and therapeutic products and incompatibility in the pH of the solution.

Due to the pH of ciprofloxacin solution is 3.5-4.6, incompatibility arises especially in alkaline solutions adjusted to pH.

In the third section of package leaflet “Instructions for appropriate use and dose/ frequency of administration” recommended doses are located.

Unused products or waste materials must be disposaled according to “Medical Waste Control Regulation” and “Packaging and Packaging Waste Control Regulation”.