PATIENT INFORMATION LEAFLET

WARNING: TENDINITIS AND TENDON DETACHMENT (inflammation or detachment in the tissues binding the muscles to the bones), **PERIPHERAL NEUROPATHY** (disorders seen in the nerves located far from the centre-sensory loss for any reason), **SERIOUS SIDE EFFECTS INCLUDING CENTRAL NERVOUS SYSTEM EFFECTS AND MYASTHENIA GRAVIS** (a type of muscular weakness)

- Antibiotic belonging to fluoroquinolone group, including VONECİP, can cause following irreversible side effects which can cause disability:
- Inflammation of the tissues which bind the muscles to the bones (tendinitis with the possible symptoms of severe pain in the joints, swelling and redness) and tear of the tissues binding muscles to the bones (tendon) (sypmtoms may be severe pain in the muscles, sudden and fast bruising, weakness, limitation of the movement ability)
- Disorders seen for any reason in the distant nerves from the centre-loss of sensation (peripheral neuropathy; symptoms may be pain in nerves, tenderness, numbness in the feet and hands, weakness in the muscles, tremor in the hands.)
- Central nervous system effects may be hallucinations, anxiety, mental depression, suicidality, insomnia, severe headache and confusion.

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

- Antibiotics called fluoroquinolones, including Ciprofloxacin which is the active ingredient contained in VONECİP, may cause an increase in muscle weakness in patients with myasthenia gravis (a type of muscle weakness). If you have a known illness of muscle weakness, talk to your doctor or pharmacist before using VONECİP.
- Since fluoroquinolone group drugs, including VONECİP, are known to be associated with serious side effects, they may be used if there are no other alternatives to the following indications:
- Acute bacterial sinusitis (an infection in the nasal cavity and sinuses)
- Uncomplicated urinary tract infection (urinary tract infection in healthy individuals without structural and physical disorders)
- Acute bacterial exacerbation of chronic bronchitis (an increase in the amount of sputum, a darker sputum and an increase in shortness of breath.)

VONECİP 400 mg/200 ml Solution for I.V. Infusion

For intravenous use only.
Sterile

- ***Active ingredient:*** 200 ml of infusion solution contains 508.0 mg Ciprofloxacin lactate equivalent to 400 mg Ciprofloxacin.
- ***Excipients:*** Lactic acid solution, sodium chloride, hydrochloric acid, water for injection.

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

- *Keep this 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 only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.*
- *If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.*

What is in this leaflet:

headlines are included.

1. What VONECİP is and what it is used for

• VONECİP is available in a vial. Each vial contains 508.0 mg Ciprofloxacin lactate equivalent to 400 mg Ciprofloxacin.
• VONECİP contains Ciprofloxacin as active ingredient which is an antibiotic belonging to the fluoroquinolone group. Ciprofloxacin is used to kill the bacteria that cause infections.
• VONECİP is presented in 250 ml vials. Solution in the vial is colorless to slightly yellow and clear.
• VONECİP is used in adults for the treatment of respiratory tract infections, long lasting or recurring ear or sinus infections, urinary tract infections, infections on kidney, 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. VONECİP, 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.

2. What you need to know before you are given VONECİP

DO NOT USE VONECİP in the following cases:
If;
• You are allergic (hypersensitive) to the active substance, to other quinolone drugs or to any of the other ingredients,
• You are taking tizanidine which is used as a muscle relaxant.

Serious side effects can be seen and potentially irreversible, including injury to the tendon and tendon rupture (inflammation or tearing of the muscles in the bones), peripheral neuropathy (impairments in the nasal nerves - sensory loss) and the effects of the central nervous system.
Fluoroquinolones, including VONECİP, have been associated with serious and potentially irreversible side effects that can lead to disability. Common side effects include musculoskeletal and peripheral nervous system (tendinitis, tendon rupture, swelling or inflammation of the tendons, tingling or numbness, numbness in the arms and legs, muscle pain, muscle weakness, joint pain, swelling in the joints), arthralgia, myalgia, peripheral neuropathy and central nervous system effects (hallucinations), anxiety (anxiety), depression, suicidality, insomnia, severe headache and confusion (confusion).
These reactions can be observed in hours or weeks after VONECİP initiation. Patients without any age group or pre-existing risk factors experienced these side effects. VONECİP should be discontinued immediately if any initial symptoms or symptoms of any serious side effects occur. In addition, the use of fluoroquinolones, including VONECİP, should be avoided in patients experiencing any of these serious side effects associated with fluoroquinolones.
Acute bacterial sinusitis should not be used because of acute bacterial exacerbation of chronic bronchitis and the risk of serious side effects in the presence of alternative treatment options in uncomplicated urinary infections.
These indications can only be used with the approval of an infectious disease specialist in the absence of other alternative treatments.

Use VONECİP with CAUTION in following cases:
Tell your doctor immediately if any of the following cases occurs before or during treatment with VONECİP.

Take the following into consideration before using VONECİP:
If;
• .You have ever had kidney problems, dose adjustment may be needed,
• You suffer from epilepsy or other neurological conditions,
• You have a history of tendon problems during previous treatment with antibiotics such as VONECİP,
• You have myasthenia gravis (a type of muscle weakness),
• You have a history of heart problems (arrhythmia).

Take the following into consideration during VONECİP treatment:
If,
• Severe, sudden allergic reaction (an anaphylactic reaction/shock, angioedema) with the following symptoms: tightness in the chest, feeling dizzy, feeling sick or faint, or experience dizziness on standing. (If one of these happens, tell your doctor immediately since your treatment needs to be ended.),
• 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 VONECİP will have to be stopped, rest the painful area. Avoid any unnecessary exercise as this might increase the risk of a tendon rupture.

• Diarrhea may develop while your treatments with antibiotics, including VONECİP, 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. VONECİP 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 VONECİP 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 VONECİP and contact your doctor immediately.
• VONECİP 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, VONECİP must be stopped immediately.
• VONECİP 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.
• 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 VONECİP.
• You may experience psychiatric reactions after first administration of VONECİP, in rare cases leading to suicidal thoughts/ideas. If you suffer from depression or psychosis, your symptoms may become worse under treatment with VONECİP. If this happens, stop taking VONECİP and contact your doctor immediately.
• You have nonhealing reactions at the application site,
• You use medicines like cortisone,
• Your skin becomes more sensitive to sunlight or ultraviolet (UV) light under treatment with VONECİP. Avoid exposure to strong sunlight or artificial UV light such as sunbeds.

Aggravation of Myasthenia Gravis (a type of muscle weakness):
Fluoroquinolones such as VONECİP may lead to worsening of muscle weakness and breathing problems like myasthenia gravis. If you experience increased muscle weakness or breathing problems, consult your doctor immediately.
Consult your doctor about microorganisms that are resistant or susceptible to VONECİP.

Tell the doctor or laboratory staff that you are taking VONECİP 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.

VONECİP with food and drinks
Food and drink does not affect your treatment with VONECİP.

Pregnancy
Ask your doctor or pharmacist for advice before taking the medicine.
VONECİP should not be used during pregnancy.
Please consult your doctor or pharmacist if you notice that you are pregnant during treatment.

Lactation
Ask your doctor or pharmacist for advice before taking the medicine.
Do not take VONECİP 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 VONECİP
This medicinal product contains 30.8 mmol sodium per vial. This situation should be considered for patients with controlled sodium diet.

Other medicines and VONECİP
VONECİP 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:

• Heart rhythm regulate Class IA or Class III drugs that prevent hearth rhythm disorder,
• Probenecid that ensure excretion uric acid from the body (an active substance for the treatment of gout),
• 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 (for example, 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,
• Phenytoin used in the treatment of epilepsy.

If you are currently using or have recently used any prescription or non-prescription medication, please give information to your doctor or pharmacist about these.

3. How to use VONECİP

Instructions for use and dose/frequency of administration:

Unless your doctor gives a separate advice, the following doses per day is recommended for adults:

Infection		Daily and single dose in adults (mg Ciprofloxacin taken intravenously)	Treatment duration (including the transition to oral therapy as soon as possible)
Respiratory tract infections		2 x 400 mg – 3 x 400 mg	7-14 days
Urinary tract infections	Simple acute inflammation in the kidneys	2 x 200 mg – 2 x 400 mg	7-21 days
	Complicated	2 x 400 mg – 3 x 400 mg	7-21 days
Genital infections Adnexitis, prostatitis, epididymoorchitis		2 x 400 mg – 3 x 400 mg	14-28 days
Diarrhea		2 x 400 mg	1-5 days
Other infections		2 x 400 mg	7-14 days
Severe and life-threatening infections	Recurrent infections in cystic fibrosis (in children between the ages of 5-17)	3 x 400 mg	7-14 days
	Bone and joint infections (ex. Bone infection)	3 x 400 mg	Maximum 3 months (maximum 2 months in bone infection)
	Septicemia	3 x 400 mg	7-14 days
	Intra-abdominal infections	3 x 400 mg	5-14 days
Immunocompromised patients		2 x 400 mg – 3 x 400 mg	During the period of white blood cells are low
Transmitted by the respiratory route (seen after exposure to *Bacillus anthracis*) anthrax		2 x 400 mg	60 days

After intravenous treatment with VONECİP, 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.

Route of administration and method:

VONECİP should be administered intravenously for 60 minutes.

Different age groups:
Usage in children and adolescent

Infection	**Recommended dose**	**Recommended treatment duration**
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	VONECİP used intravenously with 200 mg/100 ml, 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 VONECİP is added every 6 hours to per liter of dialysis fluid or 500 mg VONECİP 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 VONECİP is very strong or weak, please tell your doctor or pharmacist.

If you use more VONECİP than you should:
If you use more VONECİP than you should, talk to a doctor or pharmacist.
It is recommended to monitorize renal functions except emergency measures.

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

Effects may occur when treatment with VONECİP is terminated:
There is no data on the effects that may occur when treatment with VONECİP is terminated.

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

If you have any of the following, stop using VONECİP and IMMEDIATELY tell your doctor or contact the emergency department of the nearest hospital:
- If you have skin rashes and itching as well as symptoms such as thickening of your voice and difficulty in breathing, this means you have hypersensitivity to VONECİP.
These are all very serious side effects.
If you have one of these, you may need emergency medical care or hospitalization.

Common side effects (between 1 and 10 in every 100 people):
- Nausea, diarrhea,
- Local reaction at the injection site.

Uncommon side effects (between 1 and 10 in every 1.000 people):
- 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 (between 1 to 10 in every 10.000 people):
- 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 (edema), mouth, tongue and throat swelling,
- Increase or decrease in blood glucose,

- Not know where and at what time (loss of consciousness),
- To see things that are not real (hallucinations),
- Abnormal dreams (nightmares),
- Depression (suicidal ideation/suicide attempt or suicidal thoughts and self-harm behavior, such as the possibility of reaching),
- Tension,
- Abnormal feeling such as numbness, tingling, burning and stinging,
- Feeling decline,
- Flicker,
- Seizures (seizures continued for 30 minutes and including the state without opening intervals of consciousness often repeated),
- 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 dysfunction,
- Crystals in urine or blood,
- Kidney infection,
- Edema,
- Sweating,
- Blood clotting abnormalities,
- Digestive enzyme amylase increase.

Very rare (less than 1 in every 10,000 people):

- Special type of reduced red blood cell count (hemolytic anemia),
- 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 (suicidal ideation/suicide attempt or suicidal thoughts and self-harm behavior, such as the possibility of reaching),
- Migraine,
- Odor disorders,
- Sensory disturbances,
- Feeling rise,
- Dizziness,
- Increased intracranial 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 multiform, erythema nodosum and Stevens-Johnson syndrome (life-threatening)),
- Muscle weakness,
- Aggravation of Myasthenia Gravis (a disease causing muscle weakness),
- Inflammation or rupture in the tendons that connect muscles to bones,
- Walking disorders.

Unknown (cannot be estimated from the available data):
- 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),
- Arthropathy disease that affects the joints in children,
- 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) (In patients treated with Vitamin K antagonists).

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

5. How to store VONECİP

Keep VONECİP out of the reach and sight of children and store in the original container.
Store at room temperatures below 30°C. Protect from light. Do not refrigerate or freeze.
Use in accordance with the expiry date.
Do not use VONECİP after the expiry date which is indicated on the package.
If you notice any disorders in product and/or package, do not use VONECİP.

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

Manufacturing Site:
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FOLLOWING INFORMATION IS INTENDED FOR HEALTHCARE PROFESSIONALS
No special requirements for disposal.

Preparing for use
VONECİP 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.

Collapse can occur in cold and can resolvable again at room temperature, therefore it is not recommended infusions solution to be stored in the refrigerator.

It should be administered separately without waiting if it is compatible or not with other infusion solutions and therapeutic products. Crash, turbidity and discoloration are the visual signs of incompatibility.

It can be seen not physically or chemically stable penicillin, 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 disposed according to local regulations.