

## 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 VONECĪP, 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) (symptoms 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 VONECĪP use, stop using VONECĪP and talk to your doctor or pharmacist.

- Antibiotics called fluoroquinolones, including Ciprofloxacin which is the active ingredient contained in VONECĪP, 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 VONECĪP.
- Since fluoroquinolone group drugs, including VONECĪP, 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.)

### VONECĪP 200 mg/100 ml Solution for I.V. Infusion

#### For intravenous use only.

Sterile

- **Active ingredient:** 100 ml of infusion solution, 254 mg ciprofloxacin lactate equivalent to 200 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:**

1. *What VONECIP is and what it is used for*
2. *What you need to know before you are given VONECIP*
3. *How to use VONECIP*
4. *Possible side effects*
5. *How to store VONECIP*

**headlines are included.**

**1. What VONECIP is and what it is used for**

- VONECIP is available in a vial. Each vial contains 254 mg ciprofloxacin lactate equivalent to 200 mg ciprofloxacin.
- VONECIP contains Ciprofloxacin as active ingredient which is an antibiotic belonging to the fluoroquinolone group. Ciprofloxacin is used to kill the bacteria that cause infections.
- VONECIP is presented in 100 ml vials. Solution in the vial is colorless to slightly yellow and clear.
- It should not be used for acute inflammation of the air cavities in the facial bones caused by bacteria (acute bacterial sinusitis) and in the presence of alternative treatment options in uncomplicated urinary tract infections due to the risk of serious side effects. In addition, the sensitivity of the urinary tract with antibiogram should be proved.
- VONECIP 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 immuno-compromised patients. VONECIP, 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 VONECIP

### **DO NOT USE VONECIP in the following cases:**

If;

- you are allergic to one of the ingredients in the drug or to quinolone-derived drugs,
- you are using a medicine containing the active ingredient of tizanidine, which is used as a muscle relaxant

### **Use VONECIP with CAUTION in following cases:**

Tell your doctor immediately if any of the following cases occurs before or during treatment with VONECIP.

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 VONECIP,
- You have myasthenia gravis (a type of muscle weakness),
- You have a history of heart problems (arrhythmia).

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 VONECIP 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 VONECIP, 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. VONECIP 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 VONECIP 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 VONECIP and contact your doctor immediately.

- VONECIP 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, VONECIP must be stopped immediately.
- VONECIP 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 VONECIP.
- You may experience psychiatric reactions after first administration of VONECIP, in rare cases leading to suicidal thoughts/ideas. If you suffer from depression or psychosis, your symptoms may become worse under treatment with VONECIP. If this happens, stop taking VONECIP 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 VONECIP. Avoid exposure to strong sunlight or artificial UV light such as sun beds.

If you have any of the following during VONECIP use, stop using VONECIP immediately and talk to your doctor or pharmacist:

- Tissue inflammation that connects the muscles to the bones (tendinitis; symptoms can 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 of the central nerves for any reason - loss of sensation (peripheral neuropathy; symptoms of pain in the nerves, tenderness, numbness in the feet and hands, numbness in the muscles, tremors in the hands)
- Central nervous system (central nervous system) effects (symptoms can be imagination (hallucination), anxiety (anxiety), mental breakdown (depression), suicidal tendency, insomnia, severe headache and confusion (confusion))
- If you have previously had muscle weakness (myasthenia gravis)

These reactions can be seen within hours or weeks after starting VONECIP. Patients of any age group or without pre-existing risk factors experienced these side effects. VONECIP should be discontinued immediately if the first signs or symptoms of any serious side effects occur. In

addition, the use of fluoroquinolones, including VONECIP, should be avoided in patients experiencing any of these serious side effects associated with fluoroquinolones.

**Aggravation of Myasthenia Gravis (a type of muscle weakness):**

Fluoroquinolones such as VONECIP 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 VONECIP.

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

**VONECIP with food and drinks**

Food and drink does not affect your treatment with VONECIP.

**Pregnancy**

*Ask your doctor or pharmacist for advice before taking the medicine.*

VONECIP 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 VONECIP during breast feeding because ciprofloxacin is excreted in breast milk and can be harmful for your child.

**Driving and using machines**

It may affect the response speed negatively in the case of driving and using machines. This is especially true when taken with alcohol.

**Important information about some of the ingredients of VONECIP**

This medicinal product contains 15,4 mmol sodium per dose. This situation should be considered for patients with controlled sodium diet.

**Other medicines and VONECIP**

VONECIP 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 VONECIP

#### **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 <i>Bacillus anthracis</i> ) anthrax	2 x 400 mg	60 days

After intravenous treatment with VONECIP, 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 determine the dose of your medicine depending on your disease and apply it to you and inform you the duration of your treatment.

**Route of administration and method:**

VONECIP will be administered intravenously and should be administered over a 60-minute period.

Preparing for use

VONECIP should be applied in 60 minutes with i.v. infusion.

Slow infusion into a wide vein minimizes patient discomfort and reduces the risk of venous irritation.

Infusion solution can be given by mixing with other infusion solutions that it is direct or compatible with.

Cold precipitation may occur and re-dissolve at room temperature; for this reason, it is recommended that the infused solution is not stored in the refrigerator.

Unless determined to be compatible for other infusion solutions and drugs, they should be administered separately. Events such as collapse, blur, color change are visual signs of incompatibility.

**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 <i>P. aeruginosa</i> lung infection	VONECIP 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 VONECIP is added every 6 hours to per liter of dialysis fluid or 500 mg VONECIP 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 VONECIP is very strong or weak, please tell your doctor or pharmacist.*

**If you use more VONECIP than you should:**

*If you use more VONECIP than you should, talk to a doctor or pharmacist.*

It is recommended to monitorize renal functions except emergency measures.

**If you forget to use VONECIP:**

*Do not take a double dose to compensate forgotten dose.*

**Effects may occur when treatment with VONECIP is terminated:**

None.

#### **4. Possible side effects**

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

**If you have any of the following, stop using VONECIP and IMMEDIATELY tell your doctor or contact the emergency department of the nearest hospital:**

- Allergic reaction (Hypersensitivity reactions such as difficulty breathing, wheezing, itching, hives and swelling)
- Angioedema (swelling of the face, tongue, lips, and throat that causes difficulty breathing)

These are all very serious side effects. If you have one of these, you have a serious allergy to VONECIP.

All of these very serious side effects are very rare.

Side effects are listed as shown in the following categories:

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 1,000 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: Frequency cannot be estimated from the available data.

Tell your doctor if you notice any of the following:

##### **Common**

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

##### **Uncommon**

- Fungal super infections,
- 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 (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**

- 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**

- 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 25°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.

Do not dispose of expired or unused drugs! Give to the collection system determined by the Ministry of Environment and Urbanization.

### ***Marketing Authorization Holder:***

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**FOLLOWING INFORMATION IS INTENDED FOR HEALTHCARE PROFESSIONALS.**

Unused products or waste materials should be disposed of in accordance with the "Medical Waste Control Regulation" and "Packaging and Packaging Waste Control Regulations".

Preparing for use

VONECIP 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.