

Rare

- Muscle pain, joint pain, increase in muscle strain and cramp, Antibiotic-associated colon inflammation (very rarely resulting in death) (see section 2 “What you need to know before you take CIPOX”),
- Decrease or increase in the number of blood cells (leukopenia, leukocytosis, neutropenia, anemia),
- Decrease or increase in the number of clotting cells on blood,
- Allergic reaction, swelling (edema) or sudden swelling of skin and mucosal surfaces (angioedema) (see section 2 “What you need to know before you take CIPOX”),
- Increase in blood sugar (hyperglycemia),
- Decrease in blood sugar (hypoglycemia) (see section 2 “What you need to know before you take CIPOX”),
- Sudden confusion,
- Orientation disorder,
- Anxiety reactions,
- Weird dreams,
- Depression (suicidal ideation / thoughts and possibility of suicidal attempt or completed suicide) (see section 2 “What you need to know before you take CIPOX”),
- Seeing, hearing or feeling things that do not exist (hallucination),
- Unusual feelings such as numbness, tingling, burning and stinging,
- Decrease of feeling,
- Loss of feeling,
- Shivering,
- Balance disorder,
- Visual impairments (including diplopia which means double vision),
- Tinnitus,
- Hearing loss,
- Decrease in hearing,
- Increased heart rate (tachycardia),
- Expansion in blood vessels (vasodilation),
- Low blood pressure,
- Fainting,
- Breathlessness (including asthma-related conditions), asthma-like symptoms,
- Liver failure,
- Jaundice due to occlusion in the bile flow,
- Liver inflammation (hepatitis),
- Light sensitivity (see section 2 “What you need to know before you take CIPOX”),
- Kidney failure,
- Blood in the urine,
- Crystals in the urine,
- Urinary infection,
- Swelling due to water retention in the body (edema),
- Excessive sweating,
- Increase in amylase, a digestive enzyme.

Very Rare

- Anemia which is accompanied by the destruction of red blood cells (hemolytic anemia) (see section 2 “What you need to know before you take CIPOX”),
- Decrease in the number of all blood cells (pancytopenia) (life-threatening),
- Dangerous decrease in the number of white blood cells (agranulocytosis) (see section 2 “What you need to know before you take CIPOX”),
- Bone marrow suppression (life-threatening),
- Serum disease like reaction (a kind of allergic reaction),
- Mental disorders (suicidal ideation / thoughts and psychological reactions with possibility of resulting suicidal attempt or completed suicide) (see section 2 “What you need to know before you take CIPOX”),
- Migraine,
- Coordination disorder,
- Walking difficulty,
- Smelling disorders,
- Intracranial pressure increase (intracranial pressure and pseudotumor cerebri),
- Visual color disturbances (vasculitis),
- Vascular inflammation,
- Pancreas inflammation,
- Liver damage which can very rarely progress to life-threatening liver failure (hepatic necrosis) (see section 2 “What you need to know before you take CIPOX”),
- Small bleeding points under the skin (petechiae); various skin rashes or rashes,
- Myasthenia gravis (a disease that causes muscle weakness) aggravation (see section 2 “What you need to know before you take CIPOX”),

Not Known

- Feeling very excited (mania) or being too optimist or hyperactive (hypomania),
- Heart beat in an abnormal high speed, life-threatening irregular heartbeat, irregularities in heartbeat (observed in ECG which shows electrical activity of heart, called “QT prolongation”),
- Effects on clotting on blood (in patients treated with Vitamin K antagonists).

If you notice any side effects not listed in this leaflet, inform your doctor or pharmacist.

Reporting of side effects

Talk with your doctor, pharmacist or nurse if you experience any side effect that is included or not included in this patient information leaflet. Also, report the side effects you have encountered, to Turkish Pharmacovigilance Center (TUFAM) via clicking “Drug Side Effect Report” icon on [www.titck.gov.tr](http://www.titck.gov.tr) or via calling the side effect report line on 0800 314 00 08. By reporting experienced side effects, you will be contributing in obtaining more information regarding the safety of your drug.

5. How to store CIPOX

Store CIPOX by keeping out of the reach and sight of children in its original package.

Store CIPOX at room temperature below 25°C.

Use in line with the expiry date.

Do not use CIPOX after the expiry date stated on the packaging.

Do not use CIPOX if you notice any failure/defect in the product and/or packaging. Do not throw away drugs that have expired or are not being used! Give them to the collection system determined by the Ministry of Environment and Urbanism.

Approval date of this patient information leaflet is 17/10/2018.

PATIENT INFORMATION LEAFLET

CIPOX 750 mg film coated tablet

It is taken orally.

- **Active substance:** Each film coated tablet contains 873 mg Ciprofloxacin HCl which is equivalent to 750 mg Ciprofloxacin.
- **Excipients:** Cellulose, Microcrystalline, Maize Starch, Crospovidone, Croscarmellose Sodium, Colloidal Anhydrous Silica, Magnesium Stearate (E572), Hydroxy Propyl Methyl Cellulose (E464), Titanium Dioxide (E171), Polyethylene Glycol.

Read this LEAFLET carefully before you start to use the medicine. It contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, please consult your doctor or pharmacist.
- This medicine is prescribed for you personally. Do not give it to others.
- During the use of this medicine, when you visit a doctor or a hospital, tell your doctor that you are using this medicine.
- Follow the directives in this leaflet strictly. Do not use **higher or lower** dose of the medicine than the one recommended to you.

In this patient information leaflet:

1. What CIPOX is and what it is used for
2. What you need to know before you take CIPOX
3. How to take CIPOX
4. Possible side effects
5. How to store CIPOX

Topics are included.

1. What CIPOX is and what it is used for

- CIPOX is presented to use in the form of film coated tablets. Each film coated tablet contains 750 mg active ingredient (Ciprofloxacin). Ciprofloxacin, the active ingredient of CIPOX, belongs to an antibiotic group called fluoroquinolones.
- CIPOX is presented to use in a box containing 14 tablets.
- CIPOX is used in the treatment of respiratory tract infections in adults, in long lasting and recurrent ear or sinus infections, in kidney and urinary tract infections, in infections of the genital organs including adnexitis (acute or chronic inflammation of ovaries and tubers with adnexa), gonorrhea, prostatitis, infections of the digestive system, abdominal cavity infections such as abdominal inflammation (peritonitis), skin and soft tissue infections, bone and joint infections, in prevention of infections caused by the bacteria called *Neisseria meningitidis* over 18 years and in case of exposure to anthrax respiratory and in malignant external ear inflammation. CIPOX can be used with other antibiotics (combination therapy) in the treatment of patients with low number of white blood cells (neutropenia) and who have fever caused by bacterial infection. Additional antibiotic treatment may be applied with CIPOX in the event of a severe infection or an infection caused by more than one type of bacteria.
- CIPOX is used for children and adolescents with cystic fibrosis (a hereditary disease causing lung, kidney or pancreatic disorder) with pulmonary and bronchial infections, in complicated urinary tract infections including those reaching to kidneys (pyelonephritis), in case of sensitiveness to the efficacy of Ciprofloxacin and when there are no alternative treatments, in case of exposure to anthrax inhalation (via inhalation).
- CIPOX can be used in cases where the doctor considers it necessary, where other agents can not be used to treat other specific severe infections seen in children and adolescents.

Fluoroquinolones, including CIPOX, should not be used in acute bacterial exacerbation of chronic bronchitis and in uncomplicated urinary infections due to the risk of serious side effects when alternative treatment options are present.

It can be used in these indications only if the other treatments are insufficient.

CIPOX can only be used in the treatment of infections which are proved to be or most probably caused by susceptible bacteria.

2. What you need to know before you take CIPOX

WARNING: SERIOUS ADVERSE REACTIONS INCLUDING TENDINITIS AND TENDON TEARING, NEUROPATHY, CENTRAL NERVOUS SYSTEM EFFECTS AND DETERIORATION OF MYASTHENIA GRAVIS

- Ciprofloxacin, active ingredient of CIPOX and fluoroquinolones, an antibiotic group, including CIPOX, can cause irreversible adverse reactions leading to disability as follows:
  - Tendinitis (tendon inflammation) and tendon (tissues binding muscles to bones) tearing
  - Peripheral neuropathy (impairment of nerves)
  - Central nervous system effects (hallucination (seeing, hearing or feeling things which do not exist), anxiety, depression, suicidality, insomnia (sleep disturbances), severe headache and confusionIn patients with any of these reactions, the use of CIPOX should be discontinued immediately and the use of fluoroquinolones should be avoided.
- Fluoroquinolones, including CIPOX, can deteriorate muscle weakness in patients with myasthenia gravis (a disease causing muscle weakness). The use of CIPOX should be avoided in patients with known myasthenia gravis history.
- Since the fluoroquinolone group, including CIPOX, is known to be associated with serious adverse reactions, they can be used if there are no other alternatives for the treatment of following indications:
  - Uncomplicated urinary infections (infections seen in healthy adults, not accompanied by structural and anatomical disorders)
  - Acute bacterial exacerbation of chronic bronchitis (re-exacerbation of permanent inflammation in membranes of bronchial tubes in lungs)

Floroquinolones, including CIPOX are being associated with adverse reactions which can cause disability and are potentially irreversible. Common adverse reactions are the effects of musculoskeletal and peripheral nervous system (such as tendinitis (tendon inflammation) and tendon (tissues binding muscles to bones) tearing, tendon swelling or inflammation, tingling or numbness, numbness in the arms and legs, muscle pain, muscle weakness, joint pain, swelling in the joints), arthralgia (joint pain), myalgia (muscle pain), peripheral neuropathy (impairment of nerves) and central nervous system effects (hallucination (seeing, hearing or feeling things which do not exist), anxiety, depression, suicidality, insomnia (sleep disturbances), severe headache and confusion) (see section 4 “Possible side effects”). These reactions can be seen within hours or weeks after starting to use CIPOX. Patients of all age groups or patients without pre-existing risk factors, have experienced these adverse reactions. CIPOX should be discontinued immediately when first signs or symptoms of any serious adverse reaction occur. In addition, in patients, who has experienced any of these fluoroquinolone related serious adverse reactions previously, floroquinolone use, including CIPOX, should be avoided.

Do not take CIPOX in the following conditions

If;

- you have allergy (hypersensitivity) to Ciprofloxacin, other fluoroquinolone group antibiotics, or any of the excipients in CIPOX,
- you are taking medication containing **tizanidine** – an active substance used as a muscle relaxant (See section taking with other medicines)

Take CIPOX with special care in the following conditions

- If you are under 18 years old,
- If you have diarrhea,
- If you have already had liver and kidney disease,
- If you have pain, swelling or tendon inflammation around the joint, or if you have had these complaints previously when you were under antibiotic treatment,
- If you are in older age and taking medicines containing corticosteroids,
- If you have nervous system disease, sara disease,
- If you are diabetic because of the risk of hypoglycemia (blood sugar reduction) with CIPOX,
- In the event of depression or psychosis,
  - You can show psychiatric reactions at first taking CIPOX. If you suffer from depression or psychosis (a type of mental disorder), your symptoms can get worse with CIPOX treatment. In rare cases, depression or psychosis can progress to suicidal thoughts, suicide attempts, or suicide. If this happens, immediately stop taking CIPOX and contact your doctor.
- If nervous system reactions occur after the first application,
- If you are using one of the medicines containing active ingredients such as theophylline (a drug used for inhalation problems), methylxanthine, caffeine, duloxetine (a drug used to treat depression, diabetic neuralgia or urinary incontinence), ropinirole (a drug used in the treatment of Parkinson's disease), clozapine (an antipsychotic drug used in the treatment of psychiatric

patients), olanzapine (an antipsychotic drug used in the treatment of psychiatric patients),

- If you are old,
- If you have kidney failure,
- If you have liver failure.

Severe, sudden allergic reaction (anaphylactic reaction / shock, angioedema). Even at the first dose, there is a small possibility of developing a severe allergic reaction, followed by symptoms such as a feeling of tightness in the chest, dizziness, nausea or fainting, or dizziness when you stand up. If this happens, you should stop using CIPOX and contact your doctor immediately. Inflammation and tendon rupture can occur from the first 48 hours of treatment to the end of several months after treatment. The risk of this tendinopathy may increase in elderly patients or in patients treated concurrently with corticosteroids. At the first sign of pain or inflammation (inflammation), stop taking medicine and relax the painful area. Any unnecessary exercise can increase the risk of tendon rupture.

If a disturbance occur in your vision, or if your eyes are effected in anyway, consult your eye doctor immediately.

When using CIPOX, your skin becomes more susceptible to sunlight or ultraviolet (UV) rays. You should avoid exposure to sunlight or artificial UV light, such as solarium.

Diarrhea can also develop weeks after the use of CIPOX. If the diarrhea is severe or persistent or contains blood or mucus, you should immediately stop the CIPOX treatment because it can be life-threatening. You should not use medication that stops or reduces bowel movements and you should contact your doctor immediately.

If you have heart disease, the conditions you need to be careful when you are using CIPOX are: If you are born with prolonged QT interval or you have related family history (a condition that is detected in the ECG, which is the electrical record of the heart), you have salt imbalance on blood (especially low level of potassium or magnesium on blood), you have slow heart rhythm (called bradycardia), or poor heart (heart failure), history of heart attack (myocardial infarction), you are female or old, you are using medicines that cause abnormal ECG changes.

Simultaneous use of CIPOX with a drug used concomitantly with methotrexate (used in some types of cancer, joint inflammation called rheumatoid arthritis, psoriasis) is not recommended.

For the treatment of some genital tract (reproductive system) infections, your doctor may prescribe another antibiotic in addition to Ciprofloxacin. If there is no improvement on the 3<sup>rd</sup> day of treatment, please consult your doctor.

When performing blood or urine analysis, tell that you are using CIPOX.

If you encounter neuropathy symptoms such as pain, burning, tingling, numbness and / or weakness while using CIPOX, stop using CIPOX and consult your doctor.

CIPOX may cause liver damage. If you notice any signs of loss of appetite, jaundice (yellowing on skin), dark urine, itching or tenderness on stomach, immediately stop taking CIPOX and contact your doctor.

If you or one of your family members has a hereditary condition called glucose-6-phosphate dehydrogenase (G6PD), you may run the risk of anemia by using CIPOX. For this reason, please tell your doctor whether you have deficiency in glucose-6-phosphate dehydrogenase (G6PD) or not.

Incorrect negative results may be seen in *Mycobacterium tuberculosis* culture test during use of CIPOX.

Consult your doctor about microorganisms that are sensitive or resistant to CIPOX.

Exacerbation of Myasthenia gravis (a disease that causes muscle weakness): Fluoroquinolones such as CIPOX may cause worsening of myasthenia gravis symptoms such as muscle weakness and respiratory problems. If you experience muscle weakness or respiratory problems, consult your doctor immediately.

CIPOX may cause a decrease in the number of white blood cells and your resistance to infections may be reduced. If you have any signs of infection such as fever and deterioration in your general condition, or signs of fever and local infection (throat, respiratory tract, mouth or urinary problems), consult your doctor immediately. Your doctor will test whether there is a decrease in the number of white cells. It is important that you warn your doctor about the medication you use.

*Please consult your doctor if these warnings are valid for you, even for a period in the past.*

**Taking CIPOX with food and drink**

Concomitant use of CIPOX with dairy products (such as milk, yoghurt or cheese) or mineral added drinks (for example calcium-fortified orange juice) may reduce the absorption of the drug. It should not be used with this type of food.

**Pregnancy**

*Consult your doctor or pharmacist before using this medicine.*  
If you are pregnant or thinking that you may be pregnant or planning to be pregnant, consult your doctor or pharmacist before using this medicine. Using CIPOX during pregnancy should be avoided. *Immediately consult your doctor if you notice that you are pregnant during your treatment.*

**Breast-feeding**

*Consult your doctor or pharmacist before using this medicine.*  
Do not use CIPOX during breastfeeding since Ciprofloxacin passes to the mother's breast milk and it can be harmful for your baby.

**Driving and using machines**

CIPOX may adversely affect the use of vehicle and machine. This is especially seen when it is taken with alcohol.

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

It does not contain any excipient which requires warning.

**Taking with other medicines**

- If you are using CIPOX with the following medicines, tell your doctor:
  - Drugs that regulate cardiac rhythm (e.g. quinidine, hyroquinidine, disopyramide, amiodarone, sotalol, dofetilide, ibutilide), tricyclic antidepressants (drugs used to treat depression), certain antimicrobials (belonging to a class called macrolide), and medicines used in the treatment of some psychiatric diseases,
  - Probenecid (a drug used in the treatment of gout),
  - Metoclopramide (nausea drug),
  - Omeprazole (stomach drug),
  - Theophylline (a drug used in the treatment of asthma),
  - Tizanidine (a drug used for severe muscle contractions in patients with multiple sclerosis which is a disease effecting central nervous system, especially functions of brain and spinal cord),
  - Methotrexate (a drug used in the treatment of rheumatism, psoriasis and cancer),
  - Cyclosporine (an immune system regulating drug in skin diseases, rheumatoid arthritis and organ transplantation),
  - Vitamin K antagonists (e.g. warfarin, acenocoumarol, phenprocoumon or fluindione) or other orally taken blood-thinning drugs,
  - Ropinirole (a drug used in Parkinson's disease),
  - Clozapine (a drug used in the treatment of psychiatric disorders),
  - Phenytoin (used for epilepsy),
  - Olanzapine (a drug used in the treatment of psychiatric disorders),
  - Zolpidem (a drug used for sleep disturbances).

CIPOX may increase the level of the following drugs in your blood.

- Pentoxifylline (for circulatory problems),
- Caffeine,
- Duloxetine (for depression, diabetic nerve damage and urinary incontinence),
- Lidocaine (for heart disorders or anesthesia),
- Sildenafil (for erectile dysfunction called ‘hardening’ in men),
- Agomelatine (a drug used in the treatment for depression).

Some medicines may reduce the effect of CIPOX.

- Antacids (used for digestive disorder treatment),

- Mineral supplementary drugs,
- Sucralfate (used in the treatment of gastric inflammation, digestion disorder, stomach or intestinal ulcer),
- A polymeric phosphate binder (sevelamer, lanthanum carbonate) (used to reduce phosphate levels in patients with renal insufficiency),
- Medicines or supplements containing magnesium, calcium, aluminum or iron.

If the use of these preparations is necessary, CIPOX should be taken 2 hours before or at the earliest 4 hours after these medications.

*Please tell your doctor or pharmacist if you are using or have recently used any prescribed or non-prescribed medicine.*

**3. How to take CIPOX**

**Instructions for proper use and dose/dosing intervals:**

Your doctor will tell you for how long and in which frequency you will use CIPOX. This period depends on the type and severity of your infection.

If you have kidney disease, tell your doctor because your treatment dose will need to be adjusted accordingly.

Treatment usually takes 5 – 21 days but it can dure longer in some severe infections. Always take CIPOX as directed by your doctor. If you are not sure, ask your doctor or pharmacist to learn how you should use it, how many tablets you should take.

**Method and route of administration:**

It is applied orally.

- Take CIPOX tablets with sufficient amount of water.
- Try to take the tablets at the same time every day.
- You can take the tablets on an empty stomach or on a full stomach. Taking calcium with food will not effect the absorption of medicine; but tablets should not be taken with dairy products (e.g. milk or yoghurt) or mineral added drinks (e.g. calcium-fortified orange juice).

Always keep in mind to take sufficient amount of liquid while using this medicine.

**Different age groups:**

**Use in children:** It should be used as recommended by your doctor.

**Use in the elderly:** It should be used as recommended by your doctor.

**Special Conditions:**

**Kidney failure:** If you have kidney failure, tell your doctor, because your treatment dose will need to be adjusted accordingly. Dose studies have not been conducted in children with kidney failure.

**Liver failure:** Should be used as prescribed by your doctor. Dose studies have not been conducted in children with liver failure.

*If you have any impression that the effect of CIPOX is too strong or too weak, consult your doctor or pharmacist.*

**If you took more CIPOX than you should:**

*If you took more CIPOX than you were told to, contact your doctor or pharmacist immediately.*

Take the tablets or box of the medicine with you for showing to doctor, if possible.

**If you forget to take CIPOX:**

Take the normal dose as soon as possible and then continue as prescribed. However, if it is almost the time for you to take the next dose, do not take the forgotten dose and continue as normal. Absolutely complete the treatment course.

*Do not take a double dose to make up for a forgotten dose.*

**Possible effects of discontinuation with CIPOX treatment:**

Even if you start feeling better in a few days, **it is important that you complete the treatment course.** If you stop taking this medicine sooner than it should be, the infection may not be completely treated and the symptoms of infection may recur or worsen. Also, resistance to antibiotics may develop.

If you have any further questions about the use of this medicine, ask your doctor.

**4. Possible side effects**

As with all medicines, there may be side effects in people sensitive to substances in the content of CIPOX.

Very common: May be observed at least one in 10 patients.

Common: May be observed in less than one in 10 patients, but more than one in 100 patients.

Uncommon: May be observed less than one in 100 patients, but more than one in 1000 patients. Rare: May be observed less than one in 1000 patients, but more than one in 10000 patients.

Very rare: May be observed in less than one in 10000 patients.

Not known: Frequency cannot be estimated from the available data.

**Stop taking CIPOX if you experience one of the conditions below and inform your doctor or apply to the emergency department of the nearest hospital IMMEDIATELY:**

**Rare**

- Seizures

**Very Rare**

- Tightness in chest, dizziness, severe and sudden allergic reaction with symptoms of feeling sick or fainted or dizziness when standing up (anaphylactic reaction/shock) (see section 2 “What you need to know before you take CIPOX”),
- Muscle weakness, inflammation or tearing in the tendons binding muscles to bones, especially for the big one which is located in the back of ankle (tissue binding muscles to bones, Achilles tendon) (see section 2 “What you need to know before you take CIPOX”),
- Wide spread pustules or pustules or wounds which can cause peeling on the skin, usually seen in mouth, throat, nose, eyes and in other mucous areas like sexual regions or severe, life-threatening skin rashes (Stevens-Johnson Syndrome, toxic epidermal necrolysis).

**Not Known**

- Extraordinary feelings like pain, burning, tingling, numbness and weakness in arm-leg muscles (neuropathy) (see section 2 “What you need to know before you take CIPOX”),
- Rash, fever, inflammation in internal organs, abnormalities in blood values and disease effecting whole body (systemic) (drug reaction accompanied by eosinophilic and systemic symptoms (DRESS Syndrome), acute generalized exanthematous pustulosis AGEP).

Other side effects observed with CIPOX are given below in accordance with their frequency:

**Common**

- Nausea,
- Diarrhea,
- Joint pain and joint inflammation in children.

**Uncommon**

- Joint pain in adults,
- Fungal super infections (starting of a second infection in a body which is weak due to any other infection),
- Loss of appetite,
- Hyperactivity,
- Restlessness,
- Headache,
- Dizziness,
- Sleep disorders,
- Taste disorders,
- Vomiting,
- Abdominal pain,
- Digestion disorders such as stomach disease (Indigestion/heartburn) or flatulence,
- Increase in blood levels of some substances (liver enzymes and or bilirubin),
- Rash,
- Itching,
- Hives,
- Kidney dysfunction,
- Pain in muscles and bones, not feeling well (asthenia) or fever,
- Increase in alkaline phosphatase, one of the liver enzymes,
- Increase in blood level of alkaline phosphatase,