PATIENT INFORMATION LEAFLET

- The antibiotic group called fluoroquinolones, including ciprofloxacin and ciprofloxacin, the active ingredients of SIPROSAN, can cause disability and irreversible side effects such as:
  - Tendonitis (inflammation of the tendon) and rupture of the tendon (the ligaments that connect the muscles to the bones)
  - Peripheral neuropathy (damage to the nerves)
  - Central nervous system effects (hallucination (seeing, hearing, or feeling things that are not there), anxiety (anxiety), depression, suicidality, insomnia (sleep disturbances), severe headache, and confusion (sudden confusion)

In patients in whom any of these reactions are observed, the use of SIPROSAN should be discontinued immediately and the use of fluoroquinolones should be avoided.

- Fluoroquinolones, including Siprosan, may exacerbate muscle weakness in patients with myasthenia gravis (a disease causing muscle weakness). The use of SIPROSAN should be avoided in patients with a known history of myasthenia gravis.

- Since fluoroquinolone group drugs, including SIPROSAN, are known to be associated with serious side effects, they can be used in the following indications if there is no other alternative.
  - Uncomplicated urinary infection (infections in healthy individuals, not accompanied by structural and anatomical disorders of the urinary system in adults)
  - Acute bacterial exacerbation of chronic bronchitis (re-exacerbation of the state of persistent inflammation of the membranes of the bronchial tubes in the lung)

SIPROSAN® 500 mg film coated tablet

It is taken orally.

- ***Active ingredient:*** Each film-coated tablet contains 582 mg of ciprofloxacin hydrochloride monohydrate equivalent to 500 mg of ciprofloxacin.

- ***Excipients:*** Corn starch, microcrystalline cellulose, sodium starch gluconate, precipitated silica, magnesium stearate, talc, eudrogit EPO, sodium lauryl sulfate, stearic acid, titanium dioxide, magnesium stearate.

Before you start using this medicine, read these PATIENT INFORMATION LEAFLET carefully because it contains important information for you.

- *Keep this user manual. You can need to read again.*
- *If you have other questions, please talk your doctor or pharmacist.*
- *This medicine has been prescribed for you personally, do not give it to others.*
- *When you go to a doctor or hospital while using this medicine, tell your doctor that you are using this medicine.*
- *Follow exactly what is written in this instruction. Do not use **high or low** doses other than the dose recommended to you about the drug.*

In this leaflet:

Headings are included.

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

Fluoroquinolones, including Siprosan, should not be used in acute bacterial exacerbation of chronic bronchitis (re-exacerbation of persistent inflammation of the membranes of the bronchial tubes in the lung) and in the presence of alternative treatment options for uncomplicated urinary infections (urinary tract infections) because of the risk of serious adverse effects. It can be used in these indications when other treatment options have failed.

In addition, in urinary infections (urinary tract infections), sensitivity should be proven with an antibiogram. SIPROSAN can only be used in the treatment of infections that are

proven or seriously suspected to be caused by susceptible bacteria.

- SIPROSAN is available in the form of white, oblong film-coated tablets. Each film-coated tablet contains 500 mg of active substance (ciprofloxacin). Ciprofloxacin, the active ingredient of SIPROSAN, belongs to a group of antibiotics called fluoroquinolones.

- SIPROSAN is available in a box containing 14 tablets.
- SIPROSAN is used for the treatment of respiratory tract infections in adults, in long-term and recurrent ear or sinus infections, kidney and urinary tract infections, adnexitis (acute or chronic inflammation of the ovaries and tubes with the uterus appendages (adnex)), in infections of the genital organs, including gonorrhea (gonorrhea), prostatitis, in gastrointestinal tract infections, in infections of the abdominal cavity such as peritonitis, skin and soft tissue infections, bone and joint infections, in the prevention of infections caused by the bacteria *Neisseria meningitidis* over the age of 18, in case of exposure by inhalation of anthrax and in malignant otitis externa.

  SIPROSAN can be used together with other antibiotics (combination therapy) in the treatment of patients with low white blood cell (white blood cell) count (neutropenia) and fever thought to be caused by bacterial infection.

  In case of a severe infection or an infection caused by more than one type of bacteria, additional antibiotic therapy can be applied in addition to SIPROSAN.
- SIPROSAN is used in children and adolescents with cystic fibrosis (an inherited disease that causes defects in the lungs, kidneys, or pancreas), in cases of exposure to anthrax inhalation (by inhalation), when other alternative treatments are not suitable, in case of sensitivity to the active substance of ciprofloxacin in pulmonary and bronchial infections, complicated urinary tract infections, including those reaching the kidneys (pyelonephritis). SIPROSAN can be used in cases where other agents cannot be used for the treatment of other specific severe infections in children and adolescents, if deemed necessary by the physician.

2. Things to consider before using SIPROSAN

Tendinitis (inflammation of the ligament that connects muscle to bone) and tendon rupture (rupture of the ligament that connects muscle to bone), peripheral neuropathy (inflammation of nerve endings), and central nervous system effects are serious side effects that cause disability and are potentially irreversible.

Fluoroquinolones, including SIPROSAN, have been associated with serious adverse effects that can cause disability and are potentially irreversible. Common side effects are musculoskeletal and peripheral nervous system (tendinitis (tendonitis) and tendon rupture (the ligaments that attach muscles to bones) swelling or inflammation of tendons, tingling or numbness, numbness in arms and legs, myalgia, muscle weakness, joint pain) , such as swelling in the joints), arthralgia (joint pain), myalgia (muscle pain), peripheral neuropathy (damage to the nerves), central nervous system effects (hallucination (seeing, hearing or feeling things that are not there), anxiety (anxiety), depression, suicidality, insomnia (sleep disturbances), severe headache and confusion (sudden confusion) (see section 4. What are the possible side effects?).

These side effects may occur within hours or weeks after starting SIPROSAN. Patients of all age groups or without pre-existing risk factors have experienced these side effects.

SIPROSAN should be discontinued immediately at the first signs or symptoms of any serious side effect. In addition, the use of fluoroquinolones, including SIPROSAN, should be avoided in patients experiencing any of these serious adverse reactions in association with fluoroquinolones.

DO NOT USE SIPROSAN in the following situations

If;

- If you are allergic (hypersensitive) to ciprofloxacin, other quinolone group antibiotics or any of the excipients in SIPROSAN
- If you are using a drug containing the active substance **tizanidine**, which is used as a muscle relaxant (see section on use with other drugs).

USE SIPROSAN CAREFULLY in the following situations

If;

- If you are under the age of 18,
- If diarrhea is observed,
- If you have previous liver and kidney disease,
- If you have pain, swelling or tendonitis around the joint, or if you have had these complaints before under antibiotic treatment,
- If you are of advanced age and use cortisone-containing drugs,
- If you have a nervous system disease, epilepsy,

– If you have diabetes (diabetes), as there may be a risk of hypoglycemia (low blood sugar) with SIPROSAN,
– If there is depression or psychosis,
    o You may show psychiatric reactions when you first take SIPROSAN. If you suffer from depression or psychosis (a type of mental disorder), your signs (symptoms) may become worse with SIPROSAN treatment. In rare cases, depression or psychosis can progress to suicidal thoughts, suicide attempts, or committing suicide. If this happens, stop taking SIPROSAN immediately and contact your doctor.
- If nervous system reactions occur after the first administration,
- If you are using any of the drugs containing theophylline (a medicine used for breathing problems), methylxanthine, caffeine, duloxetine (a medicine used to treat depression, diabetic nerve pain, or urinary incontinence), ropinirole (a drug used in the treatment of Parkinson's disease), clozapine (an antipsychotic drug used to treat psychiatric patients), olanzapine (an antipsychotic drug used to treat psychiatric patients), active substances.
- If you are old,
- If you have kidney failure,
- If you have liver failure,

Severe, immediate allergic reaction (anaphylactic reaction/shock, angioedema). Even with the first dose, there is a small chance of developing a severe allergic reaction, the following symptoms being: chest tightness, lightheadedness, nausea or fainting, or lightheadedness upon standing up. If this happens, you should stop using SIPROSAN and contact your doctor immediately.

Inflammation and tendon rupture may occur within the first 48 hours of treatment and up to months after discontinuation of treatment. The risk of this tendinopathy may be increased in elderly patients or patients treated concomitantly with corticosteroids. At the first sign of pain or inflammation, stop taking the drug and rest the painful area. Any unnecessary exercise can increase the risk of tendon rupture.

If your vision is impaired or your eyes are affected in any way, consult an ophthalmologist immediately.

While using SIPROSAN, your skin becomes more sensitive to sunlight or ultraviolet (UV) rays. You should avoid exposure to strong sunlight or artificial UV light such as a solarium.

Diarrhea may develop weeks after stopping the use of SIPROSAN. If it is severe or persistent, or contains blood or mucus, you should stop taking SIPROSAN immediately, as it can be life-threatening. You should not use drugs that stop or reduce bowel movements and you should contact your doctor immediately.

Conditions to be careful while using SIPROSAN if you have heart disease: Being born with prolongation of the QT interval or having a related family history (a condition detected in an EKG, which is an electrical recording of the heart), salt imbalance in the blood (especially low levels of potassium or magnesium in the blood), having a very slow heart rhythm (called 'bradycardia'), weak heart (heart failure), a history of heart attack (myocardial infarction), if you are female or old, or if you are taking other medications that cause abnormal EKG changes.

The simultaneous use of SIPROSAN with a drug used in the treatment of methotrexate (some types of cancer, joint inflammation called rheumatoid arthritis, psoriasis called psoriasis) is not recommended.

For the treatment of some genital tract (reproductive system) infections, your doctor may prescribe an additional antibiotic in addition to ciprofloxacin. If there is no improvement yet on the 3rd day of treatment, please consult your doctor.

While having blood or urine analysis, tell that you are using SIPROSAN.

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

SIPROSAN can cause liver damage. If you notice any symptoms such as loss of appetite, jaundice (yellowing of the skin), dark urine, itching or stomach tenderness, stop taking Siprosan and contact your doctor immediately.

If you or someone in your family has an inherited condition called glucose-6-phosphate dehydrogenase (G6PD), you may face the risk of anemia with the use of SIPROSAN. Therefore, inform your doctor whether you have glucose-6-phosphate dehydrogenase (G6PD) deficiency.

False negative results may be seen in the *Mycobacterium tuberculosis* culture test performed while using SIPROSAN.

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

Exacerbation of myasthenia gravis (a disease that causes muscle weakness):
Fluoroquinolones such as Siprosan may cause worsening of Myasthenia gravis symptoms such as muscle weakness and breathing problems. If you experience increased muscle weakness or breathing problems, consult your doctor immediately.
SIPROSAN may cause a decrease in the number of white blood cells and your resistance to infections may decrease. If you have symptoms of infection such as fever and deterioration in your general condition, or fever and signs of local infection (throat, respiratory tract, mouth or urinary problems), consult your doctor immediately. Your doctor will test to see if there is a possible decrease in the number of white blood cells. It is important to warn your doctor about the medicine you are using.
If these warnings apply to you, even at any time in the past, please consult your doctor.

Using SIPROSAN with food and drink
Concomitant use of SIPROSAN with dairy products (such as milk, yogurt or cheese) or mineral-added beverages (eg, calcium-fortified orange juice) may reduce the absorption of the drug. It should not be used with such foods.

Pregnancy
Consult your doctor or pharmacist before using this medication.
If you are pregnant or think you may be pregnant or are planning to become pregnant, consult your doctor or pharmacist before using this medicine.
The use of SIPROSAN during pregnancy should be avoided.
There are no adequate data from the use of ciprofloxacin in women of childbearing potential. As a precaution, it is recommended to use an appropriate method of contraception.

If you find out that you are pregnant during your treatment, consult your doctor or pharmacist immediately.

Breast-feeding

Consult your doctor or pharmacist before using this medication.

Do not use SIPROSAN while breastfeeding, because ciprofloxacin passes into breast milk and may be harmful to your baby.

Vehicle and machine use

SIPROSAN may adversely affect the use of vehicles and machinery. This is especially true when taken with alcohol.

Important information about some excipients in the content of SIPROSAN

It does not contain an excipient requiring warning.

Concomitant use with other drugs

- Inform your doctor if you are using SIPROSAN together with the following drugs:

- Medicines that regulate heart rhythm (eg, quinidine, hydroquinidine, disopramide, amiodarone, sotalol, dofetilide, ibutilide), tricyclic antidepressants (drugs used to treat depression), some antimicrobials (belonging to a class called macrolides), and drugs used in the treatment of some psychiatric diseases
- probenecid (a medicine used to treat gout),
- Metoclopramide (nausea medicine),
- Omeprazole (stomach medicine),
- theophylline (a medicine used to treat asthma),
- tizanidine (a medicine for severe muscle contractions in patients with multiple sclerosis, a disease that affects the central nervous system, especially brain and spinal cord function),
- Methotrexate (a drug used in the treatment of rheumatism, psoriasis and cancer),
- Cyclosporine (an immunomodulatory drug in skin diseases, rheumatoid arthritis and organ transplantation),
- Vitamin K antagonists (eg, warfarin, acenocoumarol, phenprocoumon or fluindione) or other oral blood thinners,
- Ropinirole (a medicine used in Parkinson's disease),
- Clozapine (a drug used in the treatment of psychiatric diseases),

- Phenytoin (used for Sara (epilepsy))
- Olanzapine (a medicine used to treat psychiatric disorders)
- Zolpidem (a medicine used for sleep disorders).

SIPROSAN may increase the level of the following medicines in your blood:
- Pentoxifylline (for circulation problems),
- Caffeine,
- Duloxetine (for depression, diabetic nerve damage and urinary incontinence),
- Lidocaine (for heart conditions or anesthesia),
- Sildenafil (for erectile dysfunction called erectile dysfunction in men),
- Agomelatine (a medicine used to treat depression).

Some medicines can reduce the effect of SIPROSAN:
- Antacids (used to treat indigestion),
- Mineral supplement drugs,
- sucralfate (used to treat heartburn, indigestion, ulcers in the stomach or intestines),
- Polymeric phosphate binder (sevelamer, lanthanum carbonate) (used to reduce phosphate level in patients with kidney disease),
- Medicines or supplements containing magnesium, calcium, aluminum or iron.

If the use of these preparations is necessary, SIPROSAN should be taken 2 hours before or at the earliest 4 hours after these drugs.
If you are currently using or have recently used any prescription or non-prescription drugs, please inform your doctor or pharmacist about them.

3. How to use SIPROSAN?

Instructions for proper use and dose/frequency of administration:
Your doctor will tell you how long and how often to use SIPROSAN. This time depends on the type of infection and how severe it is.

If you have kidney disease, tell your doctor because your medication dose may need to be adjusted.

Treatment usually lasts 5 to 21 days, but sometimes longer in severe infections. Always take

this medicine exactly as your doctor has told you. If you are not sure, ask your doctor or pharmacist how many tablets you should take and how you should use them.

Application route and method:

It is administered orally.

- Take the tablets with enough liquid. Do not chew the tablets as they taste bad.
- Try to take your tablets at the same times every day.
- You can take the tablets on an empty stomach or on a full stomach. Taking calcium with meals will not significantly affect the absorption of the drug. However, the tablets **should not be taken** with dairy products such as milk or yogurt, or with mineral-fortified beverages (eg, calcium-fortified orange juice).

Remember to drink enough fluids 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 use cases:

Kidney failure: Tell your doctor if you have kidney failure, because your treatment dose will need to be adjusted accordingly. Dosage studies have not been conducted in children with renal impairment.

Liver failure: It should be used as recommended by your doctor. Dosage studies have not been conducted in children with hepatic impairment.

If you have the impression that the effect of SIPROSAN is too strong or too weak, talk to your doctor or pharmacist.

If you use more SIPROSAN than you should:

If you have used more than you should use from SIPROSAN, talk to a doctor or pharmacist immediately.

If possible, take the tablets or the box of the medicine with you to show the doctor.

If you forget to use SIPROSAN

Take the normal dose as soon as possible and then continue as prescribed. However, if it's almost time for your next dose, don't take the missed dose and continue as you normally would. Make sure to complete your course of treatment.

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

Effects that may occur when treatment with SIPROSAN is terminated

Even if you start to feel better within a few days, **it is important that you complete the course of treatment**. If you stop this medicine sooner than necessary, the infection may not be completely treated and the symptoms of the infection may reappear or worsen. In addition, antibiotic resistance may develop.

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

4. What are the possible side effects?

Like all medicines, there may be side effects in people who are sensitive to the substances in the content of SIPROSAN.

Very common : It can be seen in at least one of 10 patients.

Common : It can be seen less than one in 10 patients, but more than one in 100 patients.

Uncommon : It can be seen less than one in 100 patients, but more than one in 1,000 patients.

Rare : It can be seen less than one in 1,000 patients but more than one in 10,000 patients.

Very rare : It can be seen in less than one in 10,000 patients.

Unknown : It cannot be estimated from the available data.

If any of the following occur, stop using SIPROSAN and IMMEDIATELY inform your doctor or go to the emergency department of the nearest hospital:

Rare

- seizures

Very rare

- Severe, sudden allergic reaction (anaphylactic reaction/shock) with symptoms such as chest tightness, dizziness, feeling sick or faint, or dizziness upon standing up (See Section 2 under the heading " Things to consider before using SIPROSAN ").
- Muscle weakness, inflammation or tearing of the tendons that connect the muscles to the bones, especially the large tendon at the back of the ankle (the tissue that connects the muscles to the bones, the Achilles tendon) (See Section 2 under the heading " Things to consider before using SIPROSAN ".)
- Serious, life-threatening skin rash (Stevens-Johnson syndrome, toxic epidermal necrolysis) in the form of raised bumps or sores, usually on other mucous surfaces such as the mouth, throat, nose, eyes, and genitals, which may become widespread blisters or peeling.

Unknown

- Unusual sensations (neuropathy) such as pain, burning, tingling, numbness or weakness in the muscles of the arms and legs (See Section 2 under the heading " Things to consider before using SIPROSAN ".)
- Rash, fever, inflammation of internal organs, abnormalities in blood values and (systemic) disease affecting the whole body (drug reaction with eosinophilia and systemic symptoms (DRESS syndrome), acute generalized exanthematous pustulosis AGEP)

Other side effects observed during treatment with SIPROSAN are given below according to their frequency:

Common

- Nausea,
- Diarrhea,
- Joint pain and inflammation of the joints in children.

Uncommon

- Joint pain in adults,
- Fungal super-infections (the onset of a second infection in the body weakened by any infection),

- An increase in the number of blood cells called eosinophils, a type of white blood cell, in the blood,
- Anorexia,
- Mobility (hyperactivity),
- restlessness,
- Headache,
- Dizziness,
- Sleeping disorders,
- Taste disorders,
- Vomiting,
- Stomach ache,
- Digestive problems such as stomach upset (indigestion/heartburn) or gas bloating,
- Increased blood levels of certain substances (increased liver enzymes (transaminase) and/or bilirubin,
- Rash,
- Itching,
- Hives,
- Kidney dysfunction,
- Pain in muscles and bones, feeling unwell (asthenia) or fever,
- Increase in blood alkaline phosphatase (a certain substance in the blood).

Rare

- Muscle pain, joint inflammation, increased muscle tension and cramps,
- Antibiotic-induced inflammation of the large intestine (which may very rarely result in death) (See Section 2 under the heading " Things to consider before using SIPROSAN ".),
- Decrease or increase in the number of blood cells (leukopenia, leukocytosis, neutropenia, anemia),
- Decrease or increase in the number of coagulation cells in the blood,
- Allergic reaction swelling (edema) or sudden swelling of the skin and mucosal surfaces (angioedema) (See Section 2 under the heading " Things to consider before using SIPROSAN ".)
- Increase in blood sugar (hyperglycemia),

- Decrease in blood sugar (hypoglycemia) (See Section 2 under the heading " Things to consider before using SIPROSAN "),
- Sudden confusion (confusion),
- Disorientation (disorientation),
- Anxiety reactions,
- Strange dreams,
- Depression (suicidal ideation/thoughts and the possibility of attempting or reaching suicide) (See Section 2 under the heading " Things to consider before using SIPROSAN ".)
- Seeing, hearing or feeling things that are not real (hallucination),
- Abnormal feeling such as numbness, tingling, burning and stinging,
- Decreased feeling,
- Loss of feeling,
- Tremor,
- Balance disorder,
- Visual disturbances (including double vision called diplopia),
- tinnitus,
- Hearing loss,
- Decreased hearing,
- Increase in heart rate (tachycardia),
- Enlargement of blood vessels (vasodilation),
- Low blood pressure,
- Fainting,
- Shortness of breath (including asthma-related conditions), asthma-like symptoms (symptoms),
- Liver failure,
- Jaundice due to obstruction in the bile flow,
- Liver inflammation (hepatitis),
- Photosensitivity (See Section 2 under the heading " Things to consider before using SIPROSAN ".),
- Kidney failure,
- Having blood in the urine,
- Presence of crystals in the urine,

- Urinary tract inflammation,
- Swelling due to water retention in the body (edema),
- Excessive sweating,
- Increase in amylase, a digestive enzyme.

Very rare

- Anemia (hemolytic anemia) with the destruction of red blood cells in the blood (See Section 2 under the heading " Things to consider before using SIPROSAN ".),
- Decreased number of all blood cells (pancytopenia) (life-threatening),
- Dangerous decrease in the number of white blood cells in the blood (agranulocytosis) (See Section 2 under the heading " Things to consider before using SIPROSAN ".),
- Bone marrow suppression (life-threatening),
- Serum sickness-like reaction (a kind of allergic reaction),
- Mental health disorders (suicidal ideation/thoughts and suicidal attempts or psychological reactions that may lead to suicide) (See Section 2 under the heading " Things to consider before using SIPROSAN ".),
- Migraine,
- Coordination disorder,
- Difficulty in walking,
- Smell disorders,
- Increased intracranial pressure (intracranial pressure and pseudotumor cerebri),
- Visual discoloration,
- Vascular inflammation (vasculitis),
- Pancreatic inflammation,
- Liver damage (liver necrosis) that may progress to life-threatening liver failure very rarely (See Section 2 under the heading " Things to consider before using SIPROSAN ".),
- Small bleeding point under the skin (petechiae); various skin rashes or rashes
- Exacerbation of Myasthenia Gravis (a disease that causes muscle weakness) (See Section 2 under the heading " Things to consider before using SIPROSAN ".).

Unknown

- Feeling too excited (mania) or too much optimism or hyperactivity (hypomania)

- Abnormal rapid heart rhythm, life-threatening irregular heart rhythm, heart rhythm irregularities (called "QT interval prolongation", seen in the EKG showing the electrical activity of the heart)
- Effects on blood coagulation (in patients treated with vitamin K antagonists).

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

5. Storage of SIPROSAN

Keep SIPROSAN out of the sight and reach of children and in its package.

Store at room temperature below 25°C.

Use in accordance with expiration dates.

Do not use SIPROSAN after the expiry date on the package.

"The number written after the phrase "The Last Use." represents the month and the last day of that month is the expiration date.

Do not use SIPROSAN if you notice any defects in the product and/or its packaging.

Do not throw away expired or unused medicines! Give it to the collection system determined by the Ministry of Environment and Urbanization.

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This patient information leaflet has been approved on 08/05/2020.