Patient package insert according to Pharmacists' Regulations (Preparations) – 1986
This medicine can be sold with a physician's prescription only

Ciprodex® 500, Caplets

Each caplet contains ciprofloxacin as hydrochloride at a dose of 500 mg.

Inactive ingredients and allergens in the medicine – see section 6 "Additional information" and in section 2 "Important information about some of the ingredients of the medicine".

Read this entire leaflet carefully before you start using this medicine. This leaflet contains concise information about the medicine. If you have any further questions, ask your physician or pharmacist.
This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if you think that their illness is similar.

1. What is the medicine used for?

Ciprodex is used in adults to treat the following bacterial infections:
- respiratory tract infections
- long lasting or recurring ear or sinus infections
- urinary tract infections
- genital tract infections in men and women
- gastro-intestinal tract infections and intra-abdominal infections
- skin and soft tissue infections
- bone and joint infections
- to prevent infections due to the bacterium Neisseria meningitidis
- anthrax inhalation

Treatment for children and adolescents, under specialist medical supervision, to treat the following bacterial infections:
- lung and bronchial infections in children and adolescents suffering from cystic fibrosis
- complicated urinary tract infections, including infections that have reached the kidneys (pyelonephritis).
- anthrax inhalation exposure.
- **Ciprodex** may also be used to treat other specific severe infections in children and adolescents when your doctor considered this necessary.

Therapeutic group: antibiotic of the fluoroquinolone group.

2. Before using the medicine

Do not use the medicine if:

- You are hypersensitive (allergic) to the active ingredient (ciprofloxacin), to other medicines of the quinolone group or to one of the additional ingredients the medicine contains (see section 6).
- You are taking tizanidine (also see section "Drug interactions").

Special warning regarding the use of this medicine:
- Before treatment with **Ciprodex**

You should not take fluoroquinolone/quinolone antibacterial medicines, including **Ciprodex**, if you have experienced any serious adverse reaction in the past when taking a quinolone or fluoroquinolone. In this situation, you should inform your doctor as soon as possible.
- **Before treatment with Ciprodex, tell the physician if:**
  - you have ever had kidney problems because your treatment may need to be adjusted.

- you suffer from epilepsy or other neurological conditions, you have a history of seizures.
- you suffer from tendon problems or if you have a history of tendon problems during previous treatment with antibiotics such as **Ciprodex**.
- you are diabetic because you may experience a risk of hypoglycaemia (low blood sugar) with **Ciprodex**.
- you have myasthenia gravis (a type of muscle weakness), because symptoms can be exacerbated.
- you have been diagnosed with an enlargement or "bulge" of a large blood vessel (aortic aneurysm or large vessel peripheral aneurysm).
- you have experienced a previous episode of aortic dissection (a tear in the aorta wall).
- you have been diagnosed with a leaky heart valve (heart valve regurgitation).
- you have a family history of aortic aneurysm or aortic dissection, congenital heart valve disease or other risk factors or predisposing conditions to aortic aneurysm or dissection (e.g. connective tissue disorders such as Marfan syndrome, or Ehlers-Danlos syndrome, Turner syndrome, Sjögren's syndrome [autoimmune inflammatory disease] or vascular disorders such as Takayasu arteritis, giant cell arteritis, Behcet´s disease, high blood pressure or atherosclerosis, rheumatoid arthritis [a disease of the joints] or endocarditis [heart infection]).
- you have heart problems. Caution should be taken when using **Ciprodex** if you have or your family have a history of prolonged QT interval (seen on ECG, electrical recording of the heart), you have salt imbalance in the blood (especially low level of potassium or magnesium in the blood), you have a very slow heart rhythm (called 'bradycardia'), you have a weak heart (heart failure), you have a history of heart attack (myocardial infarction), you are female or elderly or you are taking other medicines that result in abnormal ECG changes (see section: "Drug interactions").
- 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 **Ciprodex**.
- you suffer from impaired liver function.

- For the treatment of some genital tract infections, your doctor can prescribe another antibiotic in addition to **Ciprodex**. If there is no improvement in symptoms after 3 days of treatment, please consult your doctor.
- In children under the age of 18 there is a higher risk of symptoms such as pain or swelling in the bones, joints or tendons while taking **Ciprodex**.

<u>While taking the medicine</u>
Tell your doctor immediately, if any of the following occurs **while taking Ciprodex**. Your doctor will decide whether treatment with **Ciprodex** needs to be stopped.

- **Severe, sudden allergic reaction** (an anaphylactic reaction/shock, angioedema) which may be fatal. Even with the first dose, there is a small chance that you may experience a severe allergic reaction with the following symptoms: tightness in the chest, feeling dizzy, sick or faint, or experiencing dizziness when standing up, itchy skin rashes (hives), difficulty breathing or swallowing, swelling of the lips, tongue, face, throat tightness, hoarseness, rapid pulse. **If this happens, stop taking Ciprodex and contact your doctor immediately.**
- **Severe, prolonged side effects can cause disability and may be irreversible**. Fluoroquinolone/quinolone antibacterial medicines, including **Ciprodex**, have been associated with very rare but serious side effects, some of them being long lasting (continuing months or years), disabling or potentially irreversible. This includes tendon, muscle and joint pain of the upper and lower limbs, difficulty in walking, abnormal sensations such as pins and needles, tingling, tickling, numbness or burning (paraesthesia), sensory disorders including impairment of vision, taste and smell, and

hearing, depression, memory impairment, severe fatigue, and severe sleep disorders. If you experience any of these side effects after taking **Ciprodex**, contact your doctor immediately prior to continuing treatment. You and your doctor will decide on continuing the treatment considering also an antibiotic from another class.

- **Pain and swelling in the joints and inflammation or rupture of tendons** may occur rarely. Your risk is increased if you are elderly (above 60 years of age), have received an organ transplant, have kidney problems or if you are being treated with corticosteroids. Inflammation and ruptures of tendons may occur within the first 48 hours of treatment and even up to several months after stopping the therapy. At the first sign of pain or inflammation of a tendon (for example in your ankle, wrist, elbow, shoulder or knee), stop taking **Ciprodex**, contact your doctor and rest the painful area. Avoid any unnecessary exercise, as this might increase the risk of a tendon rupture. Stop the treatment and contact medical assistance immediately with the appearance of signs or symptoms of the following which could indicate a tendon rupture: hear or feel a snap or pop in a tendon area, bruising appears right after an injury in a tendon area, inability to move or bear weight in the affected area.
- If you feel **sudden, severe pain in your abdomen, chest or back**, **which may be a sign of an aortic aneurysm or dissection**, go immediately to an emergency room. The risk may increase if you are treated with systemic corticosteroids.
- If you begin to experience rapid attacks of **shortness of breath**, especially when fully lying down or if you notice **swelling in the ankles, feet or stomach or a new instance of heart palpitations** (feeling of rapid or irregular heart beat), inform the doctor immediately.
- 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 seizure happens, stop taking the medicine and contact your doctor immediately.
- You may rarely experience symptoms of **neuropathy** (Peripheral Nerve Disease) such as pain, burning, tingling, numbness and/or weakness especially in the feet and legs or hands and arms. If this happens, stop taking the medicine and contact your doctor immediately in order to prevent the development of potentially irreversible condition.
- You may experience **psychiatric reactions** after taking antibiotics from the fluoroquinolone group, including **Ciprodex,** even after taking the first dose. If you suffer from **depression** or **psychosis**, your symptoms may become worse under treatment with **Ciprodex**. In rare cases, depression or psychosis can progress to thoughts of suicide and self-harming behaviour such as suicide attempts or completed suicide (see section 4: "Side effects"). In case of depression, psychosis, suicidal thoughts or behaviour, stop taking the medicine and contact your doctor immediately.
- Quinolone antibiotics may cause an **increase of your blood sugar levels** above normal levels (hyperglycaemia), or **lowering of your blood sugar levels** below normal levels (hypoglycaemia), potentially leading to loss of consciousness (hypoglycaemic coma) in severe cases (see section 4). This is important for people who have diabetes. If you suffer from diabetes, your blood sugar should be carefully monitored.
- **Diarrhoea** may develop while you are taking antibiotics, including **Ciprodex**, or even several weeks after you have stopped taking them. If it becomes severe or persistent or you notice that your stool contains blood or mucus, stop taking the medicine and contact your doctor immediately, as this can be life-threatening. You may have stomach cramps and a fever. Do not take medicines that stop or slow down bowel movements.
- If your **eyesight becomes impaired** or if your eyes seem to be otherwise affected, consult an eye specialist immediately.
- Your skin becomes **more sensitive to sunlight or ultraviolet (UV) light** when taking **Ciprodex**. Avoid exposure to strong sunlight or artificial UV light such as sunbeds or sunlamps. The symptoms may include a severe sunburn, blisters or swelling of your skin. If you get any of these symptoms, contact your doctor immediately. Take care of proper protection (clothes that cover your skin, hat, sunscreens etc.).

- Tell the doctor or laboratory staff that you are taking **Ciprodex** if you have to provide a **blood or urine sample.**
- If you suffer from **kidney problems**, tell the doctor because your dose may need to be adjusted. **Ciprodex** may cause **liver damage**. If you notice any symptoms such as loss of appetite, itching or tenderness of the stomach, contact your doctor immediately. If you have jaundice (yellowing of the skin and the eyes) or dark urine, stop taking the medicine and contact your doctor immediately.
- **Ciprodex** 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 the doctor immediately. A blood test will be taken to check possible reduction of white blood cells count (agranulocytosis). It is important to inform your doctor that you are taking the medicine.

Drug interactions
If you are taking, have recently taken or might take other medicines, including nonprescription medications and nutritional supplements, tell the doctor or pharmacist.
Do not take Ciprodex together with Tizanidine (a medicine used to treat muscle spasticity in multiple sclerosis), because this may cause side effects such as low blood pressure and sleepiness (see also section 2 "Do not use the medicine if").

The following medicines are known to interact with **Ciprodex**.
Taking **Ciprodex** together with these medicines can influence the therapeutic effect of those medicines and it can also increase the probability of experiencing side effects.
Tell your doctor if you are taking:
- vitamin K antagonists (e.g. warfarin, acenocoumarol, phenprocoumon or fluindione) or other oral anticoagulants (to thin the blood)
- probenecid (for gout)
- methotrexate (for certain types of cancer, psoriasis, rheumatoid arthritis)
- theophylline (for breathing problems)
- clozapine, olanzapine (an antipsychotic)
- ropinirole (for Parkinson's disease)
- phenytoin (for epilepsy)
- metoclopramide (for nausea and vomiting)
- ciclosporin (for skin conditions, rheumatoid arthritis and in organ transplantation)
- other medicines that can alter your heart rhythm: medicines that belong to the group of antiarrhythmics (e.g. quinidine, hydroquinidine, disopyramide, amiodarone, sotalol, dofetilide, ibutilide), tricyclic antidepressants, some antimicrobials (that belong to the group of macrolides), some antipsychotics
- zolpidem (for sleep disorders)
- a Non- Steroidal Anti - Inflammatory Drug (NSAID). Taking an NSAIDs while you take **Ciprodex** may increase your risk of central nervous system effects and seizures
- medicines to treat diabetes (such as glibenclamide)

Ciprodex may **increase** the levels of the following medicines in your blood:
- pentoxifylline (for circulatory disorders)
- caffeine
- duloxetine (for depression, diabetic nerve damage or incontinence)
- lidocaine (for heart conditions or anaesthetic use)
- sildenafil (e.g. for erectile dysfunction)
- agomelatine (for depression)

Some medicines **reduce** the effect of **Ciprodex**.
Tell your doctor if you take or wish to take:
- antacids
- omeprazole
- mineral supplements
- sucralfate (for ulcer)
- a polymeric phosphate binder (e.g. sevelamer or lanthanum carbonate)
- didanosine
- medicines or supplements containing calcium, magnesium, aluminum or iron

If these preparations are essential, take **Ciprodex** about two hours before or six hours after them.

Use of this medicine and food
Ciprodex should not be taken with dairy products (e.g. milk or yoghurt) or mineral-fortified drinks (e.g. calcium-fortified orange juice) alone, as they may affect the absorption of the active substance, but may be taken with a meal that contains them in addition to other products. Also see section 3 "How to use this medicine".

Pregnancy, breastfeeding and fertility
If you are pregnant or breastfeeding, think you may be pregnant, planning to have a baby or planning to breastfeed, consult your doctor or pharmacist for advice before taking this medicine.
It is preferable to avoid the use of **Ciprodex** during pregnancy.
Do not take **Ciprodex** during breastfeeding because the active ingredient is excreted in breast milk and can be harmful for your child.

Driving and use of machinery
Ciprodex may make you feel less alert and cause some neurological adverse effects. Therefore, make sure you know how you react to the medicine before driving a vehicle or operating machinery. If in doubt, consult a doctor.
As for children, they should be warned to be careful when riding a bicycle or playing near road etc.

Important information about some of the ingredients or this medicine
This medicine contains lactose. If you have been told by a doctor in the past that you are intolerant to certain sugars, consult a doctor before commencing treatment.
This medicine contains less than 1 mmol of sodium (23 mg) per caplet, that is to say essentially "sodium-free".

3. How to use this medicine?
Always use this medicine according to doctor's instructions. Check with the doctor or pharmacist if you are not sure about the dosage and manner of treatment. The dosage and administration will be determined by the doctor only.
The doctor will explain to you exactly how much **Ciprodex** you will have to take as well as how often and for how long. This will depend on the type of infection you have and how bad it is.
Tell your doctor if you suffer from kidney problems because your dose may need to be adjusted.
The treatment usually lasts from 5 to 21 days, but may take longer for severe infections.
Do not exceed the recommended dose.

Swallow the caplet with a full glass of water. Caplets can be halved/crushed. Do not chew the caplets since they are coated to mask the taste. Do try to take the medicine at around the same time every day.
You can take the medicine at mealtimes or between meals. **Do not take Ciprodex** with dairy products (e.g. milk or yoghurt) or with mineral-fortified juices (e.g. calcium-fortified orange juice) alone, as they may affect the absorption of the active substance, but **Ciprodex** may be taken with a meal that contains them in addition to other products. Also see section "Use of this medicine and food".
Drink plenty of water during treatment with the medicine.

If you have taken a higher dosage
If you have taken an overdose or if a child has accidentally swallowed the medicine, proceed immediately to a doctor or a hospital emergency room and bring the package of the medicine with you.

If you forget to take the medicine
If you forget to take **Ciprodex** and it is:
6 hours or more until the next dose, take the forgotten dose as soon as you remember. Take the next dose as usual.
Less than 6 hours until the next dose, do not take the forgotten dose. Take the next dose as usual.
Do not take a double dose to make up for a forgotten dose.
Continue with the treatment as recommended by your doctor.

If you stop taking the medicine
Even if there is improvement in your health, do not stop the treatment of this medicine without consulting the doctor.
It is important that you finish the course of treatment, even if you begin to feel better after a few days. If you stop taking this medicine too soon, your infection may not be completely cured and the symptoms of the infection may return or get worse. You might also develop resistance to the antibiotic.

Do not take medicines in the dark! Check the label and the dose each time you take a medicine. Wear glasses if you need them. If you have any further questions regarding the use of this medicine, consult your doctor or pharmacist.

4. Side effects

Like any medicine, the use of **Ciprodex** may cause side effects, in some users. Do not be alarmed while reading the list of side effects. You may not suffer from any of them.
The following section contains the most serious side effects that you can recognize yourself:
Stop taking Ciprodex and contact your doctor immediately in order to consider another antibiotic treatment if you notice any of the following serious side effects:

Rare side effects (effects which appear in 1-10 out of 10,000 users):
Seizure (see in section 2 "Special warning regarding the use of this medicine")

Very rare side effects (effects which appear in less than one out of 10,000 users):
- Severe, sudden allergic reaction with symptoms such as tightness in the chest, feeling dizzy, sick or faint, or experience dizziness when standing up (anaphylactic reaction/shock) (see in section 2 "Special warning regarding the use of this medicine").
- Muscle weakness, inflammation of the tendons which could lead to rupture of the tendon, particularly affecting the large tendon at the back of the ankle (Achilles tendon) (see in section 2 "Special warning regarding the use of this medicine").

- A serious life-threatening skin rash, usually in the form of blisters or ulcers in the mouth, throat, nose, eyes and other mucous membranes such as genitals which may progress to widespread blistering or peeling of the skin (Stevens-Johnson syndrome, toxic epidermal necrolysis).

Side effects with an unknown frequency (effects for which frequency has not yet been determined)
- Unusual feelings of pain, burning, tingling, numbness or muscle weakness in the extremities (neuropathy) (see in section 2 "Special warning regarding the use of this medicine").
- A drug reaction that causes rash, fever, inflammation of internal organs, hematologic abnormalities and systemic illness [DRESS (Drug Reaction with Eosinophilia and Systemic Symptoms), AGEP (Acute Generalised Exanthematous Pustulosis)].

Other side effects
Common side effects (effects which appear in 1-10 out of 100 users):
- nausea, diarrhoea
- joint pain and joint inflammation in children

Uncommon side effects (effects which appear in 1-10 out of 1,000 users):
- joint pain in adults
- fungal superinfections
- a high concentration of eosinophils, (a type of white blood cell)
- decreased appetite
- hyperactivity or agitation
- headache, dizziness, sleeping problems or taste disorders
- vomiting, abdominal pain, digestive problems such as stomach upset (indigestion/heartburn), or wind
- increased amounts of certain substances in the blood (transaminases and/or bilirubin)
- rash, itching or hives
- poor kidney function
- pains in your muscles and bones, feeling unwell (asthenia) or fever
- increase in blood alkaline phosphatase (a certain substance in the blood)

Rare side effects (effects which appear in 1-10 out of 10,000 users):
- muscle pain, inflammation of the joints, increased muscle tone and cramping
- inflammation of the bowel (colitis) linked to antibiotic use (can be fatal in very rare cases) (see in section 2 "Special warning regarding the use of this medicine")
- changes to the blood count (leukopenia, leukocytosis, neutropenia, anaemia), increased or decreased amounts of a blood clotting factor (thrombocytes)
- allergic reaction, swelling (oedema) or rapid swelling of the skin and mucous membranes (angio-oedema) (see in section 2 "Special warning regarding the use of this medicine")
- increased blood sugar (hyperglycaemia)
- decreased blood sugar (hypoglycaemia) (see in section 2 "Special warning regarding the use of this medicine")
- confusion, disorientation, anxiety reactions, strange dreams, depression (potentially leading to thoughts of suicide, suicide attempts or completed suicide) (see in section 2 "Special warning regarding the use of this medicine") or hallucinations
- pins and needles, unusual sensitivity to stimuli of the senses, decreased skin sensitivity, tremors or giddiness
- eyesight problems including double vision (see in section 2 "Special warning regarding the use of this medicine")
- tinnitus, loss of hearing, impaired hearing

- rapid heartbeat (tachycardia)
- expansion of blood vessels (vasodilation), low blood pressure or fainting
- shortness of breath, including asthmatic symptoms
- liver disorders, jaundice (cholestatic icterus) or hepatitis
- sensitivity to light (see in section 2 "Special warning regarding the use of this medicine")
- kidney failure, blood or crystals in the urine, urinary tract inflammation.
- fluid retention or excessive sweating
- increased levels of the enzyme amylase

Very rare side effects (effects which appear in less than one out of 10,000 users):
- a special type of reduced red blood cell count (haemolytic anaemia); a dangerous drop in a type of white blood cells (agranulocytosis) (see in section 2: "Special warning regarding the use of this medicine"); a drop in the number of red and white blood cells and platelets (pancytopenia), which may be fatal; and bone marrow depression, which may also be fatal
- allergic reaction called serum sickness-like reaction (see in section 2: "Special warning
- regarding the use of this medicine")
- mental disturbances (psychotic reactions potentially leading to thoughts of suicide, suicide attempts or completed suicide) (see in section 2: "Special warning regarding the use of this medicine")
- migraine, disturbed coordination, unsteady walk (gait disturbance), disorder of sense of smell (olfactory disorders), pressure on the brain (intracranial pressure and pseudotumor cerebri)
- visual colour distortions
- inflammation of the wall of the blood vessels (vasculitis)
- pancreatitis
- death of liver cells (liver necrosis) very rarely leading to life-threatening liver failure (see in section 2: "Special warning regarding the use of this medicine")
- small, pin-point bleeding under the skin (petechiae); various skin eruptions or rashes
- worsening of the symptoms of myasthenia gravis (see in section 2: "Special warning regarding the use of this medicine")

Side effects with an unknown frequency (effects for which frequency has not yet been determined)
- syndrome associated with impaired water excretion and low levels of sodium (SIADH)
- feeling highly excited (mania) or feeling great optimism and overactivity (hypomania)
- abnormal fast heart rhythm, life-threatening irregular heart rhythm, alteration of the heart rhythm (called ‘prolongation of QT interval’, seen on ECG, electrical activity of the heart)
- influence on blood clotting (in patients treated with Vitamin K antagonists)
- loss of consciousness due to severe decrease in blood sugar levels (hypoglycaemic coma). See section 2.

Very rare cases of long lasting (up to months or years) or permanent adverse drug reactions, such as tendon inflammations, tendon rupture, joint pain, pain in the limbs, difficulty in walking, abnormal sensations such as pins and needles, tingling, tickling, burning, numbness or pain (neuropathy), depression, fatigue, sleep disorders, memory impairment, as well as impairment of hearing, vision, and taste and smell have been associated with administration of quinolone and fluoroquinolone antibiotics, in some cases irrespective of preexisting risk factors.

Cases have been reported of enlargement and weakness of the aortic wall or a tear in the aortic wall (aneurysm and dissection), which may tear and become lethal, and cases of heart valve leak in patients taking fluoroquinolones. Also see section 2.

If a side effect appears, if one of the side effects worsens or if you suffer from any side effect which is not mentioned in this leaflet, consult the doctor.

Side effects can be reported to the Ministry of Health via the link
" דיווח על תופעות לוואי עקב טיפול תרופתי" that can be found on the homepage of the Ministry of Health website (www.health.gov.il) directing to the online form of adverse events reporting or via the following link: https://sideeffects.health.gov.il

5. How to store the medicine?

- Avoid poisoning! This medicine and any other medicine must be stored in a closed place out of the reach and sight of children and/or infants to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by your doctor.
- Do not use the medicine after the expiry date (תאריך תפוגה) stated on the package. The expiry date refers to the last day of that month.
- **Storage conditions:** store at a temperature below 25°C.
- Do not throw away any medicines via wastewater or household waste. Ask the pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Additional information

In addition to the active ingredient, this medicine also contains:
Lactose monohydrate, sodium starch glycolate, povidone, hypromellose, titanium dioxide, sodium stearyl fumarate, macrogol 400.

What the medicine looks like and what the package contains
White to off - white biconvex caplet, scored on both sides.
Approved package sizes include 2, 5, 7, 10, 14, 20 caplets. Not all package sizes may be marketed.

Revised in July 2023 according to MOH guidelines.
Drug registration number at the national medicines registry of the Ministry of Health:
123 60 30428 00

Manufacturer and registration holder: Dexcel Ltd., 1 Dexcel St., Or Akiva 3060000, Israel