

PACKAGE LEAFLET: INFORMATION FOR THE USER

Cifox 2mg/ml Solution for Infusion

Ciprofloxacin (as hydrochloride)

Read all of this leaflet carefully before you start taking 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.
- 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 Cifox is and what it is used for
2. What you need to know before you use Cifox
3. How to use Cifox
4. Possible side effects
5. How to store Cifox
6. Contents of the pack and other information

1 What Cifox is and what it is used for

Cifox 2mg/ml Solution for Infusion contains the active substance ciprofloxacin. Ciprofloxacin is an antibiotic belonging to the fluoroquinolone family. Ciprofloxacin works by killing bacteria that cause infections. It only works with specific strains of bacteria.

Adults

Cifox is used in adults to treat the following bacterial infections:

- respiratory tract infections
- long lasting or recurring ear or sinus infections
- urinary tract infections
- infections of the testicles
- genital organ infections in women
- gastro-intestinal tract infections and intra-abdominal infections
- skin and soft tissue infections
- bone and joint infections
- to treat infections in patients with a very low white blood cell count (neutropenia)
- to prevent infections in patients with a very low white blood cell count (neutropenia)
- anthrax inhalation exposure

If you have a severe infection or one that is caused by more than one type of bacterium, you may be given additional antibiotic treatment in addition to Cifox.

Children and adolescents

Cifox is used in 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

Cifox may also be used to treat other specific severe infections in children and adolescents when your doctor considers this necessary.

2 What you need to know before you use Cifox

You must not be given Cifox if you are:

- allergic to ciprofloxacin, to other quinolone drugs or to any of the other ingredients of this medicine (listed in section 6)
- taking tizanidine (see Section 2: Taking other medicines)

Warnings and precautions

Talk to your doctor before using Cifox if you:

- have ever had kidney problems because your treatment may need to be adjusted
- suffer from epilepsy or other neurological conditions
- have a history of tendon problems during previous treatment with antibiotics such as Cifox
- have myasthenia gravis (a type of muscle weakness)
- have heart problems

Caution should be taken when using this kind of medicine, if you were born with or have family history of prolonged QT interval (seen on ECG, electrical recording of the heart), have salt imbalance in the blood (especially low levels of potassium or magnesium in the blood), have a very slow heart rhythm (called 'bradycardia'), have a weak heart (heart failure), 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 *Taking other medicines*).

While under treatment with Cifox

Tell your doctor immediately, if any of the following occurs **during treatment with Cifox**. Your doctor will decide whether treatment with Cifox needs to be stopped.

- **Severe, sudden allergic reaction** (an anaphylactic reaction/shock, angio-oedema). Even with the first dose, there is a rare chance that you may experience a severe allergic reaction with the following symptoms: tightness in the chest, feeling dizzy, feeling sick or faint, or experience dizziness on standing.

If this happens, tell your doctor immediately since the administration of Cifox will have to be stopped.

- **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 stop taking Cifox and rest the painful area. Avoid any unnecessary exercise as this might increase the risk of a tendon rupture.
- 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 Cifox and contact your doctor immediately.
- You may experience **psychiatric reactions** after first administration of ciprofloxacin. If you suffer from **depression** or **psychosis**, your symptoms may become worse under treatment with Cifox. If this happens, stop taking Cifox 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 Cifox and contact your doctor immediately.
- **Diarrhoea** may develop while you are on antibiotics, including Cifox, or even several weeks after you have stopped using them. If it becomes severe or persistent or you notice that your stools

contain blood or mucus, tell your doctor immediately. Cifox treatment will have to be stopped immediately, as this can be life-threatening.

Do not take medicines that stop or slow down bowel movements.

- Tell the doctor or laboratory staff that you are taking Cifox if you have to provide a **blood or urine sample**.
- Cifox 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, Cifox must be stopped immediately.
- Cifox 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 anaemia with ciprofloxacin.
- Your skin becomes more **sensitive to sunlight or ultraviolet (UV) light** under treatment with ciprofloxacin. Avoid exposure to strong sunlight or artificial UV light such as sunbeds.

Other medicines and Cifox

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines, including medicines obtained without a prescription.

You must tell your doctor if you are taking other medicines that can alter your heart rhythm: medicines that belong to the group of anti-arrhythmics (e.g. quinidine, hydroquinidine, disopyramide, amiodarone, sotalol, dofetilide, ibutilide), tricyclic antidepressants, some antimicrobials (that belong to the group of macrolides), some antipsychotics.

Do not use Cifox together with tizanidine, because this may cause side effects such as low blood pressure and sleepiness (see Section 2: "**You must not be given Cifox if you are:**").

The following medicines are known to interact with Cifox in your body. Using Cifox together with these medicines can influence the therapeutic effect of these medicines. It can also increase the probability of experiencing side effects.

Tell your doctor if you are taking:

- warfarin or other oral anti-coagulants (to thin the blood)
- probenecid (for gout)
- methotrexate (for certain types of cancer, psoriasis, rheumatoid arthritis)
- theophylline (for breathing problems)
- tizanidine (for muscle spasticity in multiple sclerosis)
- clozapine (an antipsychotic)
- ropinirole (for Parkinson's disease)
- phenytoin (for epilepsy)
- metoclopramide (for nausea)
- ciclosporin (medicine used to prevent rejection)
- omeprazole (for stomach ulcers)
- sildenafil (for erectile problems)
- glibenclamide (for diabetes)

- duloxetine (for mood disorders)
- lidocaine (local pain reliever)
- medicines known to prolong the QT-interval

Cifox may **increase** the levels of the following medicines in your blood:

- pentoxifylline (for circulatory disorders)
- caffeine

Cifox with food and drink

Food and drink do not affect your treatment with Cifox.

Pregnancy and breast-feeding

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

It is preferable to avoid the use of Cifox during pregnancy. Tell your doctor if you are planning to get pregnant. Do not take Cifox during breast-feeding because ciprofloxacin is excreted in breast milk and can be harmful for your child.

Driving and using machines

Cifox may make you feel less alert. Some neurological adverse events can occur. Therefore, make sure you know how you react to Cifox before driving a vehicle or operating machinery. If in doubt, talk to your doctor.

Cifox contains sodium

This medicinal product contains 0.154mmol or 3.54mg sodium per ml. The 50ml bottle contains 7.7mmol sodium (equivalent to 177mg sodium, 450mg sodium chloride).

The 100ml bottle contains 15.4mmol sodium (equivalent to 354mg sodium, 900mg sodium chloride) and the 200ml bottle contains 31mmol sodium (equivalent to 708mg sodium, 1800mg sodium chloride). To be taken into consideration by patients on a controlled sodium diet.

3 How to use Cifox

Your doctor will explain to you exactly how much Cifox you will be given 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.

Treatment usually lasts between 3 and 21 days, but may be longer for severe infections.

Your doctor will give you each dose by slow infusion through a vein into your bloodstream. For children, the infusion duration is 60 minutes. In adult patients, infusion time is 60 minutes for 400mg Cifox and 30 minutes for 200mg Cifox. Administering the infusion slowly helps prevent immediate side effects occurring.

Remember to drink plenty of fluids while you are taking Cifox.

If you stop your course of Cifox

It is important that you **finish the course of treatment** even if you begin to feel better after a few days. If you stop using 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.

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

4 Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Common: may affect up to 1 in 10 people

- nausea, diarrhoea, vomiting
- joint pain in children
- local reaction at the injection site, rash
- temporary increased amounts of substance in the blood (transaminases)

Uncommon: may affect up to 1 in 100 people

- fungal superinfections
- a high concentration of eosinophils, a type of white blood cell, increased or decreased amounts of a blood clotting factor (thrombocytes)
- loss of appetite (anorexia)
- hyperactivity, agitation, confusion, disorientation, hallucinations
- headache, dizziness, sleeping problems, taste disorders, pins and needles, unusual sensitivity to stimuli of the senses, seizures (see Section 2: Take special care with Cifox), giddiness
- eyesight problems
- loss of hearing
- rapid heartbeat (tachycardia)
- expansion of the blood vessels (vasodilation), low blood pressure
- abdominal pain, digestive problems such as stomach upset (indigestion/heartburn), wind
- liver disorders, increased amounts of one substance in the blood (bilirubin), jaundice (cholestatic icterus)
- itching, hives
- joint pain in adults
- poor kidney function, kidney failure
- pains in your muscles and bones, feeling unwell (asthenia), fever, fluid retention
- increase in blood alkaline phosphatase (a certain substance in the blood)

Rare: may affect up to 1 in 1,000 people

- inflammation of the bowel (colitis) linked to antibiotic use (can be fatal in rare cases) (see Section 2: Take special care with Cifox)
- changes to the blood count (leukopenia, leukocytosis, neutropenia, anaemia), a drop in the number of red and white blood cells and platelets (pancytopenia), which may be fatal, bone marrow depression which may also be fatal (see Section 2: Take special care with Cifox)
- allergic reaction, allergic swelling (oedema), rapid swelling of the skin and mucous membranes (angiooedema), severe allergic reaction (anaphylactic shock) which can be life-threatening (see Section 2: Take special care with Cifox)
- increased blood sugar (hyperglycemia)
- anxiety reaction, strange dreams, depression, mental disturbances (psychotic reactions) (see Section 2: Take special care with Cifox)
- decreased skin sensitivity, tremor, migraine, disorder of sense of smell (olfactory disorders)
- tinnitus, impaired hearing
- fainting, inflammation of the blood vessel (vasculitis)
- shortness of breath including asthmatic symptoms
- pancreatitis
- hepatitis, death of liver cells (liver necrosis) very rarely leading to life-threatening liver failure
- sensitivity to light (see Section 2: Take special care with Cifox), small, pin-point bleeding under the skin (petechiae)
- muscle pain, inflammation of the joints, increased muscle tone, cramping, tendon rupture – especially of the large tendon at the back of the ankle (Achilles tendon) (see Section 2: Take special care with Cifox)
- blood or crystals in the urine (see Section 2: Take special care with Cifox), urinary tract inflammation
- excessive sweating

- abnormal levels of a clotting factor (prothrombin) increased levels of the enzyme amylase

Very rare: may affect up to 1 in 10,000 people

- a special type of reduced red blood cell count (haemolytic anaemia); a dangerous drop in a type of white blood cells (agranulocytosis)
- severe allergic reaction (anaphylactic reaction, anaphylactic shock, serum sickness) which can be fatal (see Section 2: Take special care with Cifox)
- mental disturbances (psychotic reactions) (See section 2: Take special care with Cifox)
- disturbed coordination, unsteady walk (gait disturbance), pressure on the brain (intracranial pressure)
- visual colour distortions
- various skin eruptions or rashes (e.g. the potentially fatal Stevens-Johnson syndrome or toxic epidermal necrolysis)
- muscle weakness, tendon inflammation, worsening of the symptoms of myasthenia gravis (see Section 2: Take special care with Cifox)

Not known: frequency cannot be estimated from the available data

- troubles associated with the nervous system such as pain, burning, tingling, numbness and/ or weakness in extremities
- 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)
- increase in international normalised ratio (INR) in patients taking Vit K antagonists

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly (see details below). By reporting side effects you can help provide more information on the safety of this medicine.

IRELAND: FREEPOST, Pharmacovigilance Section, Irish Medicines Board, Kevin O'Malley House, Earlsfort Centre, Earlsfort Terrace, Dublin 2, Ireland

Tel: +353 1 6764971, Fax: +353 1 6762517 Website: www.imb.ie
e-mail: imbpharmacovigilance@imb.ie

5 How to store Cifox

Keep this medicine out of the sight and reach of children

Keep bottle in the outer carton in order to protect from light. There are no special precautions required during administration.

Your doctor or hospital pharmacist (chemist) will store Cifox appropriately prior to use. Do not refrigerate or freeze. At cool storage conditions precipitation may occur which will re-dissolve at room temperature and does not affect the product.

After opening:

Use immediately. Discard any unused solution.

Do not use this medicine after the expiry date which is stated on the carton and on the bottle after "EXP": The expiry date refers to the last day of that month.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6 Contents of the pack and other information

What Cifox contains

- The active substance is ciprofloxacin (as hydrochloride).
Each bottle with 50ml solution for infusion contains 100mg ciprofloxacin.
Each bottle with 100ml solution for infusion contains 200mg ciprofloxacin.
Each bottle with 200ml solution for infusion contains 400mg ciprofloxacin.
- The other ingredients are lactic acid, sodium chloride, sodium hydroxide, hydrochloric acid and water for injections.

What Cifox looks like and contents of the pack

It is available in clear glass Type 2 vials with rubber stopper and aluminium crimping cap containing 50ml, 100ml or 200ml of solution at a concentration of 2mg/ml. The appearance of the product is a clear, sterile aqueous solution with a pH 3.5 - 4.5.

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturers:

Marketing Authorisation Holder:

Rowex Ltd., Bantry, Co Cork, Ireland.

Manufacturers:

Salutas Pharma GmbH, Otto-von-Guericke Allee 1, D-39179 Barleben, Germany.

Lek Pharmaceuticals d.d., Verovškova 57, 1526 Ljubljana, Slovenia.

Rowa Pharmaceuticals Ltd., Bantry, Co Cork, Ireland.

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Advice/medical education

Antibiotics are used to cure bacterial infections. They are ineffective against viral infections. If your doctor has prescribed antibiotics, you need them precisely for your current illness. Despite antibiotics, some bacteria may survive or grow. This phenomenon is called resistance: some antibiotic treatments become ineffective. Misuse of antibiotics increases resistance. You may even help bacteria become resistant and therefore delay your cure or decrease antibiotic efficacy if you do not respect appropriate:

- dosage
- schedules
- duration of treatment

Consequently, to preserve the efficacy of this drug:

- 1 - Use antibiotics only when prescribed.
- 2 - Strictly follow the prescription.
- 3 - Do not re-use an antibiotic without medical prescription, even if you want to treat a similar illness.
- 4 - Never give your antibiotic to another person; maybe it is not adapted to her/his illness.
- 5 - After completion of treatment, return all unused drugs to your chemist's shop to ensure they will be disposed of correctly.

The following information is intended for healthcare professionals only:

Cifox Solution for Infusion should be administered by intravenous infusion. For children, the infusion duration is 60 minutes. In adult patients, infusion time is 60 minutes for 400mg ciprofloxacin and 30 minutes for 100mg and 200mg ciprofloxacin. Slow infusion into a large vein will minimise patient discomfort and reduce the risk of venous irritation. The infusion solution can be infused either directly or after mixing with other compatible infusion solutions. The product should not be mixed with other

drug products which are physically or chemically unstable at its pH of 3.5-4.5. However, Cifox has been shown to be compatible with 0.9% sodium chloride solution, Ringer's solution, Ringer lactate solution, 5% and 10 % glucose solution. Unless compatibility is proven, the infusion solution must always be administered separately. After intravenous initiation of treatment, the treatment can be continued orally as well.