Applicant: Ranbaxy Pharmaceuticals (Pty) Ltd
Product names: Ciprofloxacin 250/500 Tablets
Dosage form & Strength: Film-coated tablets - Ciprofloxacin hydrochloride equivalent to ciprofloxacin 250 mg / 500 mg per tablet

PATIENT INFORMATION LEAFLET

SCHEDULING STATUS: S4

CIFRAN 250 Tablets

CIFRAN 500 Tablets

Sugar free

Read all of this eaflet carefully before you start taking CIFRAN

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist, nurse or other health care provider.
- **CIFRAN** has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

What is in this leaflet

1. What **CIFRAN** is and what it is used for
2. What you need to know before you take **CIFRAN**
3. How to take **CIFRAN**
4. Possible side effects
5. How to store **CIFRAN**
6. Contents of the pack and other information

1. What CIFRAN is and what it is used for

CIFRAN are used in adults to treat severe and/or complicated bacterial infection of the lungs, bladder, gut (diarrhoea), bone, or skin and soft tissues where other antimicrobials used for similar infections were considered not to be an appropriate treatment option, have failed, cannot be used or are not tolerated.
It is also used to prevent you getting an infection caused by a bacterium called *Neisseria meningitides*.

2. What you need to know before you take CIFRAN

Do not take CIFRAN

- If you allergic (hypersensitive) to ciprofloxacin or to other antibiotics of the same type (called a quinolone), or any of the other ingredients in these tablets (listed in section 6).
- If you have previously experienced side effects with the use of quinolone/fluoroquinolone antibiotics relating to your joints, muscles, ligaments, nerves, central nervous system (brain), epilepsy or mental health (psychiatric disorder).
- If you were born with or have any condition with abnormal heart rhythm whether related to QT time prolongation or not (seen on ECG, electrical recording of the heart).
- If you are taking other medicines that result in an abnormal heart rate and/or rhythm tracing (ECG) e.g. (prolongation of the “QT time”).
- If you have an enlargement or “bulge” of a large blood vessel (aortic aneurysm) or a previous episode of aortic dissection (a tear in the aortic wall) or a family history of aortic aneurysm/dissection or other risk factors or existing predisposing conditions).
- If you have myasthenia gravis (abnormal muscle fatigue leading to weakness and, in serious cases, paralysis).
- If you have confirmed mitral valve and /aortic valve (both names for valves in your heart) regurgitation unless no safer alternative antibiotic is available, has failed or is not well tolerated.
- If you are on treatment for high blood pressure with medicines called ACE inhibitors/angiotensin receptor blockers. Ask your doctor if you are unsure.
- If you are taking tizanidine (see Taking other medicines with CIFRAN).
- If you are pregnant, think you might be pregnant or are planning to have a baby or currently breastfeeding.
- **If you or your child are younger than 18 years.**

Warnings and precautions

Take special care with **CIFRAN**:

- Severe cutaneous adverse reactions (SCARs) including toxic epidermal necrolysis (TEN), Stevens Johnson syndrome (SJS) and drug reaction with eosinophilia and systemic symptoms (DRESS), which could be life-threatening or fatal, have been reported with **CIFRAN** (see Possible Side Effects). If signs and symptoms suggestive of these reactions appear which include skin rash, itching, peeling, crusting, severe blisters and bleeding in the lips, eyes, mouth, nose and genitals, **CIFRAN** should be discontinued immediately, and you must contact your doctor.
  If you developed a serious reaction such as SJS, TEN or DRESS with the use of **CIFRAN,** treatment with **CIFRAN** must not be restarted at any time.
- Severe, sudden allergic reaction may occur (even after the first dose) with the following symptoms: tightness in the chest, feeling dizzy, sick or faint. If this happens, stop taking **CIFRAN** and contact your doctor immediately.
- **CIFRAN** 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, stop taking **CIFRAN** and contact your doctor immediately.
- Pain and swelling in the joints and tendinitis may occur, particularly if you are elderly and also being treated with corticosteroids. Inflammation and ruptures of tendons may occur even within the first 48 hours of treatment or up to several months after discontinuing treatment with **CIFRAN**. At the first sign of any pain or inflammation stop taking **CIFRAN** and rest the painful area. Avoid any unnecessary exercise, as this might increase the risk of a tendon rupture (see Do not take **CIFRAN**).
- If you have myasthenia gravis (a type of muscle weakness) (see Do not take **CIFRAN**).
- If you have heart problems. Caution should be taken when using **CIFRAN** if you were born with or have family history of prolonged QT interval (seen on ECG); have salt imbalance in the blood (especially low level of potassium or magnesium); have a very slow heart rate; have a weak heart (heart failure); have a history of heart attack; you are female or elderly; or you are taking other medicines that result in abnormal ECG changes (see Do not take **CIFRAN** and Taking other medicines with **CIFRAN**).
- If you are currently taking other medicines that can reduce your blood potassium levels.
- If you have a family history of aortic aneurysm or aortic dissection or other risk factors or existing

predisposing conditions (e.g. connective tissue disorders such as Marfan Syndrome, Vascular Ehlers-Danlos syndrome, Takayasu arteritis, giant cell arteritis, Behcet's disease, high blood pressure or known atherosclerosis (see Do Not Take **CIFRAN**).

- If you have a damaged mitral and/or aortic heart valve which cannot close properly (see Do not take **CIFRAN**).
- If you have moderate to severe impairment of your kidney function, or if you are elderly and are treated with ACE inhibitors/angiotensin receptor blockers to control your blood pressure as this may cause further injury to your kidneys (see Do Not Take **CIFRAN**). Your kidney function will be checked before and during treatment if you are receiving fluoroquinolone antibiotics and ACE inhibitors/angiotensin receptor blockers to control your blood pressure.
- If you suffer from fits or epilepsy or have a history of convulsive disorders (see Do not take **CIFRAN**).
- If you suffer from neurological conditions such as cerebral ischaemia or stroke, you may experience side effects associated with the central nervous system. If this happens, stop taking **CIFRAN** and contact your doctor immediately (see Do not take **CIFRAN**).
- You may experience symptoms of neuropathy such as pain, burning, tingling, numbness and/or weakness. If this happens, stop taking **CIFRAN** and contact your doctor immediately (see Do not take **CIFRAN**).
- If you have or ever had kidney problems, because your dose may need to be adjusted.
- Crystals may be found in your urine. You should drink enough water and excessive alkalinity of the urine should be avoided.
- If you have diabetes, as you may experience change in blood sugar levels (low blood sugar / high blood sugar) if you have diabetes mellitus and are taking medication for the diabetes.
- Hypoglycaemia has been reported most often in diabetic patients, predominantly in elderly population. If this happens, contact your doctor immediately.
- 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 **CIFRAN**.
- If your eyesight becomes impaired or if your eyes seem to be otherwise affected, consult an eye

specialist immediately.

- If your skin becomes more sensitive to sunlight or ultraviolet (UV) light. Avoid exposure to strong sunlight, or artificial UV light such as sunbeds. If your skin becomes reddened, swollen, or blistered, like bad sunburn, call your doctor.

- **CIFRAN** may interfere with the interpretation of diagnostic culture tests for tuberculosis.
  Tell the doctor or laboratory staff that you are taking **CIFRAN** if you have to provide a blood or urine sample.

If the above applies to you or if you are not sure if any of the above applies to you, talk to your doctor before taking **CIFRAN**.

Other medicines and CIFRAN

Always tell your health care provider if you are taking any other medicine. (This includes all complementary or traditional medicines).

Do not take **CIFRAN** together with tizanidine(for muscle spasticity in multiple sclerosis), because this may cause side effects such as low blood pressure and sleepiness (see **Do not take CIFRAN**).

Do not take **CIFRAN** together with other medicines that can alter your heart rhythm: medicines that belong to the group of anti-arrhythmics (e.g. quinidine, procainamide, amiodarone and sotalol).

CIFRAN must not be used with other medicines known to have this effect (such as antihistamines, astemizole and terfenadine, cisapride, erythromycin, pentamidine, phenothiazines, or tricyclic antidepressants).

Do not take **CIFRAN** if you are on treatment with ACE inhibitors/angiotensin receptor blockers used to control your blood pressure as this may lead to acute kidney injury (see **Do not take CIFRAN**). Ask your doctor if you are not sure.

The following medicines are known to interact with **CIFRAN** in your body. Taking **CIFRAN** together with these medicines can influence the therapeutic effect of those medicines. It can also increase the probability of experiencing side effects. Ask your doctor or pharmacist for advice before taking any of the following medicines.

CIFRAN can increase the level of the following medicines in the blood:

- theophylline (for breathing problems)
- clozapine (an antipsychotic)
- ropinirole (for Parkinson's disease)
- agomelatine
- zolpidem (for insomnia)
- xanthine derivatives such as pentoxifylline (for circulatory disorders) or caffeine
- duloxetine (for depression, diabetic nerve damage or incontinence)
- lidocaine (for heart conditions or anaesthetic use)
- sildenafil (for erectile dysfunction)

Medicines which reduce the uptake of **CIFRAN**:

- sucralfate (used to treat heartburn, indigestion or ulcers in the stomach or intestines)
- antacids (used to treat indigestion)
- highly buffered medicines such as anti-retrovirals (used to treat HIV)
- a polymeric phosphate binder such as sevelamer, lanthanum carbonate (to lower the level of phosphates in patients with kidney problems)
- medicines or dietary supplements containing calcium, magnesium, aluminium or iron.

If these medicines are essential, take **CIFRAN** about two hours before or no sooner than four hours after them.

- NSAIDs (Non-steroidal anti-inflammatory drugs)-medicines for pain relief: Taking NSAIDs, such as fenbuten, with **CIFRAN** may increase the chance of seizures.
- Ciclosporin (used to treat psoriasis, dermatitis, rheumatoid arthritis and in organ transplantation): Transient increases in serum creatinine concentrations.
- Vitamin K antagonists (e.g. warfarin, acenocoumarol phenprocoumon or fluindione) or other oral anti-coagulants (used to thin the blood):

  CIFRAN can intensify the action of these medicines.
- Glibenclamide (for diabetes):**CIFRAN** can intensify the action of glibenclamide (leading to

hypoglycaemia).

- Probenecid (for gout): Use of probenecid and **CIFRAN** increases the ciprofloxacin serum concentrations.
- Metoclopramide (for nausea and vomiting) : Accelerates absorption of **CIFRAN**
- Methotrexate (for certain types of cancer, psoriasis, rheumatoid arthritis):
- Concurrent administration with methotrexate may increase the concentration of methotrexate to toxic levels.
- Phenytoin (used to treat epilepsy): Altered (decreased or increased) serum levels of phenytoin were observed leading to loss of seizure control with decreased levels or overdose related side effects with increased levels.

CIFRAN with food or drink

CIFRAN should be swallowed whole with plenty of liquid and may be taken with or without food.

Do not eat or drink any dairy products (such as milk, yoghurt or cheese) or drinks with added calcium when you take the tablets, as they may affect the absorption of **CIFRAN** and may not work properly.

Pregnancy and breastfeeding

You should not use CIFRAN during pregnancy or when breastfeeding your baby.

If you are pregnant or breastfeeding your baby, think you may be pregnant or are planning to have a baby, please consult your doctor, pharmacist or other health care provider for advice before taking this medicine .

Driving and using machines

CIFRAN may make you feel less alert and some neurological side effects can occur, which may impair the ability to drive or to operate machinery, especially when taken with alcohol. Therefore, make sure you know how you react to **CIFRAN** before driving a vehicle or operating machinery.

3. How to take CIFRAN

Do not share medicines prescribed for you with any other person.

Always take or give **CIFRAN** exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are unsure.

CIFRAN should be swallowed whole with plenty of liquid and may be taken with or without food.

Your doctor will decide on the duration of treatment. Your doctor will explain to you exactly how much **CIFRAN** you will have to take as well as how often and for how long.

This will depend on the type and severity of infection you have.

The usual treatment period is 5 to 10 days.

For severe and complicated infections more prolonged therapy may be required.

The dose range is 250 – 750 mg twice daily.

The tablet must be swallowed whole with plenty of liquid and may be taken with or without meals.

• *Severe and/ or complicated infections of the lower respiratory tract:*

750 mg twice daily

• *Severe and/ or complicated infection of the urinary tract:*

500 mg twice daily

• *Severe and/ or complicated infections of the skin and bone infections:*

750 mg twice daily

For the prophylaxis of invasive infections of *Neisseria meningitides,* take one single dose of 500 mg.

Elderly

Elderly patients should receive a dose as low as possible depending on the severity of their illness and how well their kidneys are working.

Tell your doctor if you suffer from kidney problems because your dose may need to be adjusted.

Do try to take the tablets at around the same time every day.

It is best to take **CIFRAN** at least 2 hours before or 4 hours after magnesium/aluminium antacids, polymeric phosphate binders (for example, sevelamer, lanthanum carbonate), sucralfate, or other products containing calcium, iron or zinc

If you have the impression that the effect of **CIFRAN** is too strong or too weak, talk to your doctor or

pharmacist.

If you have taken CIFRAN TABLETS than you should

In the event of overdosage, consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison control centre. Take this leaflet or some tablets with you so your doctor will know what you have taken.

If you forget to take CIFRAN

If you forget to take **CIFRAN** at the right time, take them as soon as you remember. However, if it is almost time for your next dose, do not take the missed dose and continue as usual. Do not take a double dose to make up for forgotten individual doses. Be sure to complete your course of treatment.

If you stop taking CIFRAN

It is important to take or give the full course of treatment even if you begin to feel better after a few days. If you stop taking **CIFRAN** 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 **CIFRAN**, ask your doctor or pharmacist.*

4. Possible side effects

CIFRAN can have side effects.

Not all side effects reported for **CIFRAN** are included in this leaflet. Should your general health worsen, or if you experience any untoward effects while taking **CIFRAN**, please consult your health care provider for advice.

If any of the following happens, stop taking **CIFRAN** and tell your doctor immediately or go to the casualty department at your nearest hospital:

- Swelling of the face, lips, tongue, throat and airways (breathing tubes), difficult breathing, blueness of the skin, low blood pressure, heart failure and can result in death;
- rare skin condition with severe blisters and bleeding in the lips, eyes, mouth, nose and genitals (Stevens-Johnson syndrome or toxic epidermal necrolysis or erythema multiforme or exfoliative dermatitis or drug reaction with rash, fever, inflammation of internal organs, haematologic abnormalities (including increased white blood cells (eosinophilia) and liver enzymes) and systemic illness (Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS).

These are all **very serious** side effects. If you have them you may have had a **serious allergic reaction** or other type of reaction to **CIFRAN**. You may need medical attention or hospitalisation immediately.

Tell your doctor immediately or go to the casualty department at your nearest hospital if you notice any of the following:

- Sudden severe pain in your chest, abdomen (tummy) or back;
- mitral valve and/or aortic valve regurgitation
- inflammation of the bowel (colitis) linked to antibiotic use (can be fatal in very rare cases), perforation of the bowel, bleeding from the bowel;
- liver disorders, yellowing of the skin and/or eyes, also called jaundice, hepatitis;
- death of liver cells (liver necrosis), very rarely leading to life-threatening liver failure;
- poor kidney function, kidney failure, blood or crystals in the urine;
- rapid heartbeat (tachycardia);
- muscle weakness, tendon inflammation, tendon rupture, pain, tear and inflammation of tendons including the back of the ankle (Achilles), shoulder, hand, or other tendon sites
- bleeding problems;
- a special type of reduced red blood cell count (haemolytic anaemia symptoms are tiredness, headaches, being short of breath when exercising);
- high blood pressure in the brain leading to blurred vision (intracranial pressure);
- pain, burning, tingling, numbness and/or weakness in extremities (peripheral neuropathy and

polyneuropathy);

- tremors, fits, or giddiness;
- self-endangering behaviour (psychotic reactions potentially leading to thoughts of suicide, suicide attempts, or completed suicide);
- increased blood sugar (hyperglycaemia) or decreased blood sugar (hypoglycaemia);
- 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).

These are all serious side effects. You may need urgent medical attention.

Tell your doctor if you notice any of the following:

Frequent:

- nausea;
- diarrhoea.

Less frequent:

- headache, migraine, dizziness, sleeping problems, or taste disorders, bad taste, lethargy, weakness, trembling, nervousness, sweating, disturbed coordination, unsteady walk (gait disturbance), disorder of sense of smell (olfactory disorders);
- agitation, anxiety, strange dreams, confusion, disorientation, feeling low (depression), an altered and unreal perception of oneself (hallucinations);
- buzzing, hissing, whistling, ringing or other persistent noise in the ears (tinnitus), loss of hearing, spinning movement;
- eyesight problems, visual colour distortions, eye pain, rapid involuntary movements of the eyes, double vision;
- vomiting, abdominal pain, indigestion, wind, decreased appetite;
- rash, red raised skin rash, itching, or hives, dry skin, sweating, blistering rash, flushing;
- skin condition characterised by tender red nodules on the shins and legs (erythema nodosum);
- joint pain, joint swelling, swelling of tendons and synovial joint
- fungal super infections, thrush;

- pains in your muscles and bones, weakness, increased muscle tone and cramping, feeling unwell, or fever, chills
- small, pin-point bleeding under the skin (petechiae);
- increased reactivity of skin to sunlight (photosensitivity);
- inflammation of the wall of the blood vessels (vasculitis);
- pancreatitis;
- expansion of blood vessels (vasodilation), low blood pressure, or fainting.

Frequency unknown:

- feeling highly excited (mania) or feeling great optimism and overactivity (hypomania);
- hypersensitivity reaction called Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS)

Laboratory Test Abnormalities

- abnormal liver function tests (increase in transaminases, bilirubin, blood alkaline phosphatase);
- presence of renal casts, crystals in the urine;
- increase in blood sugar level;
- changes to the blood cell count (leukopenia, leukocytosis, pancytopenia, neutropenia, anaemia, eosinophilia, increased or decreased amounts of platelets), abnormal levels of a clotting factor (prothrombin), increase or decrease in thrombocytes (thrombocytosis or thrombocytopenia), bone marrow suppression.

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

Reporting of side effects

If you get side effects, talk to your doctor, pharmacist or nurse. You can also report side effects to SAHPRA via the "**6.04 Adverse Drug Reaction Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8. By reporting side effects, you can help provide more information on the safety of **CIFRAN**.

5. How to store CIFRAN

Store all medicines out of reach of children.

Store at or below 25 °C, protected from moisture.

Do not take **CIFRAN** after the expiry date stated on the pack. The expiry date refers to the last day of that month.

Return all unused medicine to your pharmacist. Do not dispose of unused medicines in drains or sewerage systems (e.g. toilets).

6. Contents of the pack and other information

What CIFRAN contain

The active substance is ciprofloxacin.

CIFRAN250 Tablets: Each film coated tablet contains ciprofloxacin hydrochloride equivalent to 250 mg ciprofloxacin.

CIFRAN 500 Tablets: Each film coated tablet contains ciprofloxacin hydrochloride equivalent to 500 mg ciprofloxacin.

The other ingredients in **CIFRAN** are: colloidal anhydrous silica, magnesium stearate, maize starch, microcrystalline cellulose, sodium starch glycollate, purified talc and film coating: opadry white.

Sugar free

What CIFRAN looks like and contents of the pack

CIFRAN250 Tablets: White, round, film-coated tablets debossed with `250' on one side and plain on the other side, with intact coating.

CIFRAN500 Tablets: White caplet shaped, film-coated tablets debossed with `500' on one side and plain on the other side, with intact coating.

Tablets are packed in a blister strip comprising of PVC film coated with PVdC and an aluminium foil backing. Cartons contain 10 tablets each.

Holder of Certificate of Registration

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TBA

Registration numbers

CIFRAN 250: 33/20.1.1/0365

CIFRAN 500: 33/20.1.1/0366

Botswana Only : S2 CIFRAN 250 Tablets: Reg. No: BOT 0400701 CIFRAN 500 Tablets: Reg. No BOT 0400702
Namibia Only: NS2 CIFRAN 250 Tablets: 04/20.1.1/0602 CIFRAN 500 Tablets: 04/20.1.1/0603