PATIENT INFORMATION LEAFLET

DIOF / DIOF DS SUSPENSION

Ofloxacin & Metronidazole Suspension (50mg/100mg and 100mg/200mg)

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, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. WHAT DIOF / DIOF DS IS AND WHAT IT IS USED FOR

DIOF / DIOF DS suspension contains **Ofloxacin** and **Metronidazole** which belongs to group of medicines called antibiotics.

It works by killing bacteria and parasites that cause infections in your body

DIOF / DIOF DS suspension is used for the treatment of diarrhea of mixed infection in adult patients only

2. WHAT YOU NEED TO KNOW BEFORE YOU TAKE DIOF / DIOF DS

Do not use DIOF / DIOF DS

- If you are allergic to ofloxacin or metronidazole, nitroimidazoles (e.g. tinidazole)
- Signs of an allergic reaction include: a rash, swallowing or breathing problems, swelling of your lips, face, throat or tongue.
- If you have previously had an allergic reaction to another quinolone antibiotic e.g. ciprofloxacin or norfloxacin.
- If you suffer from epilepsy or are at risk of fits.

- If you have a history of inflammation and swelling of the tendons (tendonitis) which can affect areas such as the wrist or the achilles tendon after treatment with a quinolone antibiotic e.g. ciprofloxacin, norfloxacin, or nadifloxacin.
- If you suffer from or there is a family history of glucose-6-phosphate dehydrogenase deficiency (an inherited disorder that affects the red blood cells)
- If you are pregnant, think you may be pregnant or are planning to have a baby.
- If you are breastfeeding.
- If you are under the age of 18 years, or are still growing.

Warnings and precautions

Ofloxacin

Before taking this medicine

You should not take fluoroquinolone/quinolone antibacterial medicines, including Ofloxacin, 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.

Talk to your doctor or pharmacist before taking **Ofloxacin** if any of the following apply:

- if you have been diagnosed with an enlargement or "bulge" of a large blood vessel (aortic aneurysm or large vessel peripheral aneurysm)
- if you have experienced a previous episode of aortic dissection (a tear in the aorta wall)
- if you have a family history of aortic aneurysm or aortic dissection or other risk factors or predisposing conditions (e.g. connective tissue disorders such as Marfan syndrome, or vascular Ehlers- Danlos syndrome, or vascular disorders such as Takayasu arteritis, giant cell arteritis, Behcet's disease, high blood pressure, or known atherosclerosis)
- If you feel sudden, severe pain in your abdomen, chest or back, go immediately to an emergency room.
- you have or have ever had a history of mental illness.
- you have problems with your liver or kidneys.
- you have heart disease or problems with your heartbeat.
- 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 level 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.
- you are taking other medicines that result in abnormal ECG changes.
- you have an illness of the nervous system called 'myasthenia gravis' (muscle weakness).
- if you are diabetic or suffer from low blood sugar.

During treatment

When taking this medicine

If your eyesight becomes impaired or if your eyes seem to be otherwise affected, consult an eye specialist immediately.

If you:

- experience a severe skin rash or allergic reaction, or
- develop severe diarrhoea, (which may be bloody) with stomach pain and fever, or
- notice pain, tenderness, or restricted movement of the tendons, or
- notice numbness or tingling in the hands and feet

stop taking this medicine and talk to your doctor straight away.

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 of Ofloxacin therapy. At the first sign of pain or inflammation of a tendon (for example in your ankle, wrist, elbow, shoulder or knee), stop taking Ofloxacin, contact your doctor and rest the painful area. Avoid any unnecessary exercise as this might increase the risk of a tendon rupture.

You may rarely experience symptoms of nerve damage (neuropathy) such as pain, burning, tingling, numbness and/or weakness especially in the feet and legs or hands and arms. If this happens, stop taking Ofloxacin and inform your doctor immediately in order to prevent the development of potentially irreversible condition.

Prolonged, disabling and potentially irreversible serious side effects

Fluoroquinolone/quinolone antibacterial medicines, including Ofloxacin, 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 Ofloxacin, 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.

If you are not sure if any of the above apply to you, talk to your doctor or pharmacist before taking Ofloxacin.

Metronidazole

Talk to your doctor or pharmacist before taking Metronidazole if

- You suffer or have ever suffered from liver problems
- You have kidney problems and are having dialysis

- You suffer from a condition called porphyria (a blood disorder leading to abnormal sensitivity to sunlight and other problems)
- You have a disease of the nervous system
- You have intolerance to some sugars as this medicine contains lactose
- You have been prescribed this medicine for more than 10 days – your doctor may wish to carry out some tests and monitor you closely for development of side effects to your nervous system
- You are affected by Cockayne syndrome. Cases of severe liver toxicity/acute liver failure, including cases with a fatal outcome, in patients with Cockayne syndrome have been reported with product containing metronidazole. If you are affected by Cockayne syndrome, your doctor should also monitor your liver function frequently while you are being treated with metronidazole and afterwards.

Serious skin reactions including Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), acute generalised exanthematous pustulosis (AGEP) have been reported with the use of Metronidazole.

- SJS/TEN can appear initially as reddish target-like spots or circular patches often with central blisters on the trunk. Also, ulcers of the mouth, throat, nose, genitals and eyes (red and swollen eyes) can occur. These serious skin rashes are often preceded by fever and/or flu-like symptoms. The rashes may progress to widespread peeling of the skin and life- threatening complications or be fatal.
- AGEP appears at the initiation of treatment as a red, scaly widespread rash with bumps under the skin and blisters accompanied by fever. The most common location: mainly localised on the skin folds, trunk, and upper extremities.

The highest risk for occurrence of serious skin reactions is within one week, typically, within 48 hours after start of treatment. If you develop a serious rash or another of these skin symptoms, stop taking metronidazole and contact your doctor or seek medical attention immediately.

Tell your doctor immediately and stop taking metronidazole if you develop:

- Stomach pain, anorexia, nausea, vomiting, fever, malaise, fatigue, jaundice, dark urine, putty or mastic coloured stools or itching.

If you are not sure if any of the above apply to you, talk to your doctor or pharmacist before taking this medicine. Do this even if they have applied to you in the past.

Other medicines and DIOF / DIOF DS

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

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, (e.g. clomipramine, amitriptyline),
- some antimicrobials (that belong to the group of macrolides e.g. erythromycin, clarithromycin, azithromycin),
- some antipsychotics used to treat mental health conditions such as schizophrenia and bipolar disorder.

Tell your doctor if you are taking any of the following medicines:

- medicines or dietary supplements that contain iron (for anaemia) or zinc.
- sucralfate used for stomach ulcers.
- antacids used for indigestion that contain magnesium or aluminium.
- corticosteroids, used for treatment of inflammation and swelling or over-active immune system. These may increase the risk of you developing a tendon rupture.
- painkillers called non-steroidal anti-inflammatory drugs (NSAIDs) e.g. ibuprofen or diclofenac, or theophylline, used to treat asthma or chronic obstructive pulmonary disease as these could make you more prone to fits if taken with ofloxacin.
- glibenclamide, a medicine to control your blood sugar, as the amount of these medicines in the blood may increase and have a greater effect.
- drugs that may affect your kidney function e.g. cimetidine (used for stomach ulcers or indigestion), probenecid (used for gout) and methotrexate (used for rheumatism) as they can increase the level of ofloxacin in the blood.
- medicines to thin your blood, e.g. warfarin. Taking these with ofloxacin can increase the time it takes for your blood to clot.
- If you are taking didanosine (a medicine used to treat HIV infections), you should not take the chewable, buffered tablets until at least two hours after taking ofloxacin.
- water tablets (diuretics) such as furosemide.
- Medicines used to treat epilepsy (e.g. phenobarbital, phenytoin, primidone).
- Lithium (used to treat depression).
- Medicines used to treat cancer (e.g. busulfan, fluorouracil or mycophenolate).
- Disulfiram (used to treat alcohol addiction).
- Medicines used to treat stomach ulcers (e.g. cimetidine).
- Oestrogen contraceptives (known as ‘the pill’).
- Ciclosporin (used to prevent the rejection of organs after transplant).

This medicine should not be taken within two hours of taking iron or zinc tablets, antacids, or sucralfate, as these medicines can stop Ofloxacin from working properly.

If you are due to have urine tests for porphyrin (a pigment in the blood), or for opiates (strong painkillers), tell your doctor or nurse you are taking this medicine.

DIOF / DIOF DS with food and drink

Do not drink any alcohol while you are taking Metronidazole and for 48 hours after finishing your course. Drinking alcohol while using Metronidazole might cause unpleasant side effects

such as nausea (feeling sick), vomiting (being sick), stomach pain, hot flushes, very fast or uneven heartbeat (palpitations) and headache.

Pregnancy and breast-feeding

Do not take DIOF / DIOF DS if you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby. If you become pregnant while taking DIOF / DIOF DS, stop taking the medicine and contact your doctor immediately.

Driving and using machines

This medicine may make you feel drowsy, dizzy, confused or affect your vision, cause fits or hallucinations. Make sure you are not affected before you drive or operate machinery.

3. HOW TO USE DIOF / DIOF DS

Always take this medicine exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.

Dose of Ofloxacin is 15 mg/kg/day and that of Metronidazole is 30 mg/kg/day in two divided doses.

Geriatric Use

- Geriatric patients are at increased risk for developing severe tendon disorders including tendon rupture when being treated with a fluoroquinolone such as ofloxacin. This risk is further increased in patients receiving concomitant corticosteroid therapy. Tendinitis or tendon rupture can involve the Achilles, hand, shoulder, or other tendon sites and can occur during or after completion of therapy; cases occurring up to several months after fluoroquinolone treatment have been reported. Caution should be used when prescribing ofloxacin to elderly patients especially those on corticosteroids. Patients should be informed of this potential side effect and advised to discontinue ofloxacin and contact their healthcare provider if any symptoms of tendinitis or tendon rupture occur
- In elderly geriatric patients, monitoring for metronidazole associated adverse events is recommended. Decreased liver function in geriatric patients can result in increased concentrations of metronidazole that may necessitate adjustment of metronidazole dosage.

Pediatric Use

- Safety and effectiveness in pediatric patients and adolescents below the age of 18 years have not been established. Ofloxacin causes arthropathy (arthrosis) and osteochondrosis in juvenile animals of several species.
- Safety and effectiveness of metronidazole in pediatric patients have not been established, except for the treatment of amebiasis.

If you take more DIOF / DIOF DS than you should

If you take more dose than you should, Contact your doctor or nearest hospital casualty department immediately. Signs of an overdose include feeling or being sick, loss of appetite, diarrhoea, metallic taste, headache, dizziness, insomnia or drowsiness. You may become confused and dizzy or lose consciousness, you may have a seizure or fit.

If you forget to take DIOF / DIOF DS

Take the next dose as soon as you remember. However, if it is nearly time for the next dose, skip the missed dose. Do not take a double dose to make up for forgotten doses

If you stop taking DIOF / DIOF DS

Your doctor will tell you how long you need to take your medicine for. Do not suddenly stop taking this medicine without talking to your doctor first. If you stop, your infection may get worse again. If you feel the effect of your medicine is too weak or strong, do not change the dose yourself, but ask your doctor.

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

4. POSSIBLE SIDE EFFECTS

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

Ofloxacin

Stop taking Ofloxacin, tell your doctor or go to your nearest hospital casualty department straight away if you have any of the following serious side effects because you may need medical attention:

Uncommon (may affect up to 1 in 100 people):

- resistance of infection causing organisms to this treatment, (you may fail to respond to treatment)

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

- you have an allergic reaction. Such reactions may appear in the form of anaphylaxis (a severe form of allergic reaction) with symptoms such as:
    - severe skin rash
    - swelling of the face, lips, mouth, tongue or throat (angioedema)
    - anaphylactic shock (sudden wheezing, swelling of your lips, tongue and throat or body, rash, fainting or difficulties in swallowing)
- inflammation of the bowel, which may cause severe watery diarrhoea, which may have blood in it, possibly with stomach cramps and a high temperature
- swelling of the tendons with the following symptoms; pain, tenderness, sometimes restricted movement (tendonitis). This can lead to tendon rupture, especially of the large tendon at the back of the ankle (Achilles tendon). The risk of this occurring is increased if you are also taking corticosteroids e.g. prednisolone

- numbness or tingling in the hands and feet or being very sensitive to touch, numbness or weakness of the arms and legs
- blurred, double or altered colour vision. If your eyesight becomes impaired or if your eyes seem to be otherwise affected, consult an eye specialist immediately.

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

- a condition in which the amount of oxygen-carrying pigment (haemoglobin) in the blood is below normal or an illness resulting from the destruction of red blood cells with the following symptoms; feeling tired, faint, dizzy, being short of breath when exercising and having pale skin. These may be signs of anaemia or haemolytic anaemia.
- other blood disorders when the numbers of different types of cells in the blood may fall, which may cause fever, chills, sore throat, ulcers in the mouth and throat (leucopenia, agranulocytosis)
- fits (seizures)
- skin rash, which may blister, and looks like small targets (central dark spots surrounded by a paler area, with dark ring around the edge) (erythema multiforme)
- a widespread rash with blisters and skin peeling on much of the body surface (toxic epidermal necrolysis).
- narrowing, blockage or leakage of blood vessels, in exceptional cases leading to severe skin reactions and death of areas of the skin
- severe kidney problems, which may result in your kidneys stopping working. Signs may include a rash, high temperature, general aches and pains, or blood in the urine
- hearing problems or hearing loss
- liver problems, such as inflammation of the liver (hepatitis) or blockage in the bile duct, that may cause your eyes or skin to go yellow (jaundice) or you may notice the following symptoms; nausea, vomiting, loss of appetite, feeling generally unwell, fever, itching, light coloured bowel motions, dark coloured urine

Not known (frequency cannot be estimated from the available data):

- 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)
- severe depression or mental illness. Some people who are depressed think of harming or killing themselves.
- a serious reduction in all types of blood cells (pancytopenia), which may result from a failure of the bone marrow to produce these
- a widespread rash with blisters and peeling skin, particularly around the mouth, nose, eyes and genitals (Stevens Johnson syndrome).
- swelling of the lungs with the following symptoms; coughing, difficulty breathing, wheezing
- temporary paralysis or weakness of the muscles (rhabdomyolysis), disease of the muscles with the following symptoms; aching muscles, muscle tenderness or weakness, not caused by exercise
- an attack of porphyria (a rare blood pigment disorder) in patients with this disease

- muscle or ligament rupture
- inflammation of the pancreas (pancreatitis) – you may have severe pain in the stomach and back
- loss of consciousness (coma), due to a severe reduction in blood sugar levels
- inflammation of the eye (uveitis)
- skin redness with excessive scaling (exfoliative dermatitis)
- loss of appetite, skin and eyes becoming yellow in colour, dark-coloured urine, itching, or tender stomach (abdomen). These may be signs of liver problems which may include a fatal failure of the liver.

Tell your doctor or pharmacist if any of the following side effects gets serious or lasts longer than a few days:

Uncommon (may affect up to 1 in 100 people)

- feeling sick (nausea) or being sick (vomiting), diarrhoea or stomach pains
- irritated or burning eyes
- headaches, sleep disturbances including difficulty sleeping (insomnia)
- feeling dizzy, having spinning sensations
- agitation, feeling restless
- cough and inflamed sore nose or throat (nasopharyngitis)
- fungal infection
- skin rash or itching

Rare (may affect up to 1 in 1,000 people)

- loss of appetite
- fast heart beat
- drowsiness
- feeling confused or anxious, nightmares, seeing, feeling or hearing things that are not there, depression and mental illness
- changes in or loss of your sense of taste or smell
- shortness of breath or wheezing
- changes in levels of liver enzymes or bilirubin, which may be seen in blood tests
- excessive sweating and hot flushes
- changes in kidney function shown in blood tests
- feeling faint, lightheaded or dizzy, which may be due to low blood pressure
- hives (urticaria)
- rash with pimples

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

- uncontrolled movements, unsteadiness and shaking
- unusual bleeding or bruising more easily than normal (thrombocytopenia)
- increase in some white blood cells (eosinophilia)
- ringing in the ears (tinnitus)
- joint and muscle pains

- skin rashes or eruptions, which may be caused by strong sunlight
- unusual purple discolouration under the skin, which may be due to bleeding or bruising due to leaky or damaged blood vessels

Not known (frequency cannot be estimated from the available data)

- a red, scaly rash with bumps under the skin and blisters (exanthemous pustolosis)
- muscular weakness, muscle tear
- feeling weak or irritable, sweating and/or trembling. This could be due to lowering of blood sugar (glucose) levels especially in patients with diabetes or existing low blood sugar
- an increase in blood sugar levels
- feeling of nervousness, tremor, unusual (involuntary) muscle movements,
- fainting
- digestive problems such as stomach upset (indigestion/heartburn), constipation, or wind
- general pain, pains in your muscles and stiffness in the bones/joints (arthritis), feeling unwell (asthenia), or fever
- persistent headache with or without blurred vision (benign intracranial hypertension).

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 pre-existing risk factors.

Metronidazole

Stop taking your medicine and see a doctor or go to a hospital immediately if:

- You have an allergic reaction (signs include skin rash, flaking skin, boils, sore lips or mouth; wheezing; fluttering or tightness of the chest or collapse; swelling of the face, tongue or throat).
- You suffer a serious but very rare brain disease (encephalopathy). Symptoms may include a fever, stiff neck, headache, hallucinations, problems using your arms and legs, problems with speaking, feeling confused.
- You develop skin rashes with blistering, peeling or bleeding of the skin around the lips, eyes, mouth, nose and genitals. You may also have flu-like symptoms and a high temperature. These could be signs of severe allergic skin reactions called Stevens - Johnson syndrome or toxic epidermal necrolysis.
- You develop a red, scaly widespread rash with bumps under the skin and blisters accompanied by fever at the initiation of treatment (acute generalised exanthematous pustulosis). Stop using Metronidazole if you develop these symptoms and contact your doctor or seek medical attention immediately.

Talk to your doctor straight away if you notice any of the following side effects:

- Blood disorders (signs may include increased bruising, sore throats, unexpected infections, mouth ulcers, bleeding gums or unusual tiredness)
- Yellowing skin and whites of the eyes
- Severe stomach pain which may reach through to your back (pancreatitis)

Tell your doctor or pharmacist if you notice any of the following side effects:

Very rare (affects less than 1 in 10 000 people)

- Fits (convulsions)
- Feelings of confusion, seeing or hearing things that are not there (hallucinations)
- Muscle weakness, muscle pain or joint pain
- Eyesight problems such as blurred or double vision
- Drowsiness, dizziness, headaches
- Skin rashes, itching, blisters, circular red patches on the skin. Darkening of urine
- Liver problems including life-threatening liver failure (hepatocellular liver injury)
- Abnormal liver function tests

Not known (frequency cannot be estimated from the available data)

- Paralysis (numbness), tingling, pain or a feeling of weakness in the arms or legs
- Unpleasant taste in the mouth. Furred tongue
- Feeling sick, being sick, upset stomach or diarrhoea
- Loss of appetite
- Fever
- Feeling depressed
- Pain in your eyes (optic neuritis)
- Hearing impairment/hearing loss
- Ringing in the ears (tinnitus)
- A group of symptoms together including fever, nausea, vomiting, headache, stiff neck and extreme sensitivity to bright light. This may be caused by an inflammation of the membranes that cover the brain and spinal cord (meningitis)
- You get a rash or skin discolouration with or without raised areas which often reoccurs at the same location each time the drug is taken

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: Website: www.zuventus.co.in and click the tab “Safety Reporting” located on the top right end of the home page.

By reporting side effects, you can help provide more information on the safety of this medicine.

You can also report the side effect with the help of your treating physician.

5. HOW TO STORE DIOF / DIOF DS

- Store below 25°C. Protect from light.
- Do not freeze.
- Keep out of reach of children.
- Shake well before use
- Do not use this medicine after the expiry date which is stated on the blister and the carton after “EXP”. The expiry date refers to the last day of that month.

6. CONTENTS OF THE PACK AND OTHER INFORMATION

What DIOF / DIOF DS contains

Diof Suspension
Each 5 ml contains:
Ofloxacin ……..…50 mg
Metronidazole Benzoate IP
equivalent to Metronidazole…….100 mg
Excipients……..q.s.
In a flavoured syrupy base

Diof DS Suspension
Each 5 ml contains:
Ofloxacin ……..…100 mg
Metronidazole Benzoate
equivalent to Metronidazole…….….200 mg
Excipients……..…..q.s.
In a flavoured syrupy base