OFLODAZOLE

ROENTGEN IMPEX

Module 1: - Administrative information and prescribing information:

1.3.1 Summary of Product Characteristics (SmPC):

Summary Product Characteristics (SPC)

1. NAME OF THE FINISHED PHARMACEUTICAL PRODUCT

OFLODAZOLE TABLETS (OFLOXACIN USP & ORNIDAZOLE TABLETS)

Strength
Each Film coated tablet contains:
Ornidazole 500 mg
Ofloxacin USP 200 mg
Excipients Q.S.
Colour: Titanium Dioxide BP

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Ingredients	**Use/Function**	**Qty./ tablet In mg**
Active Ingredient		
*Ofloxacin USP	Antibacterial Agent	200.00
*Ornidazole	Antiprotozoal agent	500.00
In-Active Ingredients		
#$Starch	Diluent	115.00
#Micro crystalline cellulose	Diluent /Disintegrant	173.00
Cross povidone XL 10	Disintegrant	24.00
Povidone (PVP K-30)	Binding agent	10.00
Sodium Benzoate BP	Preservative	1.00
Talc Powder BP	Glidant	6.00
Magnesium Stearate BP	Lubricant	6.00
Colloidal silicon dioxide (Aerosol)	Glidant	6.00
Sodium starch glycolate (Potato Base) BP	Disintegrant	9.00
Weight of Uncoated Tablets: 1050 mg		
Titanium Dioxide BP	Coating agent	20.00
Isopropyl Alcohol BP	Solvent	--
Methylene Chloride BP	Solvent	--
Weight of film coated Tablets: 1071.00 mg		

Reference:
BP = British Pharmacopoeia
* Quantity to be changed based on potency of API.
# Quantity of Micro crystalline cellulose powder & starch is to be adjusted to keep the total mass.
$ Quantity of Starch based on Moisture content

3 PHARMACEUTICAL FORMS:
Oral film-coated tablets
Off white coloured, caplet shape, plain on both sides film coated tablet.

4 CLINICAL PARTICULARS:
4.1 INDICATIONS FOR USE:
OFLODAZOLE may be used in the treatment of mixed polymicrobial infections like

- Lower Respiratory Tract (Acute bacterial exacerbations of chronic bronchitis & Community-acquired Pneumonia)
- Skin and skin structure infections
- Sexually Transmitted Diseases
- Acute, complicated urethral and cervical gonorrhea.
- Nongonococcal urethritis and cervicitis
- Mixed infections of the urethra and cervix
- Urinary Tract Infections (cystitis)
- Prostatitis due to Escherichia coli.
- Hepatic and intestinal amoebiasis, giardiasis, trichomoniasis of urogenital tract
- Bacterial vaginosis.
- ENT Infections

Also used in the treatment and prophylaxis of susceptible aerobic and anaerobic infections in dental and gastrointestinal surgery & in other mixed aerobic – anaerobic infections. OFLODAZOLE is also advocated in the management of H. pylori duodenal ulcer in combination with other drugs.

4.2 CONTRAINDICATIONS:
OFLODAZOLE is contraindicated in persons with a history of hypersensitivity to ofloxacin, to other quinolones, or to any of the components in this medication and in patients hypersensitive to ornidazole and other imidazoles. There is no evidence of accumulation when used in pregnant women. Therefore dosage regimen requires no adjustment during pregnancy.

5 SPECIAL PRECAUTIONS FOR USE:
Prescribing OFLODAZOLE TABLETS in the absence of a proven or strongly suspected bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.
Adequate hydration of patients receiving ofloxacin should be maintained to prevent the formation of highly concentrated urine.
Administer ofloxacin with caution in the presence of renal or hepatic insufficiency/impairment. In patients with known or suspected renal or hepatic insufficiency/impairment, careful clinical observation and appropriate laboratory studies should be performed prior to and during therapy since elimination of ofloxacin may be reduced. In patients with impaired renal function (creatinine clearance $\leq$ 50 mg/mL), alteration of the dosage regimen is necessary.

Moderate to severe photosensitivity/phototoxicity reactions, the latter of which may manifest as exaggerated sunburn reactions (e.g., burning, erythema, exudation, vesicles, blistering, edema) involving areas exposed to light (typically the face, "V" area of the neck, extensor surfaces of the forearms, dorsa of the hands), can be associated with the use of quinolones after sun or UV light exposure. Therefore, excessive exposure to these sources of light should be avoided. Drug therapy should be discontinued if photosensitivity/phototoxicity occurs.

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As with other quinolones, ofloxacin should be used with caution in any patient with a known or suspected CNS disorder that may predispose to seizures or lower the seizure threshold (e.g., severe cerebral arteriosclerosis, epilepsy) or in the presence of other risk factors that may predispose to seizures or lower the seizure threshold

A possible interaction between oral hypoglycemic drugs (e.g., glyburide/glibenclamide) or with insulin and fluoroquinolone antimicrobial agents have been reported resulting in a potentiation of the hypoglycemic action of these drugs. The mechanism for this interaction is not known. If a hypoglycemic reaction occurs in a patient being treated with ofloxacin, discontinue ofloxacin immediately and consult a physician.

As with any potent drug, periodic assessment of organ system functions, including renal, hepatic, and hematopoietic, is advisable during prolonged therapy.

Some quinolones, including ofloxacin, have been associated with prolongation of the QT interval on the electrocardiogram and infrequent cases of arrhythmia. Rare cases of torsade de pointes have been spontaneously reported during postmarketing surveillance in patients receiving quinolones, including ofloxacin. Ofloxacin should be avoided in patients with known prolongation of the QT interval, patients with uncorrected hypokalemia, and patients receiving Class IA (quinidine, procainamide), or Class III (amiodarone, sotalol) antiarrhythmic agents.

6 ADVERSE REACTIONS:

The most frequently encountered side effect is dizziness, alone or in combination with other adverse reactions. The other side effects occuring to a lesser extent are nausea, pyrosis, intestinal spasms and metallic taste. Vertigo, fatigue and other discomforts such as loose stools, insomnia, skin rash and headache have also been reported.

7 USES DURING PREGNANCY, LACTATION:

PREGNANCY (Category C)

Ofloxacin is safe during pregnancy as ofloxacin has not been shown to have any teratogenic effects at oral doses as high as its recommended dose of 810 mg/kg/day.

From animal studies on pregnant rats and rabbits, it was found that doses equivalent to 50 and 10 times the recommended maximum human dose of Ofloxacin were fetotoxic which leads to decreased fetal body weight and increased fetal mortality in rats and rabbits.

Ornidazole tablet is contradicted in case of pregnancy. Women before taking Ofloxacin Ornidazole are advised to notify their gynaecologist if they become pregnant or intend to become pregnant during therapy or are breastfeeding an infant.

LACTATION

It is not known whether ofloxacin or ornidazole is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when OFLODAZOLE (Ofloxacin Ornidazole tablets) Tablets are administered to a nursing woman. Animal data suggest both ofloxacin and ornidazole are excreted into breast milk. The benefits of breastfeeding to mother and infant should be weighed against potential risk from infant exposure to ofloxacin and ornidazole through breast milk.

8 DRUG INTERACTIONS:

Ofloxacin & Ornidazole can interact with the following drugs or groups of drugs:

Antacids, Sucralfate, Metal Cations, Multivitamins, Caffeine, Cimetidine, Cyclosporine, Probenecid, Theophylline, Warfarin etc.

9 DOSAGES AND ADMINISTRATION:

The usual dose of OFLODAZOLE tablets are 1 tablet orally every 12 h. These recommendations apply to patients with normal renal function (i.e., creatinine clearance > 50 ml/min).

Mixed Amoebiasis
Adults : 1 tab twice daily for 5-7 days
Children: ½ tab once daily for 5 to 10 days

Mixed Amoebic dysentery
Adults : 3 tablets once daily for 3 days
Children : 1 tablet once daily for 3 days

Mixed Giardiasis :
Adults : 3 tablets once daily for 1-2 days
Children: 1 tablet for 2 days

Trichomoniasis
Adults : 3 tablets once or 1 tablet twice daily for 5 days. Sexual partner should be simultaneously treated.

Bacterial vaginosis and STD
Adults : 3 tablets once or 1 tablet once daily for 5-7 days
Mixed bacterial infections in Lower Respiratory Tract, Gynaecology, ENT, Surgical Infections and

Dental Infections
Initiate oral therapy as soon as possible after I.V. infusion in surgical conditions.
Adults : 1 tablet twice daily for 5 to 10 days
Children : ½ tablet twice daily

10 OVERDOSAGE:
No data is available on overdosage toxicity. In the event of an overdosage the stomach may be emptied and symptomatic treatment should be given.

11 PHARMACOLOGY:
Ofloxacin has in vitroactivity against a broad spectrum of gram-positive and gram-negative aerobic and anaerobic bacteria. Ofloxacin is often bactericidal at concentrations equal to or slightly greater than inhibitory concentrations. Ofloxacin is thought to exert a bactericidal effect on susceptible microorganisms by inhibiting DNA gyrase, an essential enzyme that is a critical catalyst in the duplication, transcription, and repair of bacterial DNA.
The antimicrobial activity of Ornidazole is due to the reduction of the nitro group to a more reactive amine that attacks microbial DNA, brings about loss of helical structure of DNA and subsequent DNA breakage thus inhibiting further synthesis and causing degradation of existing DNA.

12 PHARMACOKINETICS:
Ofloxacin
Following oral administration, the bioavailability of ofloxacin in the tablet formulation is approximately 98%. Maximum serum concentrations are achieved one to two hours after an oral dose. Absorption of ofloxacin after single or multiple doses of 100 to 400 mg is predictable, and the amount of drug absorbed increases proportionately with the dose.

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Ofloxacin has biphasic elimination. Following multiple oral doses at steady-state administration, the half-lives are approximately 4-5 hours and 20-25 hours. However, the longer half-life represents less than 5% of the total AUC. Accumulation at steady-state can be estimated using a half-life of 9 hours. The total clearance and volume of distribution are approximately similar after single or multiple doses. Elimination is mainly by renal excretion.

Ornidazole

Ornidazole is readily absorbed from the gastro-intestinal tract and peak plasma concentrations of about 30 mcg per ml have been achieved within 2 hours of a single dose of 1.5 g, falling to about 9 mcg per ml after 24 hours and 2.5 mcg per ml after 48 hours.

The plasma elimination half-life of ornidazole is 12 to 14 hours. Less than 15% is bound to plasma proteins. It is widely distributed in body tissues and fluids, including the cerebrospinal fluid.

Ornidazole is metabolised in the liver and is excreted in the urine, mainly as conjugates and metabolites, and to a lesser extent in the faeces; 85% of a single oral dose has been reported to be eliminated within 5 days, 63% in the urine and 22% in the faeces. Biliary excretion may be important in the elimination of ornidazole and its metabolites.

13 Shelf life

36 months

14 Special precautions for storage

Store in cool, dry place below 30° C, protect from light
Do not use later than the date of expiry.
KEEP ALL MEDICINE OUT OF THE REACH OF CHILDREN.

15 Nature and contents of container

Blister of 10 X 1 Tablets/Monopack.

16 Special precautions for disposal and other handling

KEEP ALL MEDICINE OUT OF THE REACH OF CHILDREN.

17. APPLICANT/MANUFACTURER

APPLICANT
Exported by:
ROENTGEN IMPEX
NO. 2063/A, RABARI VAS, KHORAJ VILLAGE,
DIST. GANDHINAGAR-382735, GUJARAT, INDIA

Manufactured by:
Naxcure Healthcare Pvt. Ltd.
SURVEY NO.-889/1,B/H CHADASANA ONGC,
CHADASANA-JHULASAN ROAD, AT & POST.- JHULASAN,
TA.- KADI, DIST.- MEHSANA-382705
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