1. 3 PRODUCT INFORMATION

1.3.1 Summary of Product Characteristics (SmPC)

Attached

SUMMARY OF PRODUCTS CHARACTERISTICS

NIDOF (Ofloxacin & Ornidazole Tablets)

1.5 PRODUCT INFORMATION

1.5.1 Prescribing information (Summary of products characteristics)

1. NAME OF THE MEDICINAL PRODUCT

1.1 (Invented) name of the medicinal product

NIDOF

1.2 Strength

Each film coated tablet contains:

Ofloxacin	BP	200 mg
Ornidazole	IHS	500 mg
Excipients		q.s

Colour: Approved colour used

1.3 Pharmaceutical form

Tablet

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

S. No.	Ingredients	Pharma copeia Grade	Label Claim	Mg/tab	Ovg. (%)	Qty. for 1.0 Lac. (kg)	Function
DRY MIX							
1	Ofloxacin	BP	200 mg	200.000	NA	20.000	Active Ingredient
2	Ornidazole	IHS	500 mg	500.000	NA	50.000	Active Ingredient
BINDER							
3	Maize Starch	BP	NA	12.000	NA	1.200	Binder
4	P.V.P.K-30	BP	NA	2.000	NA	0.200	Disintegrant
5	Purified Water #	BP	NA	q.s	NA	15.000	Solvent
LUBRICATION							
6	Microcrystalline Cellulose-PH 102	BP	NA	7.000	NA	0.700	Disintegrant /Diluent
7	Colloidal Silicon dioxide	BP	NA	4.000	NA	0.400	Glidant
8	Croscarmellose Sodium	BP	NA	10.000	NA	1.000	Disintegrant
9	Purified Talc	BP	NA	3.000	NA	0.300	Lubricant
10	Magnesium Stearate	BP		12.000	NA	1.200	Lubricant
Target Weight of Compressed Tablets				**750.000 mg**		**75.000 Kg**	
FILM COATING MATERIAL							

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NIDOF (Ofloxacin & Ornidazole Tablets)

1	HPMC -15 cps	BP	NA	15.000	NA	1.500	Coating materials
2	PEG-6000	BP	NA	3.000	NA	0.300	Coating materials
3	Titanium Dioxide	BP	NA	2.850	NA	0.285	Coating materials
4	Purified Talc	BP	NA	2.850	NA	0.285	Lubricant
5	Color: Sunset Yellow Supra	IHS	NA	0.940	NA	0.094	Colouring Agent
6	Color: Tartrazine yellow supra	IHS	NA	0.320	NA	0.032	Colouring Agent
7	Purified Water	BP	NA	q.s	NA	6.000	Solvent
8	Purified Talc (For Dusting)	BP	NA	3.000	NA	0.300	Lubricant
Target Weight of Coated Tablets				**761.250 mg**	**----**	**76.125 kg**	**----**
PAN COATING MATERIAL (FOR ANY BATCH SIZE)							
1	P.V.P.K-30	BP	NA	1.500	NA	0.150	Coating materials
2	Isopropyl alcohol	BP	NA	q.s.	NA	0.375	Solvent

Ofloxacin and ornidazole* to be calculated on 100% assay basis anh the quantit to be compensated with MCC-PH 102**

l0% Extra MCC-PH 102** to be taken to compensate Loss on drying.

Purified water used as solvent.

Note : NA – Not Applicable

Abbreviations

BP **:** British Pharmacopoeia (Current edition)

IHS **:** In-House Specification

3. PHARMACEUTICAL FORM

Film coated Tablet

Description

Orange coloured, caplet shaped coated tablets having "NDF" embossed on one side and central break line on other side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Clinically, NIDOF has been shown to be effective in various bacterial infections. Available data suggest that the drug can be used in the following indications:

Urinary tract infections

Sexually transmitted diseases

Crohn's disease.

Gastrointestinal infections

Trichomoniasis, gairdiasis and amoebiasis.

Pulmonary infections

Clostridium difficult colitis.

Radiosensitization of malignancies.

Other infections (osteomyelitis, skin and soft tissue infections, use in immune-compromised host).

Susceptible anaerobic infections.

In all these clinical situations, NIDOF was clinically effective and in comparative studies it was found to be as effective as and better than the comparative agent.

4.2 Posology and Method of Administration:

It is to be taken orally, preferably with a glass of water.

In the treatment of infections, Ofloxacin with Ornidazole is used mainly as an oral medication in doses ranging from 200 mg of Ofloxacin and 500 mg to 2g of Ornidazole daily. Because of its long half-life of about 9 hours, treatment schedules using a single large dose have superseded longer and more frequent smaller dose regimens, especially in the treatment of trichomoniasis and giardiasis.

These recommendations apply to patients with normal renal function (i.e. creatinine clearance50ml/min.) and Ornidazole 1.5g single dose once a day for 3 days.

4.3 Contraindications

Ofloxacin should not be used in patients with known allergy to older or new quinolones. History of epilepsy. Its use in children with incomplete skeletal growth, pregnant women and nursing mothers is not recommended. Ornidazole should not be used in the cases like Hypersensitivity and other imidazoles.

History of serious neurologic disease, including seizures. Severe
hepatic failure.

4.4 Special Warnings and special Precautions for use

Ofloxacin should be used with caution in patients with epilepsy or a history of CNS disorders. In patients receiving ofloxacin, myalgia and arthralgia (pain) can occur. Inflammation and rupture of tendons (e.g. the Achilles tendon) may occur within 48 hours after starting the treatment and may be bilateral. This has occurred particularly in patients treated concurrently with corticosteroids. In the event of signs of inflammation of a tendon, treatment with ofloxacin must be discontinued immediately and appropriate treatment for the affected tendon, initiated. Less frequently cases of myopathy and/or rhabdomyolysis may occur.

Ornidazole should not be used in Renal and hepatic impairment. CNS diseases e.g. epilepsy or multiple sclerosis. May impair ability to drive or operate machinery. Pregnancy and lactation. This medicine may lead to drowsiness and impaired concentration which may be aggravated by simultaneous intake of alcohol or other central nervous system depressants. Patients should be warned against taking charge of vehicles or performing potentially hazardous tasks where loss of concentration may lead to accidents.

4.5 Interaction with other medicinal products and other forms of interaction

If mineral-containing antacids are taken at the same time, absorption of ofloxacin may be impaired.

Antacids and metal ions: The absorption of the medicine is reduced by antacids containing aluminium or magnesium and also by calcium, iron and zinc salts. Sucralfate releases aluminium ions in the stomach and thereby reduces absorption of ofloxacin. In such cases, ofloxacin should be taken about two hours before taking such preparations. High calcium content in dairy products might also interfere with the absorption of medicine.

Analgesics: Concurrent administration of fenbufen with quinolones may increase the incidence of CNS adverse effects.

Theophylline: Fluoroquinolones are known to inhibit hepatic drug metabolism and may interfere with the clearance of medicine metabolised by the liver such as theophylline. There are indications of a pronounced lowering of the cerebral seizure threshold when quinolones are given concurrently with medicines that lower the seizure threshold, eg. Theophylline.

Glibenclamide: Ofloxacin may cause a slight increase in serum concentrations of glibenclamide if administered concurrently. Excessive rises or falls in blood-sugar level may occur in isolated cases, especially in patients with diabetes mellitus. It is therefore recommended that patients treated concomitantly with ofloxacin and glibenclamide be monitored particularly closely.

Coumarin derivatives: As with other quinolones the effect of coumarin derivatives may be intensified when coadministered with ofloxacin. Patients undergoing concomitant treatment with coumarin derivatives should therefore be monitored carefully.

Others: Mutual impairment of excretion and an increase in serum levels must be considered when quinolones are administered together with other medicines (particularly in case of high dose therapy) that also undergo renal tubular secretion such as probenecid, cimetidine, furosemide or methotrexate.

Ornidazole Potentiates effect of coumarin-type oral anticoagulants. Prolongs the muscle-relaxant effect of vecuronium bromide.

4.6 Pregnancy and lactation

Ofloxacin has not been shown to have any teratogenic effects at oral doses as high as 810 mg/kg/day there are, however, no adequate and well-controlled studies in pregnant women. Ofloxacin should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

The safety of Ornidazole during pregnancy has not been established, Ornidazole to be used only if the potential benefits justifies potential risk to fetus / neonate.

4.7 Effects on ability to drive and use machines

Since there have been occasional reports of somnolence, impairment of skills, dizziness and visual disturbances, patients should know how they react to Tarivid before they drive or operate machinery. These effects may be enhanced by alcohol.

4.8 Undesirable effects

Allergic manifestations may occur, in particular hypersensitivity reactions of the skin. There have been fleabite-like haemorrhages (petechiae), the formation of blood blisters (haemorrhagic bullae) and small nodules (papules) with crust formation indicating vessel involvement (vasculitis).

There have been symptoms such as facial oedema, swollen tongue, glottal oedema, tachycardia, dyspnoea and signs of imminent shock and acute anaphylaxis. In the event of such reactions, ofloxacin should be discontinued immediately. Medical treatment (therapy for shock) is imperative. Erythema multiforme, Stevens Johnsons Syndrome, toxic epidermal necrolysis. Skin reactions on exposure to strong sunlight have been reported.

Seizure and less frequently extrapyramidal symptoms, disturbances of the nervous system, e.g. weakness, headaches, dizziness, sleep disturbances, insomnia, nightmares, unsteady gait and tremor (disturbance of muscular co-ordination), numbness and tingling in the limbs (paraesthesiae), visual disturbances such as double vision and abnormal colour vision, disturbances of the senses of taste and smell, hallucinations, convulsions and psychotic reactions such as restlessness, agitation, anxiety, drowsiness, depression and confusion. These reactions have occurred mainly in elderly patients and patients with impaired renal function, but not exclusively. In some cases these reactions have occurred already after the first dose. In the event of such adverse reactions, ofloxacin should be discontinued immediately and the doctor informed. Paraesthesia and peripheral neuropathy have occurred. There have been reports of pain in joints and muscles.

There have been cases of changes in the blood picture (leucopenia, eosinophilia, agranulocytosis, thrombocytopenia, anaemia), transient increases in liver enzymes and/or bilirubin and in serum creatinine.

Myalgia, gynaecomastia, cardiovascular effects including tachycardia.

Crystalluria as well as interstitial nephritis may also occur. Gastro-intestinal symptoms may occur (gastric or abdominal symptoms and pain, loss of appetite, nausea, vomiting, dyspepsia, diarrhoea).

Experience to date shows that the adverse reaction to ofloxacin treatment resolves on discontinuation of the preparation. The doctor should always be informed of side-effects that have occurred.

4.9 Overdose

The most important signs to be expected following acute overdosage are CNS symptoms such as confusion, dizziness, impairment of consciousness and seizures, increases QT interval as well as gastrointestinal reactions such as nausea and mucosal erosions.

CNS effects including confusional state, convulsion, hallucination, and tremor have been observed in post marketing experience

In the case of overdose steps to remove any unabsorbed ofloxacin eg gastric lavage, administration of adsorbants and sodium sulphate, if possible during the first 30 minutes, are recommended; antacids are recommended for protection of the gastric mucosa. A fraction of ofloxacin may be removed from the body with haemodialysis. Peritoneal dialysis and CAPD are not effective in removing ofloxacin from the body. No specific antidote exists.

Elimination of ofloxacin may be increased by forced diuresis.

In the event of overdose, symptomatic treatment should be implemented. ECG monitoring should be undertaken, because of the possibility of QT interval prolongation.

SUMMARY OF PRODUCTS CHARACTERISTICS

NIDOF (Ofloxacin & Ornidazole Tablets)

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Ofloxacin is a quinolone carboxylic acid derivative which has a broad spectrum of antibacterial activity against both Gram-positive and Gram-negative bacteria. Ofloxacin exerts its effect by inhibiting the bacterial DNA gyrase, which is responsible for coiling the genetic material as a prerequisite for bacterial multiplication.

The mode of action, range of activities, duration of action and MIC levels have been established mainly by means of *in vitro* studies using bacterial isolates.

Ornidazole is a 5-nitroimidazole derivative active against protozoa and anaerobic bacteria. It is converted to reduction products that interact with DNA to cause destruction of helical DNA structure and strand leading to a protein synthesis inhibition and cell death in susceptible organisms.

5.2 Pharmacokinetic properties:

Ofloxacin is readily absorbed and excreted mainly unchanged in the urine. The serum elimination half-life is approximately 6 to 8 hours. Following oral administration, ofloxacin peak serum concentrations are reached within one to two hours. The plasma level usually achieved by the recommended dosage regimes (3 to 4 micrograms/mL) is in excess of the average MIC which is 1 to 2 micrograms/mL for susceptible organisms.

Ornidazole:

Absorption: Readily absorbed (oral and intravaginal); peak plasma concentrations after 2 hr (oral), 12 hr (intravaginal).

Distribution: Body tissues and fluids (wide), CSF. Protein-binding: <15%.

Metabolism: Hepatic.

Excretion: Via urine (as conjugates and metabolites), via faeces (small amounts); 12-14 hr (elimination half-life).

5.3 Preclinical safety data

Not Applicable

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients:

- Maize Starch
- P.V.P.K-30
- Microcrystalline Cellulose-PH 102
- Colloidal Silicon dioxide
- Croscarmellose Sodium
- Purified Talc
- Magnesium Stearate
- Purified Water
- HPMC -15 cps

- Titanium Dioxide
- Sunset Yellow Supra
- Tartrazine Supra
- Polyethylene glycol-6000
- IsoPropyl alcohol

6.2 Incompatibilities
None

6.3 Shelf life
36 months from the date of manufacturers

6.4 Special precautions for storage
Do not store above 30°C.

6.5 Nature and contents of container

1x10, 10x10, 2x7 alu-alu blister packed in a unit carton; such cartons are packed in a corrugated box.

6.6 Special precautions for disposal
Tablets should be handled with care.

7. REGISTRANT

Name of Registrant:
Maxtar Bio-Genics

Address of Office:
310, Pearls Corporate (W Mall),
Manglam Place, Sector- 3 ,Rohini, Delhi-
85 India.

8. MANUFACTURER
Name of Manufacturer:
Maxtar Bio-Genics

Address of Manufacturer:
K. No. 705, Nalagarh road, Malku Majra,
(Baddi), Tehsil Nalagarh, Distt. Solan,
Himachal Pradesh - 173205 INDIA

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