1. Name of the medicinal product:

1.1 Name of the medicinal product:

Ofloxacin 200 mg & Ornidazole 500 mg Tablets

1.2 Strength:

Each film coated tablet contains:

Ofloxacin USP: 200 mg

Ornidazole: 500 mg

Excipients: q.s.

Colour: Sunset Yellow, Quinoline Yellow and Titanium Dioxide

1.3 Pharmaceutical form:

Film coated Tablets for Oral use

2. Qualitative and quantitative composition

Ofloxacin USP: 200 mg

Ornidazole: 500 mg

3. Pharmaceutical form

Film coated Tablets for Oral use

4. Clinical particulars:

4.1 Therapeutic indications:

Ofloxacin 200 mg & Ornidazole 500 mg Tablets is indicated in treatment of mixed amoebiasis, mixed amoebic dysentery, mixed giardiasis, trichomoniasis, bacterial vaginosis, Sexually transmitted diseases, infections of gynaecology, lower respiratory tract infections, ENT, surgical and dental infections.

4.2 Posology and method of administration

Route of administration: Oral

Dosage:

GIT infections – One tablet twice daily

Acute diarrhoea of mixed origin - One tablet twice daily

Dental infections - One tablet twice daily

Gynecological infections - One tablet twice daily

ENT infections - One tablet twice daily

Skin & soft tissue infections - One tablet twice daily

Surgical infections - One tablet twice daily

Not recommended for children below 12 yrs age or as directed by the physician

4.3. Contraindications

Hypersensitivity to quinolones; pregnancy and lactation; prolongation of the QT interval; uncorrected hypokalaemia.

Hypersensitivity to ornidazole or to other nitroimidazole derivatives.

4.4. Special warnings and precautions:

Epilepsy or other predisposition to seizures; known or suspected CNS disorders; renal, hepatic impairment; myasthaenia gravis; superinfection; children <18 yr; exposure to strong sunlight and UV light; ensure adequate hydration

4.5. Interactions with other drugs and other forms of interactions:

Probenecid decreases elimination. Antacids may reduce ofloxacin absorption, avoid for 2 hr either side of administration. Cimetidine may increase ofloxacin concentrations. Monitor blood glucose in patients on antidiabetic medication.

Potentially Fatal: Corticosteroids may increase risk of tendon rupture. Increases effects of oral anticoagulants, ciclosporin, theophylline. Increased risk of seizures with NSAIDs. Avoid in patients taking QT prolonging medication (e.g. class Ia or III antiarrythmics, astemizole, terfenadine, cisapride, erythromycin, pentamidine, phenothiazines and some TCA).

4.6. Fertility, Pregnancy and Lactation:

Ofloxacin

Based on a limited amount of human data, the use of fluoroquinolones in the first trimester of pregnancy has not been associated with an increased risk of major malformations or other adverse effects on pregnancy outcome. Animal studies have shown damage to the joint cartilage in immature animals but no teratogenic effects. Therefore Ofloxacin should not be used during pregnancy. Ofloxacin is excreted into human breast milk in small amounts. Because of the potential for arthropathy and other serious toxicity in the nursing infant, breast feeding should be discontinued during treatment with Ofloxacin.

Ornidazole

No controlled studies of effect of the drug on pregnant women are available. Ornidazole should be prescribed to pregnant and nursing women only if the potential benefit to the mother outweighs potential risk to the foetus/ neonate. Lithium therapy: 5-nitroimidazoles (mainly metronidazole) have been found to decrease renal elimination of lithium. So, in patients undergoing concurrent lithium therapy, plasma lithium concentrations as well as creatinine and electrolyte concentrations should be monitored. It should be used with caution in conditions where the individual drugs have been used with precautionary approach.

4.7. Effects on ability to drive and use machines

Ofloxacin

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

Ornidazole

Somnolence, dizziness, tremor, rigidity, poor coordination, seizures, vertigo or temporary loss of consciousness may occur in patients receiving Ornidazole. If they occur, such effects may affect tasks requiring alertness, including the patient's ability to drive and operate machinery.

4.8. Undesirable effects

Gastrointestinal effects like nausea, vomiting, anorexia and metallic or bitter taste. CNS effects lik dizziness, vertigo and somnolence, rigidity, tremor, coordination problems,

convulsions (rare), impairment of consciousness and signs of sensitive or mixed peripheral neuropathy have been observed. Blood dyscrasias like medullar aplasia and neutropenia may be encountered occasionally. Other adverse events such as fatigue, loose stools, and headache have also been reported.

Potentially Fatal: Anaphylaxis; rarely seizures.

4.9. Overdose

Ofloxacin

The most important signs to be expected following acute over dosage are CNS symptoms such as confusion, dizziness, impairment of consciousness and convulsive seizures as well as gastrointestinal reactions such as nausea and mucosal erosions. In the case of overdose steps to remove any unabsorbed Ofloxacin e.g gastric lavage, administration of adsorbents and sodium sulphate, if possible during the first 30 minutes, are recommended; antacids are recommended for protection of the gastric mucosa. 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.

Ornidazole

In cases of over dosage the symptoms mentioned under Undesirable Effects occur in more severe form. No specific antidote is known. The administration of diazepam is recommended if cramps occur.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Ofloxacin

Ofloxacin is a quinolone antimicrobial agent. The mechanism of action of Ofloxacin and other fluoroquinolone antimicrobials involves inhibition of bacterial topoisomerase IV and DNA gyrase (both of which are type II topoisomerases), enzymes required for DNA replication, transcription, repair and recombination. Ofloxacin has in vitro activity against a wide range of gram-negative and gram-positive microorganisms. Ofloxacin is often bactericidal at concentrations equal to or slightly greater than inhibitory concentrations. Fluoroquinolones, including Ofloxacin, differ in chemical structure and mode of action

from aminoglycosides, macrolides and beta-lactam antibiotics, including penicillins. Fluoroquinolones may, therefore, be active against bacteria resistant to these antimicrobials.

Resistance to Ofloxacin due to spontaneous mutation in vitro is a rare occurrence (range: 10-9 to 10-11). Although cross-resistance has been observed between Ofloxacin and some other fluoroquinolones, some microorganisms resistant to other fluoroquinolones may be susceptible to Ofloxacin.

Ornidazole:

After passive absorption into bacterium cell, the nitro group of Ornidazole is reduced to amine group by ferrodoxin type redox system. The formation of redox intermediate intracellular metabolites is believed to be the key component of microorganism killing for Ornidazole. The mechanism of action is similar in protozoa. Microbiology Microbiological results indicate that the following pathogens may be regarded as sensitive: Staphylococcus aureus (including methicillin resistant staphylococci), Staphylococcus epidermidis, Neisseria species, Escherichia coli, Citrobacter, Klebsiella, Enterobacter, Hafnia, Proteus (indole negative and indole-positive strains), Haemophilus influenzae, Chlamydiae, Legionella, and Gardnerella. Variable sensitivity is shown by Streptococci, Serratia marcescens, Pseudomonas aeruginosa and Mycoplasma. Anaerobic bacteria (e.g. Fusobacterium species, Bacteroides species, Eubacterium species, Peptococci, Peptostreptococcus) are normally resistant. Ofloxacin is not active against Treponema pallidum.

5.2. Pharmacokinetic Properties:

Ofloxacin – Pharmacokinetics

Absorption: Rapidly and well absorbed from the GI tract (oral); peak plasma concentrations after 0.5-2 hr. Rate, but not extent, delayed by the presence of food. bioavailability of ofloxacin in the tablet formulation is approximately 98%

Distribution: Widely distributed into body fluids, CSF, tissues, bile (high concentrations); crosses the placenta and enters breast milk. Protein-binding: 20-32%.

Metabolism: <10% of a single dose is metabolized. Converted to desmethyl and N-oxide metabolites; desmethyl ofloxacin has moderate antibacterial activity.

Excretion: Via urine within 24-48 hr by tubular secretion and glomerular filtration (75-80% as unchanged, <5% as metabolites); via faeces (4-8%). Elimination is biphasic with half-lives of 4-5 hr and 20-25 hr; prolonged in renal impairment (15-60 hr).

Ornidazole – Pharmacokinetics

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

Few studies have shown the combination of Nitroimidazoles and Quinolones to be effective clinically. This gives an indication for combining Ornidazole and ofloxacin especially in mixed infections. Ornidazole which is a new derivative of Nitroimidazoles series has a longer half-life. It is recommended to be given twice a day. Ofloxacin is also recommended twice daily. Therefore, it appears appropriate to combine Ornidazole and ofloxacin as fixed dose combinations. Moreover, FDC will provide broad spectrum of activity as individual drugs are active against both aerobic and anaerobic infection.

6. PHARMACEUTICAL DATA

6.1 List of excipients

Sr. No.	Material Name	Specification
1.	Lactose	BP
2.	Hydroxy propyl cellulose (Klucel LF)	BP
3.	Isopropyl Alcohol	BP
4.	Dichloromethane	BP
5.	Maize Starch	BP

6.	Microcrystalline Cellulose	BP
7.	Colloidal Anhydrous Silica	BP
8.	Magnesium Stearate	BP
9.	Purified Talc	BP
10.	Sodium Starch Glycolate	BP
11.	Hypromellose 15 CPS	BP
12.	Titanium Dioxide	BP
13.	Macrogol 400	BP
14.	Sunset Yellow Lake	IH
15.	Quinoline Yellow	IH

6.2 Incompatibilities

Not applicable

6.3 Shelf Life

36 months

6.4 Special Precautions for Storage

Store below 30°C in a dry place. Protect from light.

Keep medicine out of reach of children

6.5 Nature and contents of container:

Primary packing: 20 ml Vial

Secondary packing: A carton containing 20 ml vial along with 10 ml WFI with pack insert.

6.6. Special precautions for disposal and other handling

None

7. REGISTRANT:

MARKETING AUTHORISATION HOLDER

SEAL HEALTHCARE LIMITED
1, Ashimolowo Street,
Off 5th Avenue,
Abesan Estate,
Ipaja, Lagos State,
Nigeria.

8. Marketing Authorization Number: NA

9. Date of first authorization/renewal of the authorization: NA

10. Date of revision of the text:---

11. Name and address of Manufacturer:

CORAL LABORATORIES LTD.

Plot No. 57/1 (16), Bhenslore, Dunetha,

Nani Daman-396 210, India.

Email: exports@corallab.com

CORAL LABORATORIES LTD. MUMBAI

1.3.2 Labelling (outer & inner labels)

Enclosed