1.3.1 Summary of Product Characteristics (SPC)

1. Name of the medicinal product (DUOZOL TABLET)

Ofloxacin 200mg & Ornidazole 500mg Tablets

2. Qualitative and quantitative composition

Each film coated tablet contains:

Ofloxacin USP	200mg
Ornidazole	500mg

3. Pharmaceutical form

Orange coloured biconvex capsule shaped film coated tablets having break line on one side.

4. Clinical particulars

4.1 Therapeutic indications

Ofloxacin and Ornidazole Tablet are indicated for the treatment of diarrhoea of mixed infection in adults only.

Ofloxacin and Ornidazole Tablet is used to treat infections caused by bacteria requiring and not requiring oxygen for growth. These infections include diarrhea, stomach infection, disorders of the female reproductive system and pelvic infections. It also used to treat foot ulcers especially in patients with diabetes, lung infection, and patients with a weak immune system. This medicine works by killing bacteria that cause infections. Also, ornidazole blocks protozoal growth and Ofloxacin prevents bacterial DNA replication.

4.2 Posology and method of administration

One tablet of Ofloxacin and ornidazole combination is recommended as twice daily therapy.

Patients with hepatic impairment

In patients with liver cirrhosis the elimination half-life is longer (22 versus 14 hours) and clearance lower (35 versus 51 ml/min) than in healthy subjects. The dosing interval should be doubled in patients with severe hepatic impairment.

Patients with renal impairment

The pharmacokinetics of ornidazole are unaltered in renal impairment. Dose adjustment is therefore unnecessary in patients with impaired renal function. Ornidazole is removed by haemodialysis. An additional dose of 500 mg of ornidazole should be administered if the daily dose is 2 g/d or an additional dose of 250 mg ornidazole if the daily dose is 1 g/d, should therefore be administered before the start of haemodialysis.

4.3 Contraindications

- FDC of Ofloxacin and Ornidazole combination is contraindicated in persons with a history of hypersensitivity associated with the use of ofloxacin or ornidazole or any member of the quinolone group of antimicrobial agents or other nitro-imidazole derivatives.
- Ofloxacin should not be used in patients with a past history of tendonitis.
- FDC of Ofloxacin and Ornidazole combination is contra-indicated in patients with a history of epilepsy or with a lowered seizure threshold.
- FDC of Ofloxacin and Ornidazole combination is contra-indicated in children or growing adolescents, and in pregnant or breast-feeding women,
- FDC of Ofloxacin and Ornidazole combination is contra-indicated in patients with latent or actual defects in glucose-6-phosphate dehydrogenese activity may be prone to haemolytic reactions when treated with quinolone antibacterial agents.

4.4 Special warnings and precautions for use

Hypersensitivity and allergic reactions have been reported for fluoroquinolones after first administration. Anaphylactic and anaphylactoid reactions can progress to life-threatening shock, even after the first administration. In these cases ofloxacin should be discontinued and suitable treatment (e.g treatment for shock) should be initiated.

Clostridium difficile-associated disease

Diarrhoea, particularly if severe, persistent and/or bloody, during or after treatment with ofloxacin, may be symptomatic of pseudo-membranous colitis. If pseudo-membranous colitis is suspected, ofloxacin must be stopped immediately. Appropriate specific antibiotic therapy must be started without delay (e.g. oral vancomycin, oral teicoplanin or metronidazole). Products inhibiting the peristalsis are contraindicated in this clinical situation.

Patients with diseases of the CNS

In case of convulsive seizures, treatment with FDC of Ofloxacin and Ornidazole combination should be discontinued. Caution should be exercised in patients multiple sclerosis.

Cardiac Disorders

Very rare cases of QT interval prolongation have been reported in patients taking fluoroquinolones. Caution should be taken when using fluoroquinolones, including ofloxacin, in patients with known risk factors for prolongation of the QT interval such as, for example:

• congenital long QT syndrome

• concomitant use of drugs that are known to prolong the QT interval (e.g. Class IA and III antiarrhythmics, tricyclic antidepressants, macrolides, antipsychotics)

• uncorrected electrolyte imbalance (e.g. hypokalaemia, hypromagnesaemia) elderly

• cardiac disease (e.g. heart failure, myocardial infarction, bradycardia)

Patients being treated with FDC of Ofloxacin and Ornidazole combination should not expose themselves unnecessarily to strong sunlight and should avoid UV rays (sun lamps, solaria).

Patients with history of psychotic disorder

Psychotic reactions have been reported in patients receiving fluoroquinolones. In some cases these have progressed to suicidal thoughts or self-endangering behavior including suicide attempt, sometimes after a single dose. In the event that a patient develops these reactions, FDC of Ofloxacin and Ornidazole combination should be discontinued and

appropriate measures instituted. FDC of Ofloxacin and Ornidazole combination should be used with caution in patients with a history of psychotic disorder or in patients with psychiatric disease.

Patients with impaired liver function

FDC of Ofloxacin + Ornidazole should be used with caution in patients with impaired liver function, as liver damage may occur. Cases of fulminant hepatitis potentially leading to liver failure (including fatal cases) have been reported with fluoroquinolones. Patients should be advised to stop treatment and contact their doctor if signs and symptoms of hepatic disease develop such as anorexia, jaundice, dark urine, pruritis or tender abdomen.

Patients treated with vitamin K antagonists

Due to possible increase in coagulation tests (PT/INR) and/or bleeding in patients treated with fluoroquinolones, including ofloxacin, in combination with a vitamin K antagonist (e.g.warfarin), coagulation tests should be monitored when these drugs are given concomitantly.

Myasthenia gravis

FDC of Ofloxacin + Ornidazole should be used with caution in patients with a history of myasthenia gravis. Administration of antibiotics, especially of prolonged, may lead to proliferation of resistant microorganisms. The patient's condition must therefore be checked at regular intervals. If a secondary infection occurs, appropriate measures must be taken.

Peripheral neuropathy

Sensory or sensorimotor peripheral neuropathy has been reported in patients receiving fluoroquinolones, including ofloxacin. FDC of Ofloxacin + Ornidazole should be discontinued if the patient experiences symptoms of neuropathy in order to prevent the development of an irreversible condition.

Hypoglycaemia

As with all quinolones, hypoglycaemia has been reported, usually in diabetic patients receiving concomitant treatment with an oral hypoglycaemic agent (e.g. glibenclamide) or with insulin. In these diabetic patients, careful monitoring of blood glucose is recommended.

Patients with glucose-6-phosphate-dehydrogenase deficiency

Patients with latent or diagnosed glucose-6-phosphate-dehydrogenase deficiency may be predisposed to haemolytic reactions if they are treated with quinolones. FDC of Ofloxacin and Ornidazole combination should therefore be administered with caution in such patients.

Patients with rare hereditary disorders

Patients with rare hereditary disorders of galactose intolerance, the Lapp lactase deficiency or glucose galactose malabsorption should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction

Ofloxacin

Drug Antacids, Sucralfate, Metal Cations, Multivitamins:

Quinolones form chelates with alkaline earth and transition metal cations. Administration of quinolones with antacids containing calcium, magnesium, or aluminum, with sucralfate, with divalent or trivalent cations such as iron, or with multivitamins containing zinc or with didanosine may substantially interfere with the absorption of quinolones resulting in systemic levels considerably lower than desired. These agents should not be taken within the two-hour period before or within the two-hour period after FDC of Ofloxacin and Ornidazole combination administration.

Cimetidine:

Cimetidine has demonstrated interference with the elimination of some quinolones. This interference has resulted in significant increases in half-life and AUC of some quinolones. The potential for interaction between ofloxacin and cimetidine has not been studied.

Cyclosporine:

Elevated serum levels of cyclosporine have been reported with concomitant use of cyclosporine with some other quinolones. The potential for interaction between ofloxacin and cyclosporine has not been studied.

Drugs metabolized by Cytochrome P450 enzymes:

Most quinolone antimicrobial drugs inhibit cytochrome P450 enzyme activity. This may result in a prolonged half-life for some drugs that are also metabolized by this system (e.g., cyclosporine, theophylline/methylxanthines, warfarin) when co-administered with quinolones. The extent of this inhibition varies among different quinolones.

Non-steroidal anti-inflammatory drugs:

The concomitant administration of a non-steroidal anti-inflammatory drug with a quinolone, including ofloxacin, may increase the risk of CNS stimulation and convulsive seizures.

Probenecid:

The concomitant use of probenecid with certain other quinolones has been reported to affect renal tubular secretion. The effect of probenecid on the elimination of ofloxacin has not been studied.

Theophylline:

Steady-state theophylline levels may increase when ofloxacin and theophylline are administered concurrently. As with other quinolones, concomitant administration of ofloxacin may prolong the halflife of theophylline, elevate serum theophylline levels, and increase the risk of theophylline-related adverse reactions. Theophylline levels should be closely monitored and theophylline dosage adjustments made, if appropriate, when ofloxacin is co-administered. Adverse reactions (including seizures) may occur with or without an elevation in the serum theophylline level.

Warfarin:

Some quinolones have been reported to enhance the effects of the oral anticoagulant warfarin or its derivatives. Therefore, if a quinolone antimicrobi al is administered concomitantly with warfarin or its derivatives, the prothrombin time or other suitable coagulation test should be closely monitored.

Antidiabetic agents (e.g., insulin, glyburide/glibenclamide):

Since disturbances of blood glucose, including hyperglycemia and hypoglycemia, have been reported in patients treated concurrently with quinolones and an antidiabetic agent, careful monitoring of blood glucose is recommended when these agents are used concomitantly.

Interaction with Laboratory or Diagnostic Testing:

Some quinolones, including ofloxacin, may produce false-positive urine screening results for opiates using commercially available immunoassay kits. Confirmation of positive opiate screens by more specific methods may be necessary.

Ornidazole

Ornidazole potentiates the effect of coumarin-type oral anticoagulants. The dosage of the anticoagulant has to be adjusted accordingly. Ornidazole prolongs the muscle-relaxant effect of vecuronium bromide.

4.6 Fertility, pregnancy and lactation

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.

4.7 Effects on ability to drive and use machines

Since there have been occasional reports of somnolence, impairment of skills, poor coordination, dizziness, visual disturbances, vertigo or temporary loss of consciousness, patients should know how they react to FDC of Ofloxacin + Ornidazole before they drive or operate machinery. These effects may be enhanced by alcohol.

4.8 Undesirable effects

Ofloxacin

In clinical trials, the following events were considered likely to be drug-related in patients receiving multiple doses of ofloxacin: nausea 3%, insomnia 3%, headache 1%, dizziness 1%, diarrhea 1%, vomiting 1%, rash 1%, pruritus 1%, external genital pruritus in women 1%, vaginitis 1%, dysgeusia 1%. In clinical trials, the most frequently reported adverse events, regardless of relationship to drug, were: nausea 10%, headache 9%, insomnia 7%, external genital pruritus in women 6%, dizziness 5%, vaginitis 5%, diarrhea 4%, vomiting 4%.

In clinical trials, the following events, regardless of relationship to drug, occurred in 1 to 3% of patients: Abdominal pain and cramps, chest pain, decreased appetite, dry mouth, dysgeusia, fatigue, flatulence, gastrointestinal distress, nervousness, pharyngitis, pruritus, fever, rash, sleep disorders, somnolence, trunk pain, vaginal discharge, visual disturbances, and constipation.

Additional events, occurring in clinical trials at a rate of less than 1%, regardless of relationship to drug, were:

Body as a whole: asthenia, chills, malaise, extremity pain, pain, epistaxis

Cardiovascular System: cardiac arrest, edema, hypertension, hypotension, palpitations, vasodilation

Gastrointestinal System: Dyspepsia

Genital/Reproductive System: burning, irritation, pain and rash of the female genitalia; dysmenorrhea; menorrhagia; metrorrhagia

Musculoskeletal System: arthralgia, myalgia

Nervous System: seizures, anxiety, cognitive change, depression, dream abnormality, euphoria, hallucinations, paresthesia, syncope, vertigo, tremor, confusion

Nutritional/Metabolic: thirst, weight loss

Respiratory System: respiratory arrest, cough, rhinorrhea

Skin/Hypersensitivity: angioedema, diaphoresis, urticaria, vasculitis

Special Senses: decreased hearing acuity, tinnitus, photophobia \

Urinary System: dysuria, urinary frequency, urinary retention

The following laboratory abnormalities appeared in ≥ 1% of patients receiving multiple doses of ofloxacin. It is not known whether these abnormalities were caused by the drug or the underlying conditions being treated.

Hematopoietic: anemia, leukopenia, leukocytosis, neutropenia, neutrophilia, increased band forms, lymphocytopenia, eosinophilia, lymphocytosis, thrombocytopenia, thrombocytosis, elevated ESR

Hepatic: elevated: alkaline phosphatase, AST (SGOT), ALT (SGPT)

Serum chemistry: hyperglycemia, hypoglycemia, elevated creatinine, elevated BUN

Urinary: glucosuria, proteinuria, alkalinuria, hyposthenuria, hematuria, pyuria

Postmarketing Adverse Events: Additional adverse events, regardless of relationship to drug, reported from worldwide marketing experience with quinolones, including ofloxacin:

Clinical:

Cardiovascular System: cerebral thrombosis, pulmonary edema, tachycardia, hypotension/shock, syncope, torsades de pointes

Endocrine/Metabolic: hyper- or hypoglycemia, especially in diabetic patients on insulin or oral hypoglycemic agents

Gastrointestinal System: hepatic dysfunction including: hepatic necrosis, jaundice (cholestatic or hepatocellular), hepatitis; intestinal perforation; hepatic failure (including fatal cases); pseudomembranous colitis (the onset of pseudomembranous colitis symptoms may occur during or after antimicrobial treatment), GI hemorrhage; hiccough, painful oral mucosa, pyrosis

Genital/Reproductive System: vaginal candidiasis

Hematopoietic: anemia, including hemolytic and aplastic; hemorrhage, pancytopenia, agranulocytosis, leukopenia, reversible bone marrow depression, thrombocytopenia, thrombotic thrombocytopenic purpura, petechiae, ecchymosis/bruising

Musculoskeletal: tendinitis/rupture; weakness, rhabdomyolysis

Nervous System: nightmares; suicidal thoughts or acts, disorientation, psychotic reactions, paranoia; phobia, agitation, restlessness, aggressiveness/hostility, manic reaction, emotional lability; peripheral neuropathy, ataxia, incoordination; possible

exacerbation of: myasthenia gravis and extrapyramidal disorders; dysphasia, lightheadedness

Respiratory System: dyspnea, bronchospasm, allergic pneumonitis, stridor

Skin/Hypersensitivity: anaphylactic (-toid) reactions/shock; purpura, serum sickness, erythema multiforme/Stevens-Johnson Syndrome, erythema nodosum, exfoliative dermatitis, hyperpigmentation, toxic epidermal necrolysis, conjunctivitis, photosensitivity/phototoxicity reaction, vesiculobullous eruption

Special Senses: diplopia, nystagmus, blurred vision, disturbances of: taste, smell, hearing and equilibrium, usually reversible following discontinuation

Urinary System: anuria, polyuria, renal calculi, renal failure, interstitial nephritis, hematuria Laboratory.

Hematopoietic: prolongation of prothrombin time

Serum chemistry: acidosis, elevation of: serum triglycerides, serum cholesterol, serum potassium, liver function tests including: GGTP, LDH, bilirubin.

Urinary: albuminuria, candiduria In clinical trials using multiple-dose therapy, ophthalmologic abnormalities, including cataracts and multiple punctate lenticular opacities, have been noted in patients undergoing treatment with other quinolones. The relationship of the drugs to these events is not presently established. Crystalluria and Cylindruria have been reported with other quinolones.

Ornidazole

Mild side effects such as somnolence, headache and gastrointestinal disturbances like nausea and vomiting may occur. Disturbances of the CNS such as dizziness, tremor, rigidity, poor coordination, seizures, tiredness, vertigo, temporary loss of consciousness and signs of sensory or mixed peripheral neuropathy have been observed in isolated cases. Taste disturbances, abnormal liver function tests and skin reactions have been observed.

Blood and lymphatic system: rarely – signs of influence on formation of bone marrow and neutropenia.

Immune system: rarely – signs of skin allergic reactions and reactions of hypersensitivity.

Nervous system: rarely – tremor, rigidity, incoordination, convulsions, temporarily loss of consciousness, signs of sensor and mixed peripheral neutropenia, dizziness, somnolence, headache, fatigability.
Gastrointestinal System: nausea, vomiting, metal taste in mouth, change of taste, change of liver functional test.

4.9 Overdose

Ofloxacin

The most important signs to be expected following acute overdosage 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 adsorbants 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

Symptoms: convulsions, depression, peripheral neuritis, and symptoms mentioned in "Adverse effects" section, but in more severe form. Treatment is symptomatic, specific antidote is unknown, in convulsions – intravenous introduction of diazepam. Gastric lavage or hemodialysis is recommended for ornidazole excretion from the organism.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Ofloxacin

Pharmacotherapeutic group: Quinolone antibacterials, Fluoroquinolones. Ofloxacin is a quinolonecarboxylic acid derivative with a wide range of antibacterial activity against both gram negative and gram positive organisms. It is active after oral administration. It inhibits bacterial DNA replication by blocking DNA topo-isomerases, in particular DNA gyrase. Therapeutic doses of ofloxacin are devoid of pharmacological effects on the

voluntary or autonomic nervous systems. 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, Gardnerella. Variable sensitivity is shown by Streptococci, Serratia marcescens, Pseudomonas aeruginosa and Mycoplasmas. Anaerobic bacteria (e.g. Fusobacterium species, Bacteroides species, Eubacterium species, Peptococci, Peptostreptococci) are normally resistant.

Ornidazole

Ornidazole is an antiprotozoal and antibacterial agent; it is a derivative of 5-nitroimidazole. It is effective against Trichomonas vaginalis, Entamoeba histolitica, Giardia lamblia (Giardia intestinalis) and some other anaerobic bacteria, such as Gardnerella vaginalis, Bacteroides and Clostridium spp., Fusobacterium spp., and anaerobic coccus. By mechanism of action ornidazole is a DNA-tropic agent with selective activity against microorganisms, which have enzyme systems able to renew nitro group and catalyze an interaction of ferredoxin proteins with nitrocompounds. After preparation penetration into microbial cell the mechanism of its action is cause by renovation of nitro group under an influence of nitroreductase of microorganism and activity of renewed nitroimidazole. Products of renovation form complexes with DNA, causing its degradation, disturb processes of replication and transcription of DNA. In addition, products of preparation metabolism have cytostatic properties and disturb processes of cell respiration.

5.2 Pharmacokinetic properties

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 200 to 400 mg is predictable, and the amount of drug absorbed increases proportionately with the dose. Ofloxacin has biphasic elimination. Following multiple oral doses at steady-state

administration, the halflives are approximately 4 to 5 hours and 20 to 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. In vitro, approximately 32% of the drug in plasma is protein bound. Following oral administration of recommended therapeutic doses, ofloxacin has been detected in blister fluid, cervix, lung tissue, ovary, prostatic fluid, prostatic tissue, skin, and sputum. The mean concentration of ofloxacin in each of these various body fluids and tissues after one or more doses was 0.8 to 1.5 times the concurrent plasma level. Inadequate data are presently available on the distribution or levels of ofloxacin in the cerebrospinal fluid or brain tissue. Ofloxacin has a pyridobenzoxazine ring that appears to decrease the extent of parent compound metabolism. Between 65% and 80% of an administered oral dose of ofloxacin is excreted unchanged via the kidneys within 48 hours of dosing. Studies indicate that less than 5% of an administered dose is recovered in the urine as the desmethyl or Noxide metabolites. Four to eight percent of an ofloxacin dose is excreted in the feces. This indicates a small degree of biliary excretion of ofloxacin. The administration of ofloxacin with food does not affect the C max and AUC∞ of the drug, but Tmax is prolonged. Clearance of ofloxacin is reduced in patients with impaired renal function (creatinine clearance rate $\leq$ 50 mL/min), and dosage adjustment is necessary. Following oral administration to healthy elderly subjects (65 to 81 years of age), maximum plasma concentrations are usually achieved one to two hours after single and multiple twice-daily doses, indicating that the rate of oral absorption is unaffected by age or gender. Mean peak plasma concentrations in elderly subjects were 9 to 21% higher than those observed in younger subjects. Gender differences in the pharmacokinetic properties of elderly subjects have been observed. Peak plasma concentrations were 114% and 54% higher in elderly females compared to elderly males following single and multiple twice-daily doses. Plasma concentrations increase dose-dependently with the increase in doses after single oral dose and at steady state. No differences were observed in the volume of distribution values between elderly and younger subjects. As in younger subjects, elimination is mainly by renal excretion as unchanged drug in elderly subjects, although less drug is recovered from renal excretion in elderly subjects. Consistent with younger subjects, less than 5% of an administered

dose was recovered in the urine as the desmethyl and N-oxide metabolites in the elderly. A longer plasma half-life of approximately 6.4 to 7.4 hours was observed in elderly subjects, compared with 4 to 5 hours for young subjects. Slower elimination of ofloxacin is observed in elderly subjects as compared with younger subjects which may be attributable to the reduced renal function and renal clearance observed in the elderly subjects. Because ofloxacin is known to be substantially excreted by the kidney, and elderly patients are more likely to have decreased renal function, dosage adjustment is necessary for elderly patients with impaired renal function as recommended for all patients.

Ornidazole

Absorption

Ornidazole is rapidly absorbed. Mean absorption is 90%. Peak plasma concentrations are reached within three hours.

Distribution

The mean volume of distribution after i.v. administration is 1 litre per kg. Plasma protein binding of ornidazole is about 13%. The active ingredient of Ornidazole penetrates the cerebrospinal fluid, the body fluids and the tissues very effectively. Plasma concentrations are within the range considered to be optimal for the various indications (6 to 36 mg/l). After repeated administration of 500 mg or 1000 mg every twelve hours to healthy volunteers, an accumulation factor of 1.5-2.5 was calculated.

Metabolism

Ornidazole is mainly metabolised to 2-hydroxymethyl and a-hydroxymethyl metabolites in the liver. Both main metabolites are less active against Trichomonas vaginalis and anaerobic bacteria than the unchanged ornidazole.

Elimination

The half-life is about thirteen hours. 85% of a single dose is eliminated within the first five days, most of this being metabolised. 4% of the dose is excreted as unaltered substance in the urine.

5.3 Preclinical safety data

Sub-Chronic Toxicity Study of Fixed Dose Combination of Ofloxacin Ornidazole in Mus Musculus Mice shows no mortality. Hematological as well as physiological parameters were unaltered at three dose levels in Ofloxacin-Ornidazole treatment groups. Results suggest that the fixed dose combination of Ofloxacin-Ornidazole injection is non-toxic even at maximum dose level.

6.1 List of excipients

Microcrystalline Cellulose, Starch, PVP K-30, Purified Water, Talc, Magnesium Stearate, Crosscarmelose Sodium, Colloidal Silicon Dioxide, Readymix coat material and Sunset Yellow

6.2 Incompatibilities

None known

6.3 Shelf life

36 Months

6.4 Special precautions for storage

Store at a temperature not exceeding 30°C. Protect from light and moisture.

Keep out of reach of children.

6.5 Nature and contents of container

1 x 10 tablet packed in a carton.

6.6 Special precautions for disposal and other handling

Not applicable.

7. Marketing authorisation holder

PHARMA ETHICS LTD.

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