1.3.1 Summary of Product Characteristics (SmPC)

1- Name of the Medicinal Product:

1.1 Product Name

-Generic Name or International Non-Proprietary Name (INN)

(Ofloxacin Tablets USP 400 mg)

Brand Name-

SPEXACIN

1.2 Dosage Strength

Each Film Coated Tablet Contains:
Ofloxacin USP…… 400 mg
Excipients……q.s
Colours: Titanium Dioxide

1.3 Dosage Form

Film coated Tablets

2- Quality and Quantitative Composition:

2.1 Qualitative Declaration

Each Film Coated Tablet Contains:
Ofloxacin USP…… 400 mg
Excipients……q.s
Colours: Titanium Dioxide

2.2 **Composition: Batch Size: 1,00,000 Tablets**

Sr. No	Ingredients	Specification	mg/Tab	Overages %	Qty/ Batch 1 lac in Kg	Function
	Sifting/Mixing					
1	Ofloxacin	USP	400.000	---	40.000	Active
2	Dibasic Calcium Phosphate	BP	40.000	---	4.000	Diluent
3	Maize Starch	BP	81.890	---	8.189	Diluent
	Paste Preparation					
4	Maize starch	BP	16.000	---	1.600	Diluent
5	Gelatin	BP	2.000	---	0.200	Diluent
6	Purified water	BP	QS	---	QS	Binding solvent
7	Methyl paraben	BP	0.100	---	0.010	Preservative
8	Propyl paraben	BP	0.010	---	0.001	Preservative
	Lubrication					
9	Cross carmellose sodium (Vivasole)	BP	40.000	---	4.000	Disintegrate agent
10	Colloidal Silicon Dioxide (Light)	BP	6.000	---	0.600	Lubricant
11	Magnesium Stearate	BP	8.000	---	0.800	Lubricant
12	Talcum	BP	6.000	---	0.600	Lubricant

Sr. No	Ingredients	Specification	mg/Tab	Overages %	Qty/ Batch 1 lac in Kg	Function
Average Wt. of Uncoated Tablet			**600 mg**	**Limit: 600 ±5%**		
	Coating					
13	Titanium Dioxide	BP	1.000	---	0.100	Opacifier
14	Talcum	BP	1.500	---	0.150	Lubricant
15	H.P.M.C. E 15	BP	7.000	---	0.700	Film forming agent
16	Iso Propyl Alcohol	BP	150.000	---	15.000	Coating solvent
17	Methylene Chloride DCM	BP	210.000	---	21.000	Coating solvent
18	PEG 6000	BP	0.500	---	0.050	Plasticizer
Average Wt. of coated Tablet			**610 mg**	**Limit: 610±5%**		

Note: Active material was calculated on assay or Potency Basis.
BP = British Pharmacopoeia
IHS= In House Specification

19	Iso Propyl Alcohol*	---	BP	108.000	10.800	Coating Solvent
20	Sunset Yellow Lake	---	IH	1.750	0.175	Colour
Avg. Weight of Film coated tablet				**970.20 mg**	**Limit: 970.20± 5.0%**	

NOTE: Active material is to be calculated on Assay / Potency basis.
USP = United States Pharmacopoeia,
BP = British Pharmacopoeia.
* Does not appear in the finished Product.

3- Pharmaceutical Form:

Orange coloured capsule shaped film coated tablet having break line on one side and other side plain.

4- Clinical Particulars:

4.1 Therapeutic indications.

Ofloxacin Ornidazole Tablet is a medicine that is used for the treatment of Bacterial infections, Urinary tract infections, Bacterial infections by inflammation of the peritoneum, Inflammatory discharge from the urethra or vagina, Eye and ear infection, Bacterial infection and other conditions.

The complete list of uses and indications for Ofloxacin Ornidazole Tablet is as follows:

- Bacterial infections
- Urinary tract infections
- Bacterial infections by inflammation of the peritoneum
- Inflammatory discharge from the urethra or vagina
- Eye and ear infection
- Bacterial infection
- Typhoid fever
- Skin infections
- Sexually transmitted infections
- Protozoan infections
- Respiratory infections
- Typhoid
- Infections of the skin

- Vaginal infections
- Soft tissue infections
- Infections during surgical procedures
- Vaginal infection
- Tuberculosis
- Skin infection
- Infections of the urinary tract
- Infections of vagina
- Infection of respiratory tract
- Phthisis
- Vagina infection
- Sexually transmitted infection
- Infection of the vagina
- Respiratory infection
- Urinary tract infection

Ofloxacin Ornidazole Tablet may also be used for purposes not listed here.

4.2 Posology and method of administration

Ofloxacin and ornidazole tablet dosage and duration of treatment are depended on bacteria sensitivity, and infection kind and severity. The average dose for adults is 1-2 tablets two times per day during 7-10 days. The treatment should be prolonged not less than 3 days after the disappearing of clinical symptoms.

In general doctors prefer the combination of Ofloxacin &ornidazole in the dosage of one tablet twice daily for 5-10 days.

In 1. Diarrhea& Dysentery,

2. Gastroenteritis,

3. Lower respiratory & Urinary tract infection & pelvic inflammatory diseases,

4. Septic abortion,

5. Puerperal sepsis

6. Post-surgical infection,

7. Skin & soft tissue infection,

8. ENT infections,

9. Oro-dental Infections.

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

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

4.3 Contraindications

The drug is contraindicated in patients with known hypersensitivity to this product or any of its ingredients. It is not advocated during the first trimester of pregnancy and in those with history of tendinitis or tendon rupture following use of quinolones. Because of the potential for serious adverse reactions in the nursing infant, the drug must be either stopped or discontinued during lactation for at least 3 days, depending on the importance of the drug to the lactating mother.

4.4 Special warning and precautions for use

If you use other drugs or over the counter products at the same time, the effects of Ofloxacin Ornidazole Tablet may change. This may increase your risk for side-effects or cause your drug not to work properly. Tell your doctor about all the drugs, vitamins, and herbal supplements you are using, so that you doctor can help you prevent or manage drug interactions. Ofloxacin Ornidazole Tablet may interact with the following drugs and products:

Amiodarone

Anti-psychotics

Azithromycin

Disopyramide

Dofetilide

Hydroquinidine

Ibutilide

Quinidine

Sotalol

Tricyclic antidepressants

Vecuronium bromide

Warfarin

Before using Ofloxacin Ornidazole Tablet, inform your doctor about your current list of medications, over the counter products (e.g. vitamins, herbal supplements, etc.), allergies, pre-existing diseases, and current health conditions (e.g. pregnancy, upcoming surgery, etc.). Some health conditions may make you more susceptible to the side-effects of the drug. Take as directed by your doctor or follow the direction printed on the product insert. Dosage is based on your condition. Tell your doctor if your condition persists or worsens. Important counseling points are listed below.

- Avoid consuming milk and dairy products
- Consult the doctor in case of pregnancy or breastfeeding
- Consult your doctor before taking this medicine if having epilepsy and multiple sclerosis
- Do not consume if you have any disease condition like epilepsy or kidney problems
- Do not consume ofloxacin if allergic to it
- Do not drive a vehicle or operate heavy machinery after consuming the medicine
- Do not drive or operate heavy machinery
- Do not take the medicine on empty stomach
- Swallow the tablet whole with water

4.5 Interaction with other medicinal products and other forms of interaction

Antacids, Sucralfate, Metal Cations

Co-administered magnesium/aluminum antacids, sucralfate, zinc or iron preparations and didanosine chewable/buffered tablets can reduce absorption of ofloxacin tablets. Therefore, ofloxacin should be taken 2 hours before such preparations.

Theophylline, fenbufen or similar non-steroidal anti-inflammatory drugs

No pharmacokinetic interactions of ofloxacin were found with theophylline in a clinical study. However, a pronounced lowering of the cerebral seizure threshold may occur when quinolones are given concurrently with theophylline, nonsteroidal anti-inflammatory drugs, or other agents, which lower the seizure threshold.

Probenecid, cimetidine, furosemide, and methotrexate

Probenecid decreased the total clearance of ofloxacin by 24%, and increased AUC by 16%. The proposed mechanism is a competition or inhibition for active transport at the renal tubular excretion. Caution should be exercised when ofloxacin is coadministered with drugs that affect the tubular renal secretion such as probenecid, cimetidine, furosemide and methotrexate.

Drugs known to prolong QT interval

Ofloxacin, like other fluoroquinolones, should be used with caution in patients receiving drugs known to prolong the QT interval (e.g. Class IA and III antiarrhythmics, tricyclic antidepressants, macrolides, and antipsychotics)

Vitamin K antagonists

Increased coagulation tests (PT/INR) and/or bleeding, which may be severe, have been reported in patients treated with ofloxacin in combination with a vitamin K antagonist (e.g. warfarin). Coagulation tests should, therefore, be monitored in patients treated with vitamin K antagonists because of a possible increase in the effect of coumarin derivatives.

Glibenclamide

Ofloxacin may cause a slight increase in plasma glibenclamide levels when administered concurrently, it is therefore recommended that patients treated concomitantly with ofloxacin and glibenclamide be monitored particularly closely.

Since hypoglycaemia is then more likely to occur, close monitoring of blood sugar levels is recommended in such cases.

4.6 Fertility, Pregnancy and lactation

Pregnancy

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 must not be used during pregnancy

Breast-feeding

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 (see section 4.3).

4.7 Effects on ability to drive and use machine

Since there have been occasional reports of drowsiness/somnolence, impairment of skills, dizziness/vertigo and visual disturbances, which may impair the patient's ability to concentrate and react, and therefore may constitute a risk in situations where these abilities are of special importance (e.g. driving a car or operating machinery), patients should know how they react to ofloxacin before they drive or operate machinery. These effects may be enhanced by alcohol.

4.8 Undesirable effects

The information given below is based on data from clinical studies and on extensive post marketing experience.

System organ class	**Uncommon (≥1/1,000 to <1/100)**	**Rare (≥1/10,000 to <1/1,000)**	**Very rare (< 1/10,000)**	**Not known (cannot be estimated from available data)***
Infections and infestations	Fungal infection, Pathogen resistance			
Blood and lymphatic system disorders			Anaemia, Haemolyticanaemia, Leucopenia, Eosinophilia, Thrombocytopenia	Agranulocytosis, Bone marrow failure, Pancytopenia
Immune system disorders		Anaphylactic reaction*, Anaphylactoid	Anaphylactic shock*, Anaphylactoid shock*	

		reaction*, Angioedema*		
Metabolism and Nutrition disorders		Anorexia		Hypoglycaemia in diabetics treated with hypoglycaemic agents (see section 4.4), Hyperglycaemia, Hypoglycaemic coma
Psychiatric disorders	Agitation, Sleep disorder, Insomnia	Psychotic disorder (for e.g. hallucination), Anxiety, Confusional state, Nightmares, Depression		Psychotic disorder and depression with self-endangering behaviour including suicidal ideation or suicide attempt (see Section 4.4), Nervousness
Nervous system disorders	Dizziness, Headache	Somnolence, Paraesthesia, Dysgeusia, Parosmia	Peripheral sensory neuropathy*, Peripheral sensory motor neuropathy*, Convulsion*, Extra-pyramidal symptoms or other disorders of muscular coordination	Tremor, Dykinesia, Ageusia, Syncope
Eye disorders	Eye irritation	Visual disturbance		Uveitis
Ear and labyrinth disorders	Vertigo		Tinnitus, Hearing loss	Hearing impaired
Cardiac disorders		Tachycardia		Ventricular arrhythmias and torsades de pointes (reported predominantly in patients with risk factors for QT prolongation), ECG QT prolonged (see section 4.4 and 4.9)
Vascular disorders		Hypotension		
Respiratory, thoracic and mediastinal disorders	Cough, Nasopharyngitis	Dyspnoea, Bronchospasm		Allergic pneumonitis, Severe dyspnoea
Gastrointestinal disorders	Abdominal pain, Diarrhoea, Nausea, Vomiting	Enterocolitis, sometimes haemorrhagic	Pseudomembranous colitis*	Dyspepsia, Flatulence, Constipation, Pancreatitis
Hepatobiliary disorders		Hepatic enzymes increased (ALAT, ASAT, LDH, gamma-GT and/or alkaline phosphatase), Blood bilirubin increased	Jaundice cholestatic	Hepatitis, which may be severe* Severe liver injury, including cases with acute liver failure, sometimes fatal, have been reported with ofloxacin, primarily in patients with underlying liver disorders (see section 4.4).
Skin and subcutaneous tissue disorders	Pruritus, Rash	Urticaria, Hot flushes, Hyperhidrosis Pustular rash	Erythema multiforme, Toxic epidermal necrolysis, Photo-sensitivity reaction*,	Stevens-Johnson syndrome, Acute generalisedexanthemouspustulosis, Drug rash, Stomatitis

			Drug eruption , Vascular purpura, Vasculitis, which can lead in exceptional cases to skin necrosis	Exfoliative dermatitis
Musculoskeletal and connective tissue disorders		Tendonitis	Arthralgia, Myalgia, Tendon rupture (e.g. Achilles tendon) which may occur within 48 hours of treatment start and may be bilateral	Rhabdomyolysis and/or Myopathy, Muscular weakness, Muscle tear, Muscle rupture, Ligament rupture, Arthritis
Renal and urinary disorders		Serum creatinine increased	Acute renal failure	Acute interstitial nephritis
Congenital, familial and genetic disorders				Attacks of porphyria in patients with porphyria
General disorders and administration site conditions				Asthenia, Pyrexia, Pain (including pain in back, chest and extremities)

* postmarketing experience

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard.

4.9 Overdose and treatment

Symptoms

The most important signs to be expected following acute overdose are CNS symptoms such as confusion, dizziness, impairment of consciousness and convulsive seizures increases in 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.

Management

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.

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

5- Pharmacological Properties:

5.1 Pharmacodynamic Properties

Pharmacotherapeutic group: Quinolone Antibacterials, Fluoroquinolones

ATC code:J01 MA 01

Mechanism of action

Ofloxacin inhibits bacterial DNA replication by inhibiting bacterial topoisomerases, particularly DNA gyrase and topoisomerase IV. It is active after oral administration.

Therapeutic doses of ofloxacin are devoid of pharmacological effects on the voluntary or autonomic nervous system.

The NCCLS MIC breakpoint recommendations are as follows:

S ≤ 2 mg/l and R ≥ 1 mg/l

Haemophilus influenzae and *Neisseria gonorrhoea* are exceptions with breakpoints at S ≤ 0.25 mg/l and R ≥ 1 mg/l

The BSAC general recommendations are S ≤ 2 mg/l and R ≥ 4 mg/l

According to DIN 58 940, the following limits apply for ofloxacin:

S ≤ 1 mg/L, I = 2 mg/L, R ≥ 4 mg/L.

The prevalence of resistance may vary geographically and with time for selected species and local information on resistance is desirable, particularly when treating severe infections. This information gives only an approximate guidance on probabilities whether micro-organisms will be susceptible to ofloxacin or not.

Only those pathogens relevant to the indications are listed.

	European range of acquired bacterial resistance to ofloxacin
Normally susceptible	
Aerobic Gram-positive micro organisms	
S. aureus - methicillin-sensitive	0.3-12.6%
S. pyogenes	2-5%

Aerobic Gram-negative micro organisms	
Acinetobacter spp	0.3-7.3%
Citrobacter spp.	3-15%
Enterobacter spp.	2-13%
E. coli	1-8%
H. influenzae	1%
Klebsiella spp.	1-10%
Moraxella spp.	0-0.2%
Morganellamorganii	0-6.9%
N. gonorrhoeae	25%
Proteus spp.	1-15%
Serratiamarcescens	2-2.4%
Others	
Chlamydia spp	
L. pneumophila	
Intermediately susceptible	
Aerobic Gram-positive micro organisms	
S. pneumoniae	70%
Providentia	17.1%
Aerobic Gram-negative micro organisms	
E. faecalis	50%
P. aeruginosa	20-30%
Serratia spp.	20-40%
Stenotrophomonasmaltophilia	5.1-11%
Others	
Mycoplasma spp.	0-5.3%
Ureaplasma spp.	0-2.1%
Resistant	
Anaerobic bacteria	
S. aureus - methicillin-resistant	69.2-85.7%
T. pallidum	

Resistance

The main mechanism of bacterial resistance to ofloxacin involves one or more mutations in the target enzymes, which generally confer resistance to other active substances in the class. Efflux pump and impermeability mechanisms of resistance have also been described and may confer variable resistance to active substances in other classes.

5.2 Pharmacokinetic Properties

Absorption

The administration of oral doses to fasting volunteers was followed by a rapid and almost complete absorption of ofloxacin. The peak plasma concentration after a single oral dose of 200mg averaged 2.6 µg/ml and was reached within one hour. The plasma elimination half-life was 5.7 to 7.0 hours and was not dose related.

Distribution

The apparent distribution volume was 120 litres. The plasma concentration did not materially rise with repeat doses (accumulation factor for twice daily dosage: 1.5). The plasma protein binding was approx. 25%.

Biotransformation

The biotransformation of ofloxacin was below 5%. The two main metabolites found in the urine were N-desmethyl-ofloxacin and ofloxacin-N-oxide.

Elimination

Excretion is primarily renal. Between 80 and 90% of the dose were recovered from the urine as unchanged substance.

Ofloxacin was present in the bile in glucuronidised form. The pharmacokinetics of ofloxacin after intravenous infusion are very similar to those after oral doses. The plasma half-life is prolonged in persons with renal insufficiency; total and renal clearance decrease in accordance with the creatinine clearance. In renal insufficiency the dose should be reduced.

No clinically relevant interactions were seen with food and no interaction was found between ofloxacin and theophylline.

5.3 Preclinical safety Data

Preclinical effects in conventional studies of safety pharmacology, acute toxicity, repeated dose toxicity, reproductive studies were observed only at exposures considered sufficiently in excess of the maximum human exposure indicating little relevance to clinical use. Joint toxicity was observed at exposure in the human therapeutic range in juvenile rats and dogs. Ofloxacin exhibits a neurotoxic potential and causes reversible testicular alterations at high doses.

Mutagenicity studies showed no evidence for mutagenicity of ofloxacin. However, like some other quinolones Ofloxacin is phototoxic in animals at exposure in the human therapeutic range. The phototoxic, photomutagenic and photocarcinogenic potential of ofloxacin is comparable with that of other gyrase inhibitors.

Preclinical data from conventional genotoxicity studies reveal no special hazard to humans, carcinogen potential has not be investigated.

6- Pharmaceutical Particulars :

6.1 List of Excipients

Dibasic Calcium Phosphate
Maize Starch
Gelatin
Purified water
Cross Carmellose sodium (Vivasole)
Magnesium Stearate
Talcum
Titanium Dioxide
Tartrazine Yellow Lake
Sodium Starch Glycolate
H.P.M.C. E 15
Lack of Tartrazine
Sunset Yellow Lake
Iso Propyl Alcohol
Methylene Chloride DCM
PEG 6000

6.2 Incompatibilities

None known

6.3 Shelf life

36 months from the date of manufacture.

6.4 Special precautions for storage

Store in a cool and dry place, protected from light

6.5 Nature and contents of container

10 tablets packed in one blister. Such 1 blister packed in unit printed duplex board carton along with its package insert. Such 10 unit printed carton packed in box and such box add in export worthy shipper.

7- Marketing Authorization Holder:

- **Name** : APHANTEE FORMULATION NIG. LTD.

- **Address** : Suit FF11, First Floor,
Pacific Complex No. 9,
Awka Road, Onitsha,
Anambra State, Nigeria..

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8- Marketing Authorization Number (s) :

-Product license / registration Number (s)

9- Manufacturer Name:

- **Name** : **GLOBELA PHARMA PVT. LTD.**

- **Address** : Plot No. 357, G.I.D.C.,
Sachin,
Surat – 394 230,
Gujarat,
India.

- **Phone** : +91– 261–2398058
- **Fax** : +91– 261–2398058
- **E-mail** : info@globelapharma.com

10- Date of first authorization/renewal of the authorization:

11- Date of revision of the text:
