1.3 Product Information

1.3.1 Summary of product characteristics (SmPC)

1. 3.1.1 Name of the medicinal product: BGVID 400
(Ofloxacin Tablets USP 400 mg)

1.3. 1.2 Qualitative and quantitative composition:

Each film coated tablet contains:
Ofloxacin USP .....400 mg
Excipients. ..... q.s
Approved colour used.

Sr. No.	Name of Ingredient	Specification	Label Claim	Overages added (In %)	Quantity/ Tablet in mg	Reason for Function
a)	**Dry Mixing**					
1.	Ofloxacin	USP	400mg	NA	400.00	Medicament
2.	Lactose monohydrate	BP	NA	NA	130.00	Diluent
3.	Maize starch	BP	NA	NA	78.28	Diluent
b)	**Binder Preparation**					
4.	Maize starch	BP	NA	NA	28.41	Binder
5.	Povidone (K 30)	BP	NA	NA	5.00	Binder
6.	Methyl hydroxybenzoate	BP	NA	NA	0.38	Preservative
7.	Propyl hydroxybenzoate	BP	NA	NA	0.09	Preservative
8.	Purified water	BP	NA	NA	----	Vehicle
c)	**Lubrication**					
9.	Croscarmellose sodium	BP	NA	NA	19.89	Disintergrant
10.	Colloidal anhydrous silica	BP	NA	NA	5.00	Disintergrant
11.	Purified talc	BP	NA	NA	7.95	Lubricant
12.	Magnesium stearate	BP	NA	NA	5.00	Lubricant
		Compressed weight per tablet (in mg)			**680.000**	
d)	**Film Coating**					
13.	Hypromellose (15 CPS)	BP	NA	NA	8.00	Film Former
14.	Titanium dioxide	BP	NA	NA		Colour
15.	Purified talc	BP	NA	NA		Antiadherant
16.	Macrogol-6000	BP	NA	NA		Plasticizer
17.	Purified water	BP	NA	NA	----	Vehicle
		Average weight of film coated tablet (in mg)				

BGVID 400
(Ofloxacin Tablets USP 400 mg)

1. 3.1.3 Pharmaceutical form: Film coated Tablet

Description: An off-white coloured, capsule shaped, biconvex, film coated tablet, breakline on one side, plain on other side.

1.3.1.4 Clinical Particulars
1.3.1.4.1 Therapeutic indications:
BGVID 400 (Ofloxacin Tablets USP 400 mg) are indicated for the treatment of Lower respiratory tract infections including pneumonia, bronchitits and acute exacerbations of chronic bronchitis caused by gram negative aerobic bacteria, Upper and lower urinary tract infections, including uncomplicated (cystitis) and complicated urinary tract infections and Uncomplicated urethral and cervical gonorrhoea, non-gonococcal urethritis and cervicitis.

1.3.1.4.2 Posology and method of administration
Route: Oral

Method of Administration:
Always take this medicine exactly as your doctor or pharmacist has told you.
Check with your doctor or pharmacist if you are not sure.
The usual dose of Ofloxacin tablets is 400 mg orally every 12 hrs.

Indications	Single and Daily Doses
Gonococcal urethritis and cervicitis due to susceptible Neisseria gonorrhoeae	400 mg
Uncomplicated cystitis	200 mg-400 mg daily
Acute pyelonephritis and complicated urinary tract infections	400 mg daily, increasing if necessary, to 400 mg twice a day
Community-acquired pneumonia. Acute exacerbations of chronic obstructive pulmonary disease including bronchitis.	400 mg daily, increasing, if necessary, to 400 mg twice a day
Non-gonococcal urethritis and cervicitis	400 mg daily

A single dose of 400 mg of ofloxacin is sufficient for the treatment of gonococcal urethritis and cervicitis due to susceptible *Neisseria gonorrhoeae*.

1.3.1.4.3 Contraindications
BGVID 400(Ofloxacin Tablets USP 400 mg) are contraindicated-
- In persons with a history of hypersensitivity associated with the use of ofloxacin or any member of the quinolone or nitroimidazole group of antimicrobial agents.
- In patients with a history of epilepsy or an existing central nervous system disorder with a lowered seizure threshold.
- In patients with a history of tendon disorders related to fluoroquinolone administration
- In children or growing adolescents, and in pregnant or breastfeeding women, since animal experiments do not entirely exclude the risk of damage to the growth-plate cartilage in the growing organism cannot be entirely excluded.
- In patients with latent or actual defects in glucose-6-phosphate dehydrogenase activity because they may be prone to haemolytic reactions when treated with quinolone antibacterial agents.

1.3.1.4.4 Special warnings and precautions for use
• **Methicillin-resistant S. aureus :** Are very likely to possess co-resistance to fluoroquinolones, including ofloxacin. Therefore ofloxacin is not recommended for the treatment of known or

suspected MRSA infections unless laboratory results have confirmed susceptibility of the organism to ofloxacin.

- **Resistance to fluoroquinolones of E. coli :** The most common pathogen involved in urinary tract infections – varies across the European Union. Prescribers are advised to take into account the local prevalence of resistance in E. coli to fluoroquinolones.
- **Severe bullous reactions :** Cases of severe bullous skin reactions such as Stevens-Johnson syndrome or toxic epidermal necrolysis have been reported with ofloxacin. Patients should be advised to contact their doctor immediately prior to continuing treatment if skin and/or mucosal reactions occur.
- **Tendonitis :** Ofloxacin have been associated with an increased risk of tendinitis and tendon rupture in all ages. This adverse reaction most frequently involves the Achilles tendon and rupture of the Achilles tendon, and has also been reported with the rotator cuff (the shoulder), the hand, the biceps, the thumb, and other tendons. Tendinitis or tendon rupture can occur within hours or days of starting ofloxacin, or as long as several months after completion of fluoroquinolone therapy. Tendinitis and tendon rupture can occur bilaterally.
- **Hypersensitivity :** 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 should be initiated.
- **Diseases caused by Clostridium difficile :** Diarrhoea, especially if severe, persistent and/or bloody, occurring during or after treatment with ofloxacin (including several weeks after treatment), may indicate a condition caused by Clostridium difficile, the most severe form of which is pseudomembranous colitis (CDAD) CDAD may range in severity from mild to life threatening, the most severe form of which is pseudomembranous colitis. It is therefore important to consider this diagnosis in patients who develop serious diarrhoea during or after treatment with ofloxacin. If pseudo-membraneous colitis is suspected, treatment should be discontinued immediately.
- **Patients predisposed to seizures :** Quinolones may lower the seizure threshold and may trigger seizures. Ofloxacin is contraindicated in patients with a history epilepsy or with a known predisposition to seizures. Patients with a known predisposition to seizures may include those with pre-existing central nervous system lesions, concomitant treatment with fenbufen and similar non-steroidal anti-inflammatory drugs (NSAIDs), or with drugs which lower the cerebral seizure threshold, such as theophylline.In case of convulsive seizures, treatment with ofloxacin should be discontinued.
- **Patients with impaired renal function :** Since ofloxacin is eliminated primarily via the kidneys, the dose should be adjusted in patients with impaired renal function.
- **Patients with history of psychotic disorder :** Psychotic reactions have been reported in patients receiving fluoroquinolones including ofloxacin. Ofloxacin should be used with caution in patients with a history of psychotic disorder or in patients with psychiatric disease.
- **Patients with impaired liver function :** Ofloxacin should be used with caution in patients with impaired liver function, as liver damage may occur.
- **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 :** Ofloxacin have neuromuscular-blocking activity and may exacerbate muscle weakness in persons with myasthenia gravis.
- **Prevention of photosensitisation :** Photosensitisation has been reported with ofloxacin. It is recommended that patients should not expose themselves unnecessarily to strong sunlight or to

artificial UV rays (e.g. sunray lamp, solarium), during treatment and for 48 hours following treatment discontinuation in order to prevent photosensitisation.

- **QT interval prolongation :** Ofloxacin have been associated with prolongation of the QT interval on the electrocardiogram and infrequent cases of arrhythmia.
- **Peripheral neuropathy :** Ofloxacin have been associated with an increased risk of peripheral neuropathy. Cases of sensory or sensorimotor axonal polyneuropathy affecting small and/or large axons, resulting in paraesthesia, hypoesthesia, dysaesthesia and weakness, have been reported in patients receiving fluoroquinolones, including ofloxacin.

1.3.1.4.5 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

However, a pronounced lowering of the cerebral seizure threshold may occur when quinolones are given concurrently with theophylline, nonsteroidal antiinflammatory 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.

1.3.1.4.6 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

Lactation

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.

1.3.1.4.7 Effects on the ability to drive and use machines

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.

1.3.1.4.8 Undesirable effects

The most common side effects are

- Peeling or blistering of the skin
- Unusual bruising or bleeding
- Loss of appetite
- Pain, swelling, or itching of the vagina
- Stomach pain or cramps

Adverse reactions reported are as follows:

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, Haemolytic anaemia, Leucopenia, Eosinophilia, Thrombocytopenia	Agranulocytosis, Bone marrow failure, Pancytopenia
Immune system disorders		Anaphylactic reaction, Anaphylactoid reaction, Angioedema	Anaphylactic shock, Anaphylactoid shock	
Metabolism and Nutrition disorders		Anorexia		Hypoglycaemia in diabetics treated with hypoglycaemic agents, 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, 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
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.
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 generalised exanthemous pustulosis, Drug rash,

			Drug eruption , Vascular purpura, Vasculitis, which can lead in exceptional cases to skin necrosis	Stomatitis 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)

1.3.1.4.9 Overdoses

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.

Treatment

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.

1.3.1.5 Pharmacological properties

1.3.1.5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Quinolone Antibacterials, Fluoroquinolones.
ATC code: J01 MA 01
Mechanism of Action

Ofloxacin is a quinolone/ fluoroquinolone antibiotic. Ofloxacin is bactericidal and its mode of action depends on blocking of bacterial DNA replication by binding itself to an enzyme called DNA gyrase, which allows the untwisting required to replicate one DNA double helix into two. Notably the drug has 100 times higher affinity for bacterial DNA gyrase than for mammalian. Ofloxacin is a broad-spectrum antibiotic that is active against both Gram-positive and Gram-negative bacteria.

1.3.1.5.2 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 200 mg averaged 2.6 µg/ml and was reached within one hour. The plasma elimination half-life was 5.7 to 7 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.

1.3.1.5.3 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 been investigated.

1.3.1.6 Pharmaceutical particulars

1.3.1.6.1 List of excipients

Lactose monohydrate, Maize starch, Povidone (K 30), Methyl hydroxybenzoate, Propyl hydroxybenzoate, Croscarmellose sodium, Colloidal anhydrous silica, Purified talc, Magnesium stearate, Hypromellose (15 CPS), Titanium dioxide, Macrogol-6000.

1.3.1.6.2 Incompatibilities
Not applicable

1.3.1.6.3 Shelf life
36 months

1.3.1.6.4 Special precautions for storage
Store below 30°C in a dry & dark place.
Keep all medicines out of reach of children.

1.3.1.6.5 Nature and contents of container
Primary packing: 10 Tablets in an ALU-ALU Blister
Secondary packing: 1 Blister is packed in a carton along with leaflet.
Tertiary packing: Such 10 cartons are packed in a shrink. Such 100 Shrinks are packed in a 5 Ply shipper sealed with BOPP tape & strap with strapping roll.

1.3.1.6.5 Special precautions for disposal and other handling
None.

1.3.1.7 Applicant / Manufacturer Applicant	
Applicant name and address	**M/s. BG PHARMA & HEALTHCARE LTD\ PLOT 859 GUDU DISTRICT, ABUJA FCT NIGERIA**

Contact person's phone number

Contact person's email

Manufacturer	
Manufacturer name and address	**M/s. STALLIONS LABORATORIES PVT LTD**
	C-1B, 305/2,1 ,4 & 5 G.I.D.C KERALA (BAVLA) DISTRICT AHMEDABAD 382 220 GUJARAT INDIA Dist. Palghar - 401506, Maharashtra State, India.