Summary of Product Characteristics

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1. NAME OF THE MEDICINAL PRODUCT

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Norfloxacin Tablets BP 400 mg

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each Film coated tablet contains

Norfloxacin BP 400 mg

For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Tablets [Film Coated]

White to off white round biconvex film coated tablets

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

Urinary tract infections

Uncomplicated urinary tract infections (including cystitis) due to Enterococcus faecalis, Escherichia coli, Klebsiella pneumoniae, Proteus mirabilis, Pseudomonas aeruginosa, Staphylococcus epidermidis, Staphylococcus saprophyticus, Citrobacter freundii, Enterobacter aerogenes, Enterobacter cloacae, Proteus vulgaris, Staphylococcus aureus, or Streptococcus agalactiae.

Complicated urinary tract infections due to Enterococcus faecalis, Escherichia coli, Klebsiella pneumoniae, Proteus mirabilis, Pseudomonas aeruginosa, or Serratia marcescens.

Sexually transmitted diseases

Uncomplicated urethral and cervical gonorrhea due to Neisseria gonorrhoeae.

Prostatitis

Prostatitis due to Escherichia coli.

4.2 Posology and Method of administration

Infection	Description	Unit Dose	Frequency	Duration	Daily Dose
UTI Infection	Uncomplicated UTI's (cystitis) due to *E. coli*, *K. pneumoniae*, or *P. mirabilis*	400 mg	q12h	3 days	800 mg
	Uncomplicated UTI's due to other indicated	400 mg	q12h	7-10 days	800 mg

	organisms				
	Complicated UTI's	400 mg	q12h	10-21 days	800 mg
Sexually Transmitted Diseases	Uncomplicated Gonorrhea	800 mg	Single Dose	1 day	800 mg
Prostatitis	Acute or Chronic	400 mg	q12h	28 days	800 mg

Oral: route of administration

4.3 Contraindications

Norfloxacin is contraindicated in persons with a history of hypersensitivity, tendinitis, or tendon rupture associated with the use of Norfloxacin or any member of the quinolone group of antimicrobial agents.

4.4 Special warnings and precautions for use

Tendinopathy and Tendon Rupture

Fluoroquinolones, including Norfloxacin, are associated with an increased risk of tendinitis and tendon rupture in all ages. Norfloxacin should be discontinued if the patient experiences pain, swelling, inflammation or rupture of a tendon.

Exacerbation of Myasthenia Gravis

Fluoroquinolones, including Norfloxacin, have neuromuscular blocking activity and may exacerbate muscle weakness in persons with myasthenia gravis.

Central Nervous System Effects/Disorders

Convulsions have been reported in patients receiving Norfloxacin. Convulsions, increased intracranial pressure (including pseudotumor cerebri), and toxic psychoses have been reported in patients receiving drugs in this class.

Hypersensitivity Reactions

Serious and occasionally fatal hypersensitivity (anaphylactic) reactions, some following the first dose, have been reported in patients receiving quinolone therapy, including Norfloxacin. If an allergic reaction to Norfloxacin occurs, discontinue the drug.

Peripheral Neuropathy

Rare cases of sensory or sensorimotor axonal polyneuropathy affecting small and/or large axons resulting in paresthesias, hypoesthesias, dysesthesias and weakness have been reported in patients receiving quinolones, including norfloxacin.

Syphilis Treatment

Patients treated with Norfloxacin should have a follow up serologic test for syphilis after 3 months.

4.5 Interaction with other medicinal products and other forms of interact.

- Quinolones, including Norfloxacin, have been shown in vitro to inhibit CYP1A2. Concomitant use with drugs metabolized by CYP1A2 (e.g., Caffeine, Clozapine, Ropinirole, Tacrine, Theophylline, Tizanidine) may result in increased substrate drug concentrations when given in usual doses.
- Elevated plasma levels of Theophylline have been reported with concomitant Quinolone use. Therefore, monitoring of Theophylline plasma levels should be considered and dosage of theophylline adjusted as required.
- Elevated serum levels of Cyclosporine have been reported with concomitant use of cyclosporine with Norfloxacin. Therefore, Cyclosporine serum levels should be monitored and appropriate Cyclosporine dosage adjustments made when these drugs are used concomitantly.
- Quinolones, including Norfloxacin, may enhance the effects of oral anticoagulants, including Warfarin or its derivatives or similar agents. When these products are administered concomitantly, Prothrombin time or other suitable coagulation tests should be closely monitored.
- The concomitant administration of Quinolones including Norfloxacin with Glyburide (a sulfonylurea agent) has, on rare occasions, resulted in severe hypoglycemia. Therefore, monitoring of blood glucose is recommended when these agents are co-administered.
- Diminished urinary excretion of Norfloxacin has been reported during the concomitant administration of probenecid and Norfloxacin.
- The concomitant use of Nitrofurantoin is not recommended since Nitrofurantoin may antagonize the antibacterial effect of Norfloxacin in the urinary tract.
- Multivitamins, or other products containing iron or Zinc, antacids or Sucralfate, should not be administered concomitantly with, or within 2 hours of, the administration of Norfloxacin, because they may interfere with absorption resulting in lower serum and urine levels of Norfloxacin.
- Some Quinolones have also been shown to interfere with the metabolism of caffeine. This may lead to reduced clearance of caffeine and a prolongation of the plasma half-life that may lead to accumulation of Caffeine in plasma when products containing caffeine are consumed while taking Norfloxacin.

4.6 Fertility, Pregnancy and Lactation

There are, however, no adequate and well-controlled studies in pregnant women. Norfloxacin should be used during pregnancy only if the potential benefit justifies the potential risk to the foetus.

It is not known whether Norfloxacin is excreted in human milk. However, because of the potential for serious adverse reactions from Norfloxacin in nursing infants, a decision should be made to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

4.7 Effects on ability to drive and use machines

None reported.

4.8 Undesirable effects

Gastrointestinal experiences including: abdominal pain, constipation, diarrhea, dyspepsia, flatulence, gross bleeding/perforation, heartburn, nausea, GI ulcers (gastric/duodenal) and vomiting.

Abnormal renal function, anemia, dizziness, edema, elevated liver enzymes, headaches, increased bleeding time, pruritus, rashes and tinnitus.

Additional adverse experiences reported occasionally include:

Body as a Whole

fever, infection, sepsis

Cardiovascular System

congestive heart failure, hypertension, tachycardia, syncope

Digestive System

dry mouth, esophagitis, gastric/peptic ulcers, gastritis, gastrointestinal bleeding, glossitis, hematemesis, hepatitis, jaundice

Hemic and Lymphatic System

ecchymosis, eosinophilia, leukopenia, melena, purpura, rectal bleeding, stomatitis, thrombocytopenia

Metabolic and Nutritional

weight changes

Nervous System

anxiety, asthenia, confusion, depression, dream abnormalities, drowsiness, insomnia, malaise, nervousness, paresthesia, somnolence, tremors, vertigo

Respiratory System

asthma, dyspnea

Skin and Appendages

alopecia, photosensitivity, sweating increased

Special Senses

blurred vision

Urogenital System

cystitis, dysuria, hematuria, interstitial nephritis, oliguria/polyuria, proteinuria, renal failure

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 EFDA yellow Card Scheme, online at https://primaryreporting.who-umc.org/ET or toll free call 8482 to Ethiopian food and drug authority (EFDA

4.9 Overdose

Symptoms: vomiting, gastrointestinal haemorrhage, diarrhoea, dizziness, tinnitus or convulsions. In the event of significant poisoning, acute renal failure and liver damage are possible.

Treatment

- Special measures such as forced diuresis,
- dialysis or haemoperfusion are probably of no help in eliminating NSAIDs due to the high protein binding and extensive metabolism.
- Activated charcoal may be considered after ingestion of a potentially toxic overdose, and
- gastric decontamination (e.g. vomiting, gastric lavage) after ingestion of a potentially life-threatening overdose.

5.0 Pharmacological Properties

5.1 Pharmacodynamic Properties

Norfloxacin is a quinolone/fluoroquinolone antibiotic. Norfloxacin 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.

The bactericidal action of Norfloxacin results from inhibition of the enzymes topoisomerase II (DNA gyrase) and topoisomerase IV, which are required for bacterial DNA replication, transcription, repair, and recombination.

Hydrochlorothiazide acts directly on the kidney, increasing the excretion of sodium chloride and potassium and consequently water, mainly in the distal tubule.

5.2 Pharmacokinetic properties

In fasting healthy volunteers, at least 30-40% of an oral dose of Norfloxacin is absorbed. Absorption is rapid following single doses of 200 mg, 400 mg and 800 mg. At the respective doses, mean peak serum and plasma concentrations of 0.8, 1.5 and 2.4 µg/mL are attained approximately one hour after dosing.

The disposition of Norfloxacin in patients with creatinine clearance rates greater than 30 mL/min/1.73 m² is similar to that in healthy volunteers. In patients with creatinine clearance rates equal to or less than 30 mL/min/1.73 m², the renal elimination of Norfloxacin decreases so that the effective serum half-life is 6.5 hours. In these patients, alteration of dosage is necessary.

Norfloxacin is eliminated through metabolism, biliary excretion, and renal excretion. After a single 400-mg dose of Norfloxacin, mean antimicrobial activities equivalent to 278, 773, and 82 µg of Norfloxacin/g of feces were obtained at 12, 24, and 48 hours, respectively.

5.3 Preclinical safety data

None stated.

6.0 Pharmaceutical particulars

6.1 List of excipients

Microcrystalline Cellulose, Maize Starch , Lactose , Povidone K-30, Purified Talc, Magnesium Stearate , Sodium Starch Glycolate (Type A) , Colloidal Anhydrous Silica , Microcrystalline Cellulose (PH-102), Isopropyl Alcohol* , Purified Water*, Cellulose Acetate Phthalate, Titanium Dioxide , Diethyl Phthalate , Ethyl Cellulose , Colour Ferric Oxide, Colour Ferric Oxide, Dichloromethane*.

* Lost during processing

6.2 Incompatibilities

None reported

6.3 Shelf life

36 months.

6.4 Special precautions for storage

Store at temperature not exceeding 30°C in a dry place. Protect from light.

6.5 Nature and contents of container

10 Tablets packed in Blister Aluminium Foil and Clear PVC Film and such 10 blisters packed in a unit carton along with package insert.

6.6 Special precautions for disposal and other handling

None reported

7. Marketing Authorisation Holder

MEDICAMEN BIOTECH LIMITED

SP-1192 A & B, Phase-IV,

Industrial Area, Bhiwadi-301019,

Distt Alwar, Rajasthan India

8. Number(s) in the national register of finished pharmaceutical products

Certificate No: 07697/08283/REN/2021

9. Date of first authorisation/renewal of the authorisation

August 8, 2022

10. Date of revision of the text

August 2023