SUMMARY PRODUCT CHARACTERISTICS

1. Name of the medicinal product

BERLIN CIPRO (CIPROFLOXACIN HYDROCHLORIDE TABLETS USP 500 MG)

2. Qualitative and quantitative composition

Each film coated tablet contains:

Ciprofloxacin Hydrochloride USP

eq. to Ciprofloxacin 500 mg

Excipients Q.S.

Colour: Titanium Dioxide BP

3. Pharmaceutical form

Solid oral dosage form

4. Clinical particulars

4.1 Therapeutic indications

Ciprofloxacin 500mg Tablets are an antibiotic belonging to the fluoroquinolones family. Ciprofloxacin Tablets are used for the treatment of severe bacterial infections. They only work with specific strains of bacteria.

4.2 Posology and method of administration

Use in adults

Your doctor will decide the dosage and how long your treatment should continue. It is essential to follow your doctor's instructions strictly to derive the maximum benefit from Ciprofloxacin.

Do not stop the therapy prematurely, even if you feel better, because the signs of illness often begin to disappear before the infection has been completely cured. Not using the medicine for long enough or stopping treatment too early can result in the illness flaring up again. Ciprofloxacin Tablets are best taken on an empty stomach with a little liquid. Your doctor will prescribe one of the following dosages depending on the severity of your illness, the sensitivity of the organism causing it and the location of the infection: Single/daily doses for adults: Simple

infections of the lower and upper urinary tract: 2 x 250 mg. Severe infections of the urinary tract (depending on degree):2 x 250 mg to 2 x 500 mg. Infections of the airways (e.g. bronchitis): 2x250 mg to2x500 mg. Other infections (see Indications): 2 x 500 mg. Severe infections (e.g. bone infections, airway infections, or in patients with cystic fibrosis): 3 x 500 mg. For children and young people (5-17 years old) with cystic fibrosis, the recommended dosage in acute episodes of infection is 2 x 20 mg Ciprofloxacin per kg body weight, divided into 2 single doses at 12-hourly intervals. The daily dose should not exceed 3 x 500 mg. The recommended duration of treatment is 10-14 days. There is no experience of the dosage for children with impaired kidney or liver function. In acute, uncomplicated gonorrhea (clap) in men, a single dose of 250 mg is sufficient if only the urethra is affected. If the symptoms (discharge etc.) in gonorrhea do not disappear within a few days, your doctor should be consulted to give you a check-up, in particular to rule out a secondary infection which was not cured by the administration of a single dose.

4.3 Contraindications

Patients who are hypersensitive to Ciprofloxacin or similar medicines (ask your doctor or pharmacist) must not use Ciprofloxacin 500mg Tablets. Children and young people: Children and young people who are still growing should not take Ciprofloxacin 500mg Tablets. An exception to this is the treatment of acute episodes of infection in patients with cystic fibrosis (a hereditary metabolic disorder with increased production and increased viscosity of the glandular secretions of the bronchi and digestive tract), or with anthrax.

4.4 Special warnings and precautions for use

Warnings and precautions:

This medicine has been prescribed for you by your doctor to treat your current illness. The antibiotic In Ciprofloxacin Tablet is not effective against all micro-organisms that cause infectious diseases. The use of the wrong antibiotic or incorrect dosage of an antibiotic may cause complications. So never use it except on medical advice to treat other illnesses or to treat anyone else. This medicine may impair your reactions, your ability to drive and to use tools or operate machines. This is especially the case if alcohol is consumed at the same time. An adequate fluid intake is necessary during treatment with Ciprofloxacin Tablet because,

otherwise, the active substance may crystallize out in the urine. If your kidney function is impaired, it may be necessary to adjust the dosage in some circumstances. Your doctor has the information he needs about this. Patients with known cerebral disease, especially seizures (epilepsy) or disturbed circulation in the brain should only take Ciprofloxacin Tablet if they are also receiving treatment for cerebral attacks at the same timexcessive exposure to the sun (or time spent in a solarium) should be avoided while under treatment with ciprofloxacin Tablet as sensitive patients may suffer unpleasant reddening of the skin or inflammation (photosensitization)

4.5 Interaction with other medicinal products and other forms of interaction

Pharmacodynamic interactions:-

Effects of other medicinal products on sildenafil: Chelation Complex Formation The simultaneous administration of ciprofloxacin (oral) and multivalent cation-containing drugs and mineral supplements (e.g. calcium, magnesium, aluminium, iron), polymeric phosphate binders (e.g. sevelamer), sucralfate or antacids, and highly buffered drugs (e.g. didanosine tablets) containing magnesium, aluminium, or calcium reduces the absorption of ciprofloxacin. Consequently, ciprofloxacin should be administered either 1 2 hours before or at least 4 hours after these preparations. The restriction does not apply to antacids belonging to the class of H2 receptor blockers.

Food and Dairy Products: Dietary calcium as part of a meal does not significantly affect absorption. However, the concurrent administration of dairy products or mineral-fortified drinks alone (e.g. milk, yoghurt, calcium-fortified orange juice) with ciprofloxacin should be avoided because absorption of ciprofloxacin may be reduced.

Probenecid: Probenecid interferes with renal secretion of ciprofloxacin. Co-administration of probenecid and ciprofloxacin increases ciprofloxacin serum concentrations.

Effects of ciprofloxacin on other medicinal products:

Tizanidine

Tizanidine must not be administered together with ciprofloxacin (see section 4.3). In a clinical study with healthy subjects, there was an increase in serum tizanidine concentration (Cmax increase: 7-fold, range: 4 to 21-fold; AUC increase: 10-fold, range: 6 to 24-fold) when given

concomitantly with ciprofloxacin. Increased serum tizanidine concentration is associated with a potentiated hypertensive and sedative effect.

Methotrexate: Renal tubular transport of methotrexate may be inhibited by concomitant administration of ciprofloxacin, potentially leading to increased plasma levels of methotrexate and increased risk of methotrexate-associated toxic reactions. The concomitant use is not recommended.

Theophylline: Concurrent administration of ciprofloxacin and theophylline can cause an undesirable increase in serum theophylline concentration. This can lead to theophylline-induced side effects that may rarely be life threatening or fatal. During the combination, serum theophylline concentrations should be checked and the theophylline dose reduced as necessary.

4.6 Fertility, pregnancy and Breast feeding

Pregnancy:

The data that are available on administration of ciprofloxacin to pregnant women indicates no malformative or feto/neonatal toxicity of ciprofloxacin. Animal studies do not indicate direct or Indirect harmful effects with respect to reproductive toxicity. In juvenile and prenatal animals. Exposed to quinolone, effects on immature cartilage have been observed, thus, it cannot be excluded that the drug could cause damage to articular cartilage in the human immature organism / fetus. As a precautionary measure, it is preferable to avoid the use of ciprofloxacin during pregnancy.

Lactation:

Ciprofloxacin is excreted in breast milk. Due to the potential risk of articular damage, ciprofloxacin should not be used during breast-feeding.

4.7 Effects on ability to drive and use machines

Due to its neurological effects, Ciprofloxacin 500mg Tablets may affect reaction time. Thus, the ability to drive or to operate machinery may be impaired.

4.8 Undesirable effects

Like all medicines, this medicine can cause side-effects although not everybody gets them.

Muscle pain or weakness, inflammation of the joints and joint pain, increased muscle tone and cramping, inflammation of the tendons or tendon rupture, particularly affecting the large tendon

at the back of the ankle (Achilles tendon) Unusual feelings of pain, burning tingling, numbness or muscle weakness in the extremities (neuropathy) severe allergic reactions (anaphylactic reaction or anaphylactic shock, which can be fatal serum sickness) Mental disturbances (psychotic reactions potentially leading to thoughts of suicide, suicide attempts, or completed suicide) (potentially leading to thoughts of suicide, suicide attempts, or completed suicide) flu-like symptoms, followed by a painful red or purplish rash that spreads, blisters on your skin, mouth, nose or genitals, or red, painful, watery eyes, signs of the potentially fatal Stevens-Johnson syndrome or toxic epidermal necrolysis Yellow or itchy skin, a sign of jaundice (cholestatic icterus) Hypersensitivity reaction called DRESS (Drug Reaction with Eosinophilia and Systemic Symptoms).

4.9 Overdose

In the event of acute, excessive oral over dosage, reversible renal toxicity has been reported in some cases. Therefore, apart from routine emergency measures, it is recommended to monitor renal function and to administer Mg-or Ca-containing antacids which reduce the absorption of ciprofloxacin.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Urological; Fluoroquinolones,

ATC code: J01MA02

Mechanism of action: As a fluoroquinolones antibacterial agent, the bactericidal action of ciprofloxacin results from the inhibition of both type II topoisomerase (DNA-gyrate) and topoisomerase IV, required for bacterial DNA replication, transcription, repair and recombination.

PK/PD relationship:

Efficacy mainly depends on the relation between the maximum concentration in serum (C max) and the minimum inhibitory concentration (MIC) of ciprofloxacin for a bacterial pathogen and the relation between the area under the curve (AUC) and the MIC.

Mechanism of resistance:

In-vitro resistance to ciprofloxacin can be acquired through a stepwise process by target site mutations in both DNA gyrase and topoisomerase IV. The degree of cross-resistance between ciprofloxacin and other fluoroquinolones that results is variable. Single mutations may not result in clinical resistance, but multiple mutations generally result in clinical resistance to many or all active substances within the class. Impermeability and/or active substance efflux pump mechanisms of resistance may have a variable effect on susceptibility to fluoroquinolones, which depends on the physiochemical properties of the various active substances within the class and the affinity of transport systems for each active substance. All in-vitro mechanisms of resistance are commonly observed in clinical isolates. Resistance mechanisms that inactivate other antibiotics such as permeation barriers (common in Pseudomonas aeruginosa) and efflux mechanisms may affect susceptibility to ciprofloxacin. Plasmid-mediated resistance encoded by qnr-genes has been reported.

Pharmacodynamic effects

Studies in vitro have shown that sildenafil is selective for PDE5, which is involved in the erection process. Its effect is more potent on PDE5 than on other known phosphodiesterases. There is a 10-fold selectivity over PDE6 which is involved in the photo transduction pathway in the retina. At maximum recommended doses, there is an 80-fold selectivity over PDE1, and over 700-fold over PDE2, 3, 4, 7, 8, 9, 10 and 11. In particular, sildenafil has greater than 4,000-fold selectivity for PDE5 over PDE3, the cAMP-specific phosphodiesterases is form involved in the control of cardiac contractility.

5.2 Pharmacokinetic properties

Absorption

Following oral administration of single doses of 250 mg, 500 mg, and 750 mg of ciprofloxacin Tablets, ciprofloxacin is absorbed rapidly and extensively, mainly from the small intestine, reaching maximum serum concentrations 1 2 hours later. Single doses of 100 750 mg produced dose-dependent maximum serum concentrations (Cmax) between 0.56 and 3.7 mg/L. Serum concentrations increase proportionately with doses up to 1000 mg. The absolute bioavailability is approximately 70 80%. A 500 mg oral dose given every 12 hours has been shown to produce an area under the serum concentration-time curve (AUC) equivalent to that produced by an

intravenous infusion of 400 mg ciprofloxacin given over 60 minutes every 12 hours.

Distribution

Protein binding of ciprofloxacin is low (20 30%). Ciprofloxacin is present in plasma largely in a Non-ionized form and has a large steady state distribution volume of 2 3 L/kg body weight. Ciprofloxacin reaches high concentrations in a variety of tissues such as lung (epithelial fluid, Alveolar macrophages, biopsy tissue), sinuses, inflamed lesions (cantharides blister fluid), and the Urogenital tract (urine, prostate, endometrial) where total concentrations exceeding those of plasma concentrations are reached.

Metabolism

Low concentrations of four metabolites have been reported, which were identified as: desethyleneciprofloxacin (M 1), sulphociprofloxacin (M 2), ox ciprofloxacin (M 3) and formylciprofloxacin (M 4). The metabolites display in-vitro antimicrobial activity but to a lower degree than the parent compound. Ciprofloxacin is known to be a moderate inhibitor of the CYP 450 1A2 Iso-enzymes.

Elimination

Ciprofloxacin is largely excreted unchanged both really and, to a smaller extent, faecally. The serum elimination half-life in subjects with normal renal function is approximately 4 7 hours.

5.3 Preclinical safety data

Not applicable

6. Pharmaceutical particulars

6.1 List of Excipients: Croscarmellose Sodium**,** Starch, Purified Water, Colloidal Silicone Dioxide,*Purified Talc, Magnesium Stearate, Redimix Colour Titanium Dioxide, Isopropyl Alcohol, Methylene Dichloride

6.2 Incompatibilities

Not applicable

6.3 Shelf life: 3 YEAR

6.4 Special precautions for storage

Keep this medicine out of the sight and reach of children.

Do not store above 25°C and keep in the original container.

6.5 Nature and contents of container

Alu-Alu Blister containing 10 tablets is packed in a primary carton along with Pack Insert.

6.6 Special precautions for disposal and other handling

Not applicable

7. Manufacturer

KESAR PHARMA (P) LIMITED

Plot Survey No.50-P/2, Po Chhatral. Gandhinagar, INDIA

8. Marketing authorization holder

Berlin Pharma & Healthcare Ltd.
42, Comfort Oboh, Kiri-Kiri industrial area. Apapa-Lagos, Nigeria.

9. Marketing authorization number(s)

NAFDAC REG. NO. B4 - 7283

10. Date of first authorization/renewal of the authorization

Not Applicable

11. Date of revision of the text:

Not Applicable