SUMMARY OF THE PRODUCT CHARACTERISTICS

1. NAME OF THE FINISHED PHARMACEUTICAL PRODUCT

Ciprofloxacin Tablets USP 500mg F/C- CIPROKANT-500

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film coated tablet contains:
Ciprofloxacin Hydrochloride USP
Equivalent to Ciprofloxacin……500 mg
Excipients……q.s.
Colour:Titanium Dioxide

3. PHARMACEUTICAL FORM

Oral Solid Dosage Form- Tablets

4. CLINICAL PARTICULARS

4.1 Therapeutic Indication:

Ciprofloxacin Tablets 500 mg is indicated for the treatment of a wide variety of infections caused by susceptible gram-positive and gramnegative organisms including mixed infections caused by two or more organisms. It may also be used for infections caused by multi-drug resistant bacteria. Ciprofloxacin Tablets 500 mg is indicated for the treatment of the following infections caused by susceptible bacteria:
Respiratory Tract Infections: Acute and chronic bronchitis, obstructive airways disease (COPD) , empyema , lungabscess , bronchiectasis, lobar and bronchopneumonia, acute exacerbation of cystic fibrosis, otitis media, sinusitis and mastoiditis especially due to gram-neg ative bacteria (including Pseudomonas sp.)
Urinary Tract Infections: Acute and chronic pyelonephritis, cystitis, urethritis, prostatitis,

epididymitis and chronic complicated or recurrent UTI caused by multi-drug resistant organisms and/or Pseudomonas aeruginosa.

Skin and Soft Tissue Infections: In surgical and post-operative wound infections due to gram - negative organisms such as Pseudomonas aeruginosa. Also useful in infections caused by resistant Staphylococci including infected ulcers, wound infections,abscesses, cellulitis, erysipelas, infected burns.

Surgical Infections: Peritonitis, intra - abdominal abscess, cholecystitis, empyema of gall bladder, cholangitis.

Bone And Joint Infections: Acute and chronic osteomyelitis, septic arthritis.

Pelvic Infections: Salpingitis, endometritis,pelvic inflammatory disease.

Sexually Transmitted Diseases: Gonorrhoea including that caused by betalactamase producing strains and chancroid caused by H.ducreyi.

Gastrointestinal Infections: Enteric fever, infective diarrhoea.

Severe Systemic Infections: Septicaemia, bacteraemia, infections in immunocompromised patients.

4.2 Posology and method of administration:

Ciprofloxacin Tablets 500 mg should be swallowed whole with adequate amount of liquid. Ciprofloxacin tablets can be taken without regard to meals. Fluids should be taken liberally. Antacids should not be taken concomitantly or within two hours of dosing.

Adults: Respiratory tract, bone and joint infections :

Mild/Moderate 500 mg twice daily.

Severe/Complicated 750 mg twice daily.

Urinary tract infections : Mild/moderate 250 mg twice daily. Severe/complicated 500 mg twice daily.

Infectious diarrhoea : Mild/moderate/severe 500 mg twice daily.

Gonorrhoea : 500 mg single dose.

Non-gonococcal urethritis : 750 mg twice daily.

Chancroid : 500 mg twice daily.

Other infections : 500-750 mg twice daily

4.3 Contraindications:

Hypersensitivity to the active substance, to other quinolones or to any of the excipients listed.

Concomitant administration of ciprofloxacin and tizanidine

4.4 Special warnings and precautions for use:

Paediatric use: As with other drugs of this class, ciprofloxacin has been shown to cause arthropathy in weight-bearing joints of immature animals. Hence ciprofloxacin is usually not recommended for use in children.

However, if benefits are considered to outweigh the potential risk, it may be administered.

In impaired renal damage : Dosage adjustments will be required in patients with moderate to severe impairment of renal function. Monitoring of serum drug levels is the most reliable basis for dosage adjustment.

If creatinine clearance is less than 20 ml/min, half the recommended dosage may be administered.

Others:

CNS stimulation: As ciprofloxacin may cause CNS stimulation, it should be used with caution in patients with CNS disorders such as severe cerebral arteriosclerosis or epilepsy.

Crystalluria: Inadequate intake of water, when on ciprofloxacin, can cause crystalluria.

Phototoxicity : Moderate to severe phototoxicity manifested by an exaggerated sunburn reaction has been observed in patients who are exposed to direct sunlight with some members of the quinolone class of drugs.

Therapy should be discontinued if phototoxicity occurs.

4.5 Interaction with other medicinal products and other forms of interaction:

Theophylline: Serum concentrations and elimination half-life of theophylline may be increased when it is used concurrently with ciprofloxacin. Theophylline doses should be reduced and plasma levels monitored.

Antacids: Antacids containing magnesium hydroxide and/or aluminium hydroxide may

interfere with the absorption of ciprofloxacin, resulting in lower serum and urine levels; concurrent administration of antacids with ciprofloxacin should be avoided.
Anticoagulants: Prolongation of bleeding time has been reported during concomitant administration of ciprofloxacin and anticoagulants.
Cyclosporin: Transient increases in serum creatinine have been seen following concomitant administration of cyclosporin and ciprofloxacin.
Caffeine: Ciprofloxacin may interfere with the metabolism of caffeine, resulting in reduced clearance of caffeine.

4.6 Fertility, pregnancy and lactation

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 quinolones, 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 / foetus
As a precautionary measure, it is preferable to avoid the use of ciprofloxacin during pregnancy.

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

4.7 Effects on ability to drive and use machines:
Due to its neurological effects, ciprofloxacin may affect reaction time. Thus, the ability to drive or to operate machinery may be impaired.

4.8 Undesirable effects

Ciprofloxacin is generally well tolerated.

Diarrhoea, vomiting, abdominal pain,headache, restlessness and rash, have been reported. Other side effects which have been reported very rarely include myalgia, tendinitis/rupture, exacerbation of myasthenia gravis and increases in serum transaminase levels.

Potentially life-threatening effects : A series of 15 cases of anaphylactoid reactions has been reported associated with ciprofloxacin.

Stevens-Johnson syndrome, toxic epidermal necrolysis, fulminant hepatic failure have been reported rarely.

Severe or irreversible effects: As with all quinolones, seizures may occur and this effect may be potentiated by concurrent use of nonsteroidal anti-inflammatory drugs .

Pseudomembranous colitis has occurred with ciprofloxacin therapy.

Transient disturbance of hearing has been reported, particularly during high-dose therapy.

Symtomatic adverse effects: Probable or possible drug-related reactions were reported in 93% of 9473 patients treated with ciprofloxacin worldwide. The incidence of severe reactions was 0.6%. The most frequent reactions were from the gastro intestinal system(nausea,diarrhea,vomiting,dyspepsia),central nervous system(dizziness, headache, nervousness, tremors, seizures, confusion) and skin (rash, pruritus, urticaria, photosensitivity).

Other effects: Elevation of AST (SGOT) and ALT (SGPT), blood creatinine, and blood urea have been observed. Eosinophilia, leucopenia and thrombocytopenia have also been related to ciprofloxacin use.

Interference with clinical pathology tests:No technical interferences of this kind have been reported.

4.9 Overdose:

An overdose of 12g has been reported to lead to mild symptoms of toxicity. An acute overdose of 16g has been reported to cause acute renal failure.

Symptoms of overdose may include dizziness,tremor, headaches, tiredness, seizures, hallucinations,confusion,abdominal discomfort, renal and hepatic impairment as well as crystalluria and haematuria. Reversible renal toxicity has been reported.

Apart from routine emergency measures e.g.ventricular emptying followed by medical carbon, it is recommended to monitor renal function, including urinary pH and acidify, if required, to prevent crystalluria. Patients should be kept well hydrated.

Calcium or magnesium containing antacids may theoretically reduce the absorption of ciprofloxacin in overdoses.

Only a small quantity of ciprofloxacin (<10%) is eliminated by haemodialysis or peritoneal dialysis.

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

5.0 PHARMACOLOGICAL PROPERTIES:

5.1 PHARMACODYNAMIC PROPERTIES:

Pharmacotherapeutic group: Fluoroquinolones Mechanism of Action:

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

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 concentration 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 400mg 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-ionised 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, endometrium) where total concentrations exceeding those of plasma concentrations are reached.

Biotransformation

Low concentrations of four metabolites have been reported, which were identified as: desethyleneciprofloxacin (M 1) , sulphociprofloxacin (M 2), oxociprofloxacin (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 isoenzymes.

Elimination

Ciprofloxacin is largely excreted unchanged both renally 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

Non-clinical data reveal no special hazards for humans based on conventional studies of single dose toxicity, repeated dose toxicity, carcinogenic potential, or toxicity to reproduction.

Like a number of other quinolones, ciprofloxacin is phototoxic in animals at clinically relevant exposure levels. Data on photomutagenicity/photocarcinogenicity show a weak photomutagenic or phototumorigenic effect of ciprofloxacin *in-vitro* and in animal experiments. This effect was comparable to that of other gyrase inhibitors.

Articular tolerability:

As reported for other gyrase inhibitors, ciprofloxacin causes damage to the large weight-bearing joints in immature animals. The extent of the cartilage damage varies according to age, species and dose; the damage can be reduced by taking the weight off the joints. Studies with mature animals (rat, dog) revealed no evidence of cartilage lesions. In a study in young beagle dogs, ciprofloxacin caused severe articular changes at therapeutic doses after two weeks of treatment, which were still observed after 5 months.

6. Pharmaceutical Particulars

6.1 List of excipients

Microcrystalline Cellulose, Maize Starch, Purified Water, Magnesium Stearate, Colloidal Anhydrous Silica, Stearic Acid, Sodium Starch Glycolate, Wincoat White, Isopropyl alcohol, Dichloromethane.

6.2 Incompatibilities

Not known

6.3 Shelf Life

36 months from the date of manufacture

6.4 Special precautions for storage:

Do not store above 30°C. Protect from light.
Keep the medicine out of reach of children.

6.5 Nature and contents of container

Ciprofloxacin film-coated tablets are available in PVC-Aluminum foil blister pack.
Pack sizes: 10x10 Alu-PVC Blister pack

6.6 Instructions for use and handling <and disposal>

Not known

7.0 NAME AND ADDRESS OF MANUFACTURER

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8. REGISTRATION NUMBER: Not Applicable.

9. CATEGORY FOR DISTRIBUTION: Prescription Only Medicine

10. DATE OF PUBLICATION OF THIS PACKAGE INSERT: {02/2017}