SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Name of the proprietary product: Ciprofloxacin Tablets USP 500mg

Name of the nonproprietary International Product:
HABICIP

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film coated tablet contains:

Ciprofloxacin Hydrochloride USP

equivalent to Ciprofloxacin……..500 mg

Excipients…….q.s.

Colour: Titanium Dioxide

For a full list of excipients, see Section 6.1.

3. PHARMACEUTICAL FORM:

White film coated, oval shaped tablets having one side breakline and "500" embossed on other side of tablet.

4. CLINICAL PARTICULARS:

4.1. Therapeutic Indications:

Ciprofloxacin is indicated for the treatment of the following infections caused by ciprofloxacin sensitive bacteria:

Lower Respiratory Tract Infections caused by Escherichia coli, Klebsiella pneumoniae, Enterobacter cloacae, Proteus mirabilis, Pseudomonas aeruginosa, Haemophilus influenzae and Haemophilus para-influenzae.

Urinary Tract Infections caused by Escherichia coli, Klebsiella pneumoniae, Enterobacter cloacae, Serratia marcescens, Proteus mirabilis, Providencia rettgeri, Morganella morganii, Citrobacter diversus, Citrobacter freundii, Pseudomonas aeruginosa, Staphylococcus epidermidis and Streptococcus faecalis.

Skin and Soft Tissue Infections caused by Escherichia coli, Klebsiella pneumoniae, Enterobacter cloacae, Proteus mirabilis, Proteus vulgaris, Providencia stuartii, Morganella morganii, Citrobacter freundii, Pseudomonas aeruginosa, Staphylococcus aureus, Staphylococcus epidermidis and Streptococcus pyogenes.

Gastro-intestinal Infections: Infective diarrhoea caused by E. coli, Campylobacter jejuni,

Shigella flexneri and Shigella sonnei.

Bone Infections: Osteomyelitis due to susceptible gram-negative organisms.

Gonorrhoea: Ciprofloxacin is ineffective against Treponema pallidum.

In the treatment of infections caused by Pseudomonas aeruginosa, an aminoglycoside must be administered concomitantly.

4.2. Posology and method of administration:

Ciprofloxacin tablets should be swallowed whole with plenty of liquid and may be taken with or without meals.

Dosage and duration of treatment: The dosage range is 250-750 mg twice daily.

The duration of treatment depends upon the severity of the infection, clinical response and bacteriological findings. For acute uncomplicated cystitis in women, the treatment period is 3 days. Generally, treatment should be continued for at least 3 days after the signs and symptoms of the infection have disappeared. For acute infections the usual treatment period is 5 to 10 days with ciprofloxacin tablets.

For severe and complicated infections more prolonged therapy may be required.

In streptococcal infections the treatment must last at least 10 days because of the risk of late complications.

Infections of the lower respiratory tract: Mild to moderate - 250 to 500 mg twice daily; severe or complicated - 750 mg twice daily. In cystic fibrosis patients the dose is 750 mg twice daily. The low body mass of these patients should, however, be taken into consideration when determining dosage (7.5 to 15 mg/kg/day).

Infectious diarrhoea: 500 mg twice daily.

Infections of the urinary tract: Acute uncomplicated cystitis - 250 mg twice daily; mild to moderate - 250 mg twice daily; severe or complicated - 500 mg twice daily.

Infections of the skin: Mild to moderate - 500 mg twice daily; severe or complicated - 750 mg twice daily.

Bone infections: Mild to moderate 500 mg twice daily; severe or complicated - 750 mg twice daily. Treatment may be required for 4-6 weeks or longer.

Gonorrhoea: A single dose of 250 mg.

Elderly patients should receive a dose as low as possible; this will depend on the severity of the illness and on the creatinine clearance.

Impaired renal or liver function: In patients with reduced renal function, the half-life of ciprofloxacin is prolonged and the dosage needs to be adjusted.

For patients with changing renal function or patients with renal impairment and hepatic insufficiency, monitoring of drug serum levels provides the most reliable basis for dose adjustment

Method of administration -oral administration

4.3. Contraindications

Safety during pregnancy and lactation has not been established.

Ciprofloxacin is contra-indicated in children under 18 years and in growing adolescents, except where the benefits of treatment exceed the risks. Experimental evidence indicates that, species variable, reversible lesions of the cartilage of weight bearing joints has been seen in immature members of certain animal species.

Ciprofloxacin is contra-indicated in patients who have shown hypersensitivity to ciprofloxacin or any other quinolones.

4.4. Special warnings and precautions for use

Ciprofloxacin should be used with caution in patients with a history of convulsive disorders.

Crystalluria related to the use of ciprofloxacin has been observed. Patients receiving ciprofloxacin should be well hydrated and excessive alkalinity of the urine should be avoided.

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4.5. Interaction with other medicinal products and other forms of interaction: Interactions resulting in a contraindication

Concurrent administration of ciprofloxacin with theophylline may lead to elevated plasma concentrations of theophylline and prolongation of its elimination half-life. This may result in increased risk of theophylline-related adverse reactions. If concomitant use cannot be avoided, plasma levels of theophylline should be monitored and dosage adjustments made as appropriate.

Ciprofloxacin tablets should be administered 1-2 hours before, or at least 4 hours after taking iron preparations, antacids containing magnesium, aluminium, calcium or sucralfate as interference with absorption may occur. This restriction does not apply to antacids belonging to the class of H2 receptor blockers.

Concomitant-administration of the nonsteroidal anti-inflammatory drug fenbufen with

quinolones has been reported to increase the risk of central nervous system stimulation and convulsive seizures.

Monitoring of serum creatinine concentrations is advised in patients on concomitant cyclosporin therapy, as transient increases in serum creatinine concentrations have been observed.

The simultaneous administration of ciprofloxacin and warfarin may intensify the action of warfarin.

In particular cases, concurrent administration of ciprofloxacin and glibenclamide can intensify the action of glibenclamide (hypoglycaemia).

4.6. Pregnancy and Lactation:

Safety during pregnancy and lactation has not been established.

4.7. Effects on the ability to drive and use machines

Not reported.

4.8. Undesirable effects: Summary of the safety profile

Adverse drug reactions from spontaneous reports and literature cases (frequency not known)

The following side-effects have been observed: Effects on the gastro-intestinal tract: Nausea, diarrhoea, vomiting, dyspepsia, abdominal pain, flatulence, anorexia. In the event of severe and persistent diarrhoea during or after treatment, a doctor must be consulted since this symptom can hide a serious intestinal disease (pseudomembranous colitis), requiring immediate treatment. In such cases ciprofloxacin must be discontinued and appropriate therapy initiated (e.g. vancomycin, orally, 4 x 250 mg/day). Drugs that inhibit peristalsis are contraindicated.

Effects on the nervous system: Dizziness, headache, tiredness, nervousness, agitation, trembling. Infrequently: insomnia, peripheral paralgesia, sweating, unsteady gait, convulsions, increase in intracranial pressure, anxiety states, nightmares, confusion, depression, hallucinations, in individual cases psychotic reactions (even progressing to self endangering behaviour).

In some instances, these reactions occurred already after the first administration of ciprofloxacin. In these cases ciproflxoacin has to be discontinued and the doctor should be informed immediately.

Reactions of sensory organs: Impaired taste and smell, visual disturbances (e.g. diplopia, colour vision), tinnitus, transitory impairment of hearing, especially at high frequencies.

Hypersensitivity reactions: Skin reactions, e.g. rashes, pruritus, drug fever.

Infrequently: Punctate skin haemorrhages (petechiae), blister formation with accompanying haemorrhages (haemorrhagic bullae) and small nodules (papules) with crust formation showing vascular involvement (vasculitis).

Erythema nodosum, Erythema exudativum multiforme (minor), Stevens Johnson Syndrome, Lyell Syndrome.

Intestitial nephritis, hepatitis, hepatic necrosis very seldom progressing to life-threatening hepatic failure.

Anaphylactic/anaphylactoid reactions (e.g. facial, vascular and laryngeal oedema, dyspnoea progressing to life-threatening shock), in some instances after the first adminsitration. In these cases ciprofloxacin has to be discontinued and medical treatment (e.g. treatment for shock) is required.

Effects on the cardiovascular system: Tachycardia, hot flushes, migraine, fainting.

Other side effects: Joint pain, joint swelling. Very rarely: general feeling of weakness, muscular pains, tendosynovitis, photosensitivity, transient impairment in kidney function including transient kidney failure.

In single cases during the administration of ciprofloxacin, achillotendinitis was observed. Cases of partial or complete rupture of the achilles tendon have been reported predominantly in the elderly on prior systemic treatment with glucocorticoids. Therefore, at any signs of an achillotendinitis (e.g. painful swelling) the administration of ciprofloxacin should be discontinued and a physician be consulted.

Long-term or repeated administration of ciprofloxacin can lead to superinfections with resistant bacteria or yeast-like fungi.

Effects on the blood and blood constituents

Eosinophilia, leucocytopenia, granulocytopenia, anaemia, thrombocytopenia.

Very rarely: leucocytosis, thrombocytosis, haemolytic anaemia, altered prothrombin values.

Influence on laboratory parameters/urinary sediment: There can be a temporary increase in transaminases, alkaline phosphatase or cholestatic jaundice, especially in patients with previous liver damage; temporary increase in urea, creatinine or bilirubin in the serum; in individual cases hyperglycaemia, crystalluria or haematuria.

Other Information

Even when the medicine is taken as prescribed, it can affect the speed of reaction to such an extent that the ability to drive or to operate machinery is impaired. This applies

particularly in combination with alcohol.

4.9. Overdose

In the event of acute, excessive oral overdosage, reversible renal toxicity has been reported. 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. Only a small amount of ciprofloxacin (<10%) is removed from the body after haemodialysis or peritoneal dialysis. Treatment should be symptomatic and supportive.

5. Pharmacological Particulars:

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: Fluoroquinolones **ATC code:**

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 iso-enzymes.

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. Pre-clinical Safety: Dose

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 ,Sodium Starch Glycolate, Type A (Explotab®) Colloidal Anhydrous Silica, Purified Water, Stearic Acid, Magnesium Stearate, Wincoat white WT-1003,Dichloromethane,Isopropyl Alcohol

6.2. Incompatibilities: Nil

6.3. Shelf Life: 36 months.

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:

10 tablets in a blister, 10 blisters packed in a printed carton with a printed insert

6.6. Special precautions for disposal and other handling:

No special requirements.

7. APPLICANT:

M/s HABMAY PHARMACY LTD.

P.O.BOX AN 18113, ACCRA

ADABRAKA OPPOSITE THE POLICE STATION, ACCRA.

TEL: 0302-260259/ 0244483933.

8. FDA APPLICATION NUMBER: NA

9. DATE OF FIRST REGISTRATION/RENEWAL OF THE REGISTRATION: NA

10. DATE OF REVISION OF TEXT: NA

Manufactured by:

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