SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)

1. NAME OF MEDICINAL PRODUCT:

M & B Cipro Caplet (Ciprofloxacin 500mg)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION:

Each film coated caplet contains Ciprofloxacin 500mg

3. PHARMACOLOGICAL FORM:

Film coated caplet

4. CLINICAL PARTICULARS:

4.1 THERAPUETIC INDICATIONS:

Ciprofloxacin tablets 500mg are indicated for the treatment of infections caused by susceptible strains of the designated microorganisms in the conditions listed below:

1) Lower respiratory tract infections caused by *Haemophilus influenzae, H.parainfluenzae, E.coli, Klebsiella pnuemoniae, Enterobacter cloacae, Proteus mirabilis,* and *Pseudomonas aeruginosa*.
2) Urinary Tract Infection
3) Skin and Skin Structure Infections
4) Acute Uncomplicated Cystitis in females caused by Escherichia coli or Staphylococcus saprophyticus. And Chronic Bacterial Prostatitis caused by *Escherichia coli or Proteus mirabilis*
5) Uncomplicated cervical and urethral gonorrhea due to *Neisseria gonorrhea.*

4.2 DOSAGE AND ADMINISTRATION:

Dosage depends on the severity and nature of the infection. Unless prescribed otherwise, the following doses are recommended:
Urinary Tract Infections: Mild to Moderate: 250mg twice daily
Severe: 500mg twice daily
Lower Respiratory Tract Infections: Mild to Moderate: 500mg twice daily
. Severe: 750mg twice daily
Urethral and Cervical Gonococcal Infection: Uncomplicated: 250mg single dose
The recommended adult dosage for chronic bacterial prostatitis is 500mg twice daily. In acute uncomplicated cystitis in females, the usual dosage is 250mg twice daily. Skin and skin structure infections may be treated with 500mg twice daily.

4.3 CONTRA-INDICATION:

Hypersensitivity to the drug and other quinolones. Growing adolescents unless benefits outweigh risks. Children below 12years & pregnancy, Lactation. Osworth Ciprofloxacin should not be administered to pregnant or lactating mothers.

4.4 SPECIAL WARNINGS AND PRECAUTION:

Ciprofloxacin should be administered cautiously in case of impaired liver functions.

In severe cases, dose reduction is advisable. In case of renal impairment the dosage should be adjusted to the creatinine clearance. If signs of tendinitis appear, Ciprofloxacin treatment is to be withdrawn. In patients with epilepsy, data about convulsions in the anamnesis, vascular diseases and organic cerebral impairment, Ciprofloxacin should only be prescribed for compelling reasons due to the risk of adverse effects (CNS stimulation or toxicity). Exposure to sun rays should be avoided during Ciprofloxacin medication because of the risk of photosensitivity. During Ciprofloxacin treatment elevated values of the alanine - aminotransferase (ALAT), alkaline phosphatase and aspartate–aminotransferase (ASAT), as well as lactate-dehydrogenase (LDH) test determinations may be observed. Ciprofloxacin administration may give rise to false negative results in the test for
Mycobacterium tuberculosis.

Ciprofloxacin should be used with caution in patients with suspected or known CNS disorders such as arteriosclerosis or epilepsy or other factors which predispose to seizures, myasthenia gravis and renal impairment.

Liberal intake of water is advised during the use of ciprofloxacin. Caution should be taken when used with products containing calcium, Iron and Zinc (see antacid interaction above). They can be taken two hours after or six hours before the drug. Should not be used for pneumococcal pneumonia and most anaerobic organism are not susceptible.

4.5 DRUG INTERACTION:

Alkalizing agents such as carboanhydrous inhibitors and sodium bicarbonate decrease the solubility of the preparation, therefore the patients should be appraised in order to prevent crystaluria and nephrotoxicity. Animal studies have established decreased seizure threshold in case of simultaneous use of non-steroid anti-inflammatory agents.

Ciprofloxacin diminishes liver metabolism, which enhances the risk of theophylline intoxication and elevated serum levels of caffeine. Antacids, magnesium-containing laxatives, ferrous sulphate, sucralfate or zinc –5 containing preparations reduce the absorption of Ciprofloxacin. It potentiates the effect of cumarine anticoagulants.

Effects of other products on ciprofloxacin:

Drugs known to prolong QT interval

Ciprofloxacin, like other fluoroquinolones, should be used with caution in patients receiving drugs known to prolong the QT interval (e.g. Class IA and III anti-arrhythmic, tricyclic antidepressants, macrolides, and antipsychotics)

Chelation complex formation

The simultaneous administration of ciprofloxacin (oral) and multivalent cation-containing drugs and mineral supplements (e.g. calcium, magnesium, aluminum, iron), polymeric phosphate binders (e.g. sevelamer or lanthanum carbonate), sucralfate or antacids, and highly buffered drugs (e.g. didanosine tablets) containing magnesium, aluminum, 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.

Metoclopramide

Metoclopramide accelerates the absorption of ciprofloxacin (oral) resulting in a shorter time to reach maximum plasma concentrations. No effect was seen on the bioavailability of ciprofloxacin.

Omeprazole

Concomitant administration of ciprofloxacin and omeprazole containing medicinal products results in a slight reduction of Cmax and AUC of ciprofloxacin.

Effects of ciprofloxacin on other medicinal products:

Tizanidine

Tizanidine must not be administered together with ciprofloxacin. 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 hypotensive and sedative effect.

Agomelatine

In clinical studies, it was demonstrated that fluvoxamine, as a strong inhibitor of the CYP450 1A2 isoenzyme, markedly inhibits the metabolism of agomelatine resulting in a 60-fold increase of agomelatine exposure. Although no clinical data are available for a possible interaction with ciprofloxacin, a moderate inhibitor of CYP450 1A2, similar effects can be expected upon concomitant administration ('Cytochrome P450' in section 'Special warnings and precautions for use).

Zolpidem
Co-administration ciprofloxacin may increase blood levels of zolpidem, concurrent use is not recommended.

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.

Other xanthine derivatives
On concurrent administration of ciprofloxacin and caffeine or pentoxifylline (oxpentifylline), raised serum concentrations of these xanthine derivatives were reported.
Phenytoin

Simultaneous administration of ciprofloxacin and phenytoin may result in increased or reduced serum levels of phenytoin such that monitoring of drug levels is recommended.

Cyclosporin
A transient rise in the concentration of serum creatinine was observed when ciprofloxacin and cyclosporin containing medicinal products were administered simultaneously. Therefore, it is frequently (twice a week) necessary to control the serum creatinine concentrations in these patients.

Vitamin K antagonists
Simultaneous administration of ciprofloxacin with a vitamin K antagonist may augment its anti-coagulant effects. The risk may vary with the underlying infection, age and general status of the patient so that the contribution of ciprofloxacin to the increase in INR (international normalised ratio) is difficult to assess. The INR should be monitored frequently during and shortly after co-

administration of ciprofloxacin with a vitamin K antagonist (e.g., warfarin, acenocoumarol, phenprocoumon, or fluindione).

Duloxetine
In clinical studies, it was demonstrated that concomitant use of duloxetine with strong inhibitors of the CYP450 1A2 isozyme such as fluvoxamine, may result in an increase of AUC and Cmax of duloxetine. Although no clinical data are available on a possible interaction with ciprofloxacin, similar effects can be expected upon concomitant administration.

Ropinirole
It was shown in a clinical study that concomitant use of ropinirole with ciprofloxacin, a moderate inhibitor of the CYP450 1A2 isozyme, results in an increase of Cmax and AUC of ropinirole by 60% and 84%, respectively. Monitoring of ropinirole-related side effects and dose adjustment as appropriate is recommended during and shortly after co- administration with ciprofloxacin

Lidocaine
It was demonstrated in healthy subjects that concomitant use of lidocaine containing medicinal products with ciprofloxacin, a moderate inhibitor of CYP450 1A2 isozyme, reduces clearance of intravenous lidocaine by 22%. Although lidocaine treatment was well tolerated, a possible interaction with ciprofloxacin associated with side effects may occur upon concomitant administration.

Clozapine
Following concomitant administration of 250 mg ciprofloxacin with clozapine for 7 days, serum concentrations of clozapine and N-desmethylclozapine were increased by 29% and 31%, respectively. Clinical surveillance and appropriate adjustment of clozapine dosage during and shortly after co-administration with ciprofloxacin are advised.

Sildenafil
Cmax and AUC of sildenafil were increased approximately twofold in healthy subjects after an oral dose of 50 mg given concomitantly with 500 mg ciprofloxacin. Therefore, caution should be used prescribing ciprofloxacin concomitantly with sildenafil taking into consideration the risks and the benefits.

4.6 EFFECT 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.

4.7 SIDE EFFECTS / ADVERSE EFFECTS

Vertigo, headache, uneasiness, insomnia; gastrointestinal reactions –abdominal or stomach pain or discomfort, diarrhea, nausea and vomiting. It is necessary to consult a physician only if the complaints persist. Adverse effects, which call for physician's advice: tendinitis, CNS disorders –acute psychosis, confusion, hallucinations, tremor; allergic reactions –itching, rashes, redness, Stevens – Johnson syndrome, face or neck edemas; breathing disorders, vasculitis; interstitial nephritis; phlebitis. Very rarely convulsions, particularly in patients with data about that in the anamnesis, in alcoholics or in case of concurrent use of theophylline.

Reports have been made of hematological changes: leucopenia, thrombopenia, eosinophylia, hemolytic anemia.

In incidental cases photosensitivity have been encountered. Crystaluria may be brought about by the relative urine insolubility of the preparation, especially in case of neutral or alkaline pH of urine.

4.8 Undesirable effects

The most commonly reported adverse drug reactions (ADRs) are nausea and diarrhoea. ADRs derived from clinical studies and post-marketing surveillance with ciprofloxacin (oral, intravenous, and sequential therapy) sorted by categories of frequency are listed below. The frequency analysis takes into account data from both oral and intravenous administration of ciprofloxacin.

System Organ Class	**Common** ≥ 1/100 to < 1/10	**Uncommon** ≥ 1/1 000 to < 1/100	**Rare** ≥ 1/10 000 to < 1/1 000	**Very Rare** < 1/10 000	**Frequency not known** (cannot be estimated from available data)
Infections and Infestations		Mycotic superinfections			
Blood and Lymphatic System Disorders		Eosinophilia	Leukopenia Anaemia Neutropenia Leukocytosis Thrombocytopenia Thrombocytaemia	Haemolytic anaemia Agranulocytosis Pancytopenia (life- threatening) Bone marrow depression (life-threatening)	
Immune System Disorders			Allergic reaction Allergic oedema / angiooedema	Anaphylactic reaction Anaphylactic shock (life-threatening) (see section 4.4) Serum sickness-like reaction	

Metabolism and Nutrition Disorders		Decreased appetite	Hyperglycaemia, Hypoglycaemia (see section 4.4)		
Psychiatric Disorders		Psychomotor hyperactivity / agitation	Confusion and disorientation Anxiety reaction Abnormal dreams Depression (potentially culminating in suicidal ideations/thoughts or suicide attempts and completed suicide) (see section 4.4) Hallucinations	Psychotic reactions (potentially culminating in suicidal ideations/ thoughts or suicide attempts and completed suicide) (see section 4.4)	Mania, hypomania
Nervous System Disorders		Headache Dizziness Sleep disorders Taste disorders	Par- and Dysaesthesia Hypoaesthesia Tremor Seizures (including status epilepticus see section 4.4) Vertigo	Migraine Disturbed coordination Gait disturbance Olfactory nerve disorders Intracranial hypertension Pseudotumor cerebral	Peripheral neuropathy and polyneuropathy (see section 4.4)
Eye Disorders			Visual disturbances (e.g. diplopia)	Visual color distortions	
Ear and Labyrinth Disorders			Tinnitus Hearing loss / Hearing impaired		
Cardiac Disorders			Tachycardia		Ventricular arrhythmia and torsades de pointes (reported predominantly in patients with risk factors for QT prolongation), ECG QT prolonged (see section 4.4 and 4.9)
Vascular Disorders			Vasodilatation Hypotension	Vasculitis	

			Syncope		
Respiratory, Thoracic and Mediastinal Disorders			Dyspnoea (including asthmatic condition)		
Gastrointestinal Disorders	Nausea Diarrhoea	Vomiting Gastro-intestinal and abdominal pains Dyspepsia Flatulence		Pancreatitis	
Hepatobiliary Disorders		Increase in transaminases Increased bilirubin	Hepatic impairment Cholestatic icterus Hepatitis	Liver necrosis (very rarely progressing to life- threatening hepatic failure) (see section 4.4)	
Skin and Subcutaneous Tissue Disorders		Rash Pruritus Urticaria	Photosensitivity reactions (see section 4.4)	Petechiae Erythema multiforme Erythema nodosum Stevens-Johnson syndrome (potentially life-threatening) Toxic epidermal necrolysis (potentially life-threatening)	Acute generalised exanthematous pustulosis (AGEP) DRESS (Drug reaction with eosinophilia and systemic symptoms) syndrome
Musculoskeletal, Connective Tissue and Bone Disorders		Musculoskeletal pain (e.g. extremity pain, back pain, chest pain) Arthralgia	Myalgia Arthritis Increased muscle tone and cramping	Muscular weakness Tendinitis Tendon rupture (predominantly Achilles tendon) (see section 4.4) Exacerbation of symptoms of myasthenia gravis (see section 4.4)	
Renal and Urinary Disorders		Renal impairment	Renal failure Haematuria Crystalluria (see section 4.4)		

			Tubulointerstitial nephritis		
General Disorders and Administration Site Conditions		Asthenia Fever	Oedema Sweating (hyperhidrosis)		
Investigations		Increase in blood alkaline phosphatase	Increased amylase		International normalised ratio increased (in patients treated with Vitamin K antagonists)

4.9 OVER DOSAGE:

Symptoms on behalf of gastrointestinal tract and CNS.
No specific antidote is available in case of intoxication. Vomiting or lavage of the stomach should be induced in order to reduce the absorption. It is also necessary to maintain adequate hydration and provide symptomatic treatment.

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

Symptoms in overdose consist of dizziness, tremor, headache, 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. PHARMACOLOGY PROPERTIES:

5.1 Pharmacodynamics properties

Pharmacotherapeutic group: Quinolone Antibacterials, Fluoroquinolones,
ATC code: J 01 MA 02

Mechanism of action:
As a fluoroquinolone 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.

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.

Spectrum of antibacterial activity:
Breakpoints separate susceptible strains from strains with intermediate susceptibility and the latter from resistant strains:

EUCAST Recommendations

Microorganisms	**Susceptible**	**Resistant**
Enterobacteriaceae	S ≤0.5 mg/L	R > 1 mg/L
Pseudomonas spp	S ≤0.5 mg/L	R > 1 mg/L
Acinetobacter spp	S ≤1 mg/L	R > 1 mg/L
Staphylococcus spp.[1]	S ≤1 mg/L	R > 1 mg/L
Haemophilus influenzae and *Moraxella catarrhalis*	S ≤0.5 mg/L	R > 0.5 mg/L
Neisseria gonorrhoeae	S ≤0.03 mg/L	R > 0.06 mg/L
Neisseria meningitidis	S ≤0.03 mg/L	R > 0.06 mg/L
Non-species-related breakpoints*****	S ≤0.5 mg/L	R > 1 mg/L

1 *Staphylococcus* spp. - breakpoints for ciprofloxacin relate to high dose therapy.
* Non-species-related breakpoints have been determined mainly on the basis of PK/PD data and are independent of MIC distributions of specific species. They are

for use only for species that have not been given a species-specific breakpoint and not for those species where susceptibility testing is not recommended.

The prevalence of acquired resistance may vary geographically and with time for selected species and local information on resistance is desirable, particularly when treating severe infections. As necessary, expert advice should be sought when the local prevalence of resistance is such that the utility of the agent in at least some types of infections is questionable.
Groupings of relevant species according to ciprofloxacin susceptibility

COMMONLY SUSCEPTIBLE SPECIES

Aerobic Gram-positive micro-organisms
Bacillus anthracis (1)

Aerobic Gram-negative micro-organisms
Aeromonas spp.
Brucella spp.
Citrobacter koseri
Francisella tularensis
Haemophilus ducreyi
*Haemophilus influenzae**
Legionella spp.
*Moraxella catarrhalis**
Neisseria meningitidis
Pasteurella spp.
Salmonella spp.*
Shigella spp.*
Vibrio spp.
Yersinia pestis

Anaerobic micro-organisms
Mobiluncus

Other micro-organisms
Chlamydia trachomatis
Chlamydia pneumoniae
Mycoplasma hominis
Mycoplasma pneumoniae

SPECIES FOR WHICH ACQUIRED RESISTANCE MAY BE A PROBLEM

Aerobic Gram-positive micro-organisms
Enterococcus faecalis ($)
Staphylococcus spp. *(2)

Aerobic Gram-negative micro-organisms
Acinetobacter baumannii^{+}
Burkholderia cepacia^{+} *
Campylobacter spp.$^{+}$ *
*Citrobacter freundii**
Enterobacter aerogenes
*Enterobacter cloacae**
*Escherichia coli**
Klebsiella oxytoca

*Klebsiella pneumoniae**
*Morganella morganii**
*Neisseria gonorrhoeae**
*Proteus mirabilis**
*Proteus vulgaris**
Providencia spp.
*Pseudomonas aeruginosa**
Pseudomonas fluorescens
*Serratia marcescens**

Anaerobic micro-organisms
Peptostreptococcus spp.
Propionibacterium acnes

INHERENTLY RESISTANT ORGANISMS

Aerobic Gram-positive micro-organisms
Actinomyces
Enteroccus faecium
Listeria monocytogenes

Aerobic Gram-negative micro-organisms
Stenotrophomonas maltophilia

Anaerobic micro-organisms
Excepted as listed above

Other micro-organisms
Mycoplasma genitalium
Ureaplasma urealitycum

* Clinical efficacy has been demonstrated for susceptible isolates in approved clinical indications

$^{+}$ Resistance rate ≥50% in one or more EU countries

($): Natural intermediate susceptibility in the absence of acquired mechanism of resistance

(1): Studies have been conducted in experimental animal infections due to inhalations of *Bacillus anthracis* spores; these studies reveal that antibiotics starting early after exposition avoid the occurrence of the disease if the treatment is made up to the decrease of the number of spores in the organism under the infective dose. The recommended use in human subjects is based primarily on *in-vitro* susceptibility and on animal experimental data together with limited human data. Two-month treatment duration in adults with oral ciprofloxacin given at the following dose, 500 mg bid, is considered as effective to prevent anthrax infection in humans. The treating physician should refer to national and/or international consensus documents regarding treatment of anthrax.

(2): Methicillin-resistant *S. aureus* very commonly express co-resistance to fluoroquinolones. The rate of resistance to methicillin is around 20 to 50% among all staphylococcal species and is usually higher in nosocomial isolates.

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 (C_{max}) 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-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: diethylene ciprofloxacin (M 1), sulphociprofloxacin (M 2), oxociprofloxacin (M 3) and formyl ciprofloxacin (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.

Excretion of ciprofloxacin (% of dose)

	Oral administration	
	Urine	**Faeces**
Ciprofloxacin	44.7	25.0
Metabolites (M1- M4)	11.3	7.5

Renal clearance is between 180-300 mL/kg/h and the total body clearance is between 480-600 mL/kg/h. Ciprofloxacin undergoes both glomerular filtration and tubular secretion. Severely impaired renal function leads to increased half-lives of ciprofloxacin of up to 12 h.
Non-renal clearance of ciprofloxacin is mainly due to active trans-intestinal secretion and metabolism. 1% of the dose is excreted via the biliary route. Ciprofloxacin is present in the bile in high concentrations.

Paediatric patients
The pharmacokinetic data in paediatric patients are limited.
In a study in children C_{max} and AUC were not age-dependent (above one year of age). No notable increase in C_{max} and AUC upon multiple dosing (10 mg/kg three times daily) was observed.

In 10 children with severe sepsis C_{max} was 6.1 mg/L (range 4.6-8.3 mg/L) after a 1-hour intravenous infusion of 10 mg/kg in children aged less than 1 year compared to 7.2 mg/L (range 4.7-11.8 mg/L) for children between 1 and 5 years of age. The AUC values were 17.4 mg*h/L (range 11.8-32.0 mg*h/L) and 16.5 mg*h/L (range 11.0-23.8 mg*h/L) in the respective age groups.
These values are within the range reported for adults at therapeutic doses. Based on population pharmacokinetic analysis of paediatric patients with various infections, the predicted mean half-life in children is approx. 4-5 hours and the bioavailability of the oral suspension ranges from 50 to 80%.

6. PHARMACEUTICAL PARTICULARS:

6.1 LIST OF EXCIPIENTS:

Ciprofloxacin Hydrochloride
Maize Starch
Microcrystalline Cellulose PH 102
Aerosil 200
Purified Water
Magnesium Stearate
Sodium starch glycolate (Type A)
Hydroxypropylmethyl cellulose
Polyethylene 6000
Titanium Oxide
Povidone K30

6.2 INCOMPATIBILITIES:

Not Applicable

6.3 SHELF LIFE:

36 Months

6.4 SPECIAL PRECAUTION FOR STORAGE:

Store below 30°C

6.5 NATURE AND CONTENT OF CONTAINER:

10 caplet are packed in an aluminum blister strips along with a leaflet in a printed carton. This is duly labelled and strapped.

6.6 SPECIAL PRECAUTION FOR DISPOSAL:

To be destroyed by NAFDAC enforcement unit

6. Manufacturer

May & Baker Nigeria Plc.

1, May & Baker Avenue off Idiroko Road

Ota

Ogun State.

7. Marketing Authorization Holder(s)

Same as Manufacturer

8. Date of revision of the text

7th June 2024