APPROVED PACKAGE INSERT

SCHEDULING STATUS: S4

PROPRIETARY NAMES AND DOSAGE FORM:

CIPROBAY® 250, 500, 750 (Tablets)

CIPROBAY® IV (Infusion)

CIPROBAY® IV Flexibag (Infusion)

CIPROBAY® Suspension 5 % (Oral Suspension)

COMPOSITION:

CIPROBAY 250 tablet contains 291 mg ciprofloxacin hydrochloride monohydrate, equivalent to 250 mg ciprofloxacin.

CIPROBAY 500 tablet contains 582 mg ciprofloxacin hydrochloride monohydrate, equivalent to 500 mg ciprofloxacin.

CIPROBAY 750 tablet contains 873 mg ciprofloxacin hydrochloride monohydrate, equivalent to 750 mg ciprofloxacin.

CIPROBAY IV contains 2,54 mg ciprofloxacin lactate equivalent to 2,0 mg ciprofloxacin per ml in 0,9 % sodium chloride solution.

CIPROBAY IV Flexibag contains 2,54 mg ciprofloxacin lactate equivalent to 2,0 mg ciprofloxacin per ml in 5 % Dextrose.

CIPROBAY Suspension 5 % when reconstituted as directed with the suspension diluent, each 5ml CIPROBAY Suspension 5 % contains ciprofloxacin microcapsules equivalent to 250 mg ciprofloxacin.

PHARMACOLOGICAL CLASSIFICATION:

20.1.1. Broad and medium spectrum antibiotics.

PHARMACOLOGICAL ACTION:

Ciprofloxacin is a synthetic, 4-quinolone derivative with *in vitro* bactericidal activity against the following Gram-negative and Gram-positive organisms. *In vitro* sensitivity does not necessarily imply *in vivo* efficacy.

Acinetobacter
Aeromonas
Brucella
Campylobacter jejuni
Citrobacter freundii
Citrobacter species
Corynebacterium
E. Coli
Edwardsiella
Enterobacter cloacae
Enterobacter species
Haemophilus influenzae
Haemophilus para-influenzae
Hafnia
Klebsiella spp.
Listeria
Moraxella catarrhalis
Morganella morganii
Neisseria gonorrhoeae
Pasteurella
Plesiomonas
Proteus mirabilis
Proteus vulgaris
Providencia rettgeri
Providencia stuartii
Pseudomonas aeruginosa
Salmonella enteritidis
Serratia marcescens
Shigella flexneri
Shigella sonnei
Staphylococcus aureus
Staphylococcus epidermidis
Streptococcus faecalis
Streptococcus pyogenes
Streptococcus spp.
Vibrio
Viridans streptococci
Yersinia

The following organisms show varying degrees of *in vitro* sensitivity to ciprofloxacin:

Alcaligenes, Enterococcus faecalis, Flavobacterium, Gardnerella, Legionella, Mycobacterium fortuitum, Mycobacterium tuberculosis, Mycoplasma hominis, Streptococcus agalactiae, Chlamydia.

The following are usually resistant:
Enterococcus faecium, Ureaplasma urealyticum, Nocardia asteroides.
With a few exceptions anaerobes are moderately sensitive (e.g. *Peptococcus, Peptostreptococcus*) to resistant (e.g. *Bacteriodes, Treponema pallidum*).

The pharmacokinetics of ciprofloxacin suspension is very similar to that of ciprofloxacin tablets.

Ciprofloxacin plasma levels are dose-related and peak 0,5 - 2 hours after oral dosing. The absolute oral bioavailability is approximately 70 % with no substantial loss by first pass metabolism. Distribution of ciprofloxacin is wide and the volume of distribution high, indicating extensive tissue penetration. Ciprofloxacin is present in lung, skin, fat, muscle, cartilage and bone. It is also present in active form in the saliva, nasal and bronchial secretions, sputum, skin blister fluid, lymph, peritoneal fluid, bile secretions, prostatic secretions, cerebrospinal fluid and the aqueous humor.

Protein binding is low. 40 % to 50 % is excreted in urine as unchanged drug. Approximately 15 % of a single dose of ciprofloxacin is eliminated as metabolites. Elimination occurs primarily by the kidneys and mainly during the first 12 hours after dosing. Renal clearance is approximately 300 ml/minute. The elimination half-life of unchanged ciprofloxacin is 3 - 5 hours. The elimination kinetics are linear; after repeated dosing at 12 hourly intervals and once steady state has been reached no accumulation occurs.

INDICATIONS:
Ciprobay 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.

Ciprobay is ineffective against *Treponema pallidum*.
In the treatment of infections caused by *Pseudomonas aeruginosa*, an aminoglycoside must be administered concomitantly

CONTRA-INDICATIONS:

Ciprobay 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.

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

WARNINGS:

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

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

Side-effects that may be potentially life-threatening are pancytopenia and marrow depression. (See side-effects and special precautions).

Concurrent administration with methotrexate may increase the concentration of methotrexate to toxic levels.

Interactions:

Concurrent administration of Ciprobay 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.

The simultaneous administration of Ciprobay (oral) and multivalent cation-containing drugs and mineral supplements (e.g. calcium, magnesium, aluminium, iron), sucralfate or antacids and highly buffered drugs (e.g. anti-retrovirals), containing magnesium, aluminium or calcium reduce the absorption of Ciprobay. Consequently, Ciprobay 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 H_2 receptor blockers.

The concurrent administration of dairy products or mineral fortified drinks alone (e.g. milk, yoghurt, calcium fortified orange juice) and Ciprobay should be avoided because the absorption of Ciprobay is reduced. Dietary calcium as part of a meal, however, does not significantly affect absorption.

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 Ciprobay and warfarin may intensify the action of warfarin.

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

Probenecid interferes with renal secretion of Ciprobay. Co-administration of probenecid and Ciprobay increases the Ciprobay serum concentrations.

Metoclopramide accelerates the absorption of Ciprobay, resulting in a shorter time to reach maximum plasma concentrations. No effect was seen on the bioavailability of Ciprobay.

Concomitant administration of Ciprobay and omeprazole results in a 20 % reduction of the C_{max} and AUC of Ciprobay.

Renal tubular transport of methotrexate may be inhibited by concomitant administration of Ciprobay potentially leading to increased plasma levels of methotrexate. This might increase the risk of methotrexate associated toxic reactions. Therefore, patients under methotrexate therapy should be carefully monitored when concomitant Ciprobay therapy is indicated.

PREGNANCY AND LACTATION:

Safety during pregnancy and lactation has not been established.

DOSAGE AND DIRECTIONS FOR USE:

CIPROBAY TABLETS

Ciprobay tablets should be swallowed whole with plenty of liquid.

CIPROBAY SUSPENSION

Always use the graduated measuring spoon to obtain the exact dose:

½ measuringspoonful (approx 2,5 ml) contains approx. 125 mg ciprofloxacin. 1 measuringspoonful (approx 5,0 ml) contains approx. 250 mg ciprofloxacin.

Ciprobay tablets and suspension can be taken independent of mealtimes.

If Ciprobay is taken on an empty stomach, the active substance is absorbed more rapidly.

It has been shown in clinical trials that a reduction of absorption can be expected if taken with dairy products or with mineral fortified drinks. The tablets or suspension should not be taken concurrently with dairy products or with mineral fortified drinks alone (e.g. milk, yoghurt, calcium fortified orange juice). However, dietary calcium as part of a meal does not significantly affect Ciprobay absorption.

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 - 10 days with Ciprobay tablets or suspension. 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).

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.

Infectious diarrhoea: 500 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.

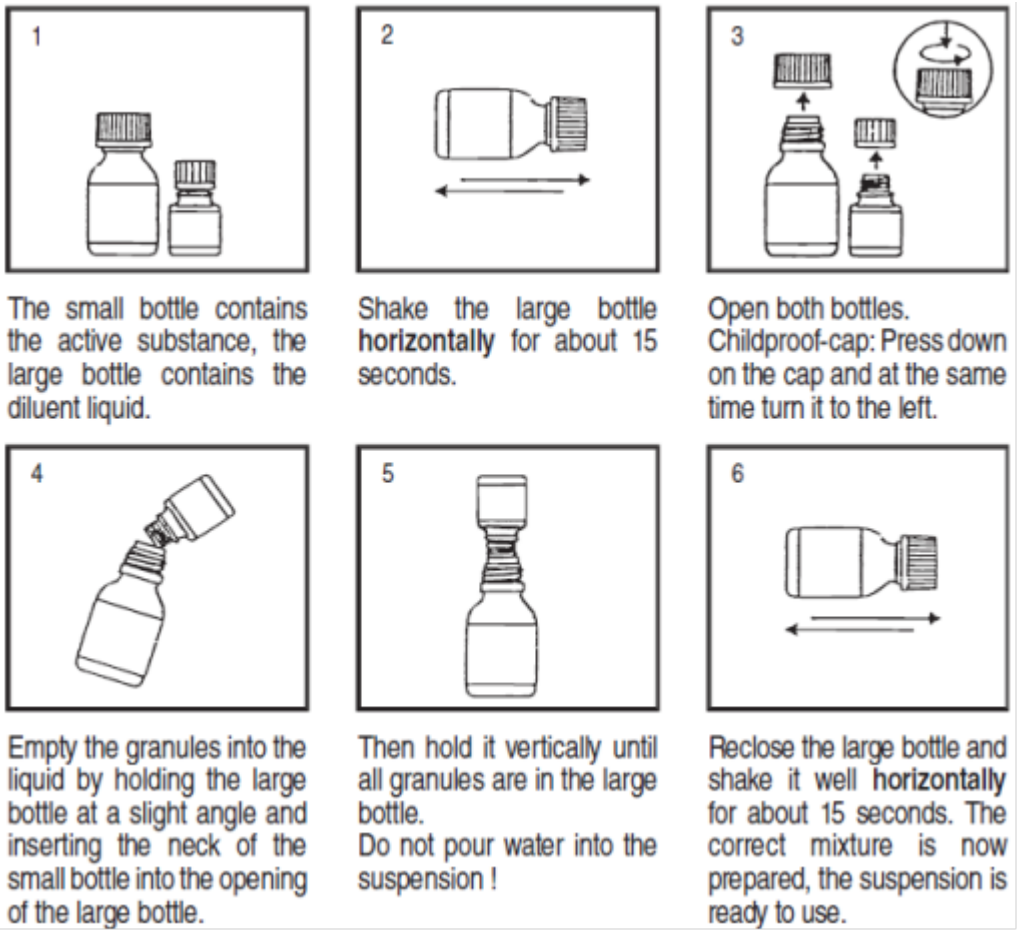
Gonorrhoea: A single dose of 250 mg.

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

If the patient is unable to take Ciprobay tablets or suspension, because of the severity of his illness or for other reasons (e.g. patients on enteral nutrition), it is recommended to commence the therapy with intravenous Ciprobay. After intravenous administration the treatment can be continued orally.

Instructions for use/handling:

Preparation of the ready-to-use suspension:



Taking the ready-to-use suspension:

Swallow the prescribed amount of suspension as quickly as possible. Do not chew the microcapsules present in the suspension, simply swallow them. A drink of water may be taken afterwards. Replace the cap on the bottle after use. It may be stored at room temperature up to 25°C. Do not store in refrigerator. The ready-to-use suspension is stable for 14 days. After treatment has been completed, it should not be re-used.

Shake well each time before use for approx. 15 seconds.

The graduated measuringspoon with the markings 1/2 is equivalent to 2,6 ml and contains 2,5 ml of final mixed suspension and 1/1 is equivalent to 5,2 ml and contains 5,0 ml of final mixed suspension. The graduated measuringspoon must be used for measuring the required prescribed amount of Ciprobay suspension.

Important incompatibilities:

No additions should be made to the mixed final suspension.

CIPROBAY IV

Dosage and Duration of Treatment:

The dosage of Ciprobay IV is determined by the severity and type of infection, the sensitivity of the causative organism(s) and the age, mass and renal function of the patient. The usual dose is 100 mg - 200 mg IV every 12

hours. For severe and / or complicated infections 400 mg may be administered every 12 hours (i.e. bd). Intravenous therapy should be discontinued as soon as oral Ciprobay therapy can be substituted. The normal duration of intravenous therapy is up to 7 days.

Cystic fibrosis:

In cystic fibrosis patients the normal dose is 200 mg IV twice daily. The low body mass of these patients should, however, be taken into consideration when determining dosage (5 - 10 mg / kg / day).

Directions for Intravenous Administration:

Ciprobay IV should be administered by intravenous infusion over a period of 60 minutes. Slow infusion into a large vein will minimize patient discomfort and reduce the risk of venous irritation. The infusion solution can be infused either directly or after mixing with the other compatible infusion solutions.

The Ciprobay IV infusion solution is compatible with physiological saline, Ringer solution and Ringer lactate solution, 5 % and 10 % glucose solutions, 10 % fructose solution, and 5 % glucose solution with 0,225 % NaCl or 0,45 % NaCl. When Ciprobay infusion solutions are mixed with compatible infusion solutions, for microbiological reasons and light sensitivity these solutions should be administered shortly after admixture.

Important incompatibilities:

Unless compatibility with other infusion solutions / drugs has been confirmed, the infusion solution must always be administered separately. The visual signs of incompatibility are e.g. precipitation, clouding and discolouration.

Incompatibility appears with all infusion solutions / drugs that are physically or chemically unstable at the pH of the solution (e.g. penicillins, heparin solutions), especially on combination with solutions adjusted to an alkaline pH (pH of the ciprofloxacin infusion solutions: 3,9-4,5).

Any remaining solution should be discarded.

Impaired Renal or Liver Function:

In patients with reduced renal function, the half-life of Ciprobay 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.

Dose adjustment of ciprofloxacin for patients with kidney and/or liver insufficiency.

1. Kidney insufficiency:
   - 1.1 CL_{cr} □ 31 ml/min/1,73m² □ 60ml/min/1,73m² — Max 1000 mg/day orally or 800 mg/day intravenously.
   - 1.2 CLcr □ 30 ml/min/1,73m² — Max 500 mg/day orally or 400 mg/day intravenously.
   - 1.3 Impaired renal function and haemodialysis — As in 1.2 above; on dialysis days after dialysis.
2. Impaired renal function and CAPD
   - 2.1 Addition of ciprofloxacin infusion solution to the dialysate (intraperitoneal) : 50 mg ciprofloxacin/litre dialysate administered 4 times a day.
   - 2.2 Oral administration of either ciprofloxacin film coated tablet as 500 mg tablet or 2 x 250 mg tablets or ciprofloxacin suspension equivalent to 500mg ciprofloxacin is indicated.
   - 2.3 For CAPD patients with peritonitis, the recommended daily oral dose is 500 mg 4 times a day.
3. Liver function disturbances: No dose adjustment.
4. Liver and kidney insufficiency: As in 1.1 and 1.2 above.

SIDE EFFECTS AND SPECIAL PRECAUTIONS:

The most common Adverse Reactions based on all clinical studies with Ciprobay (oral, parenteral)

BODY SYSTEM	
Incidence of frequency ≥ 1 % < 10 % (very common)	
Digestive system:	Nausea, diarrhoea
Skin and appendages:	Rash
Incidence of frequency ≥ 0.1 % < 1 % (common)	
Body as a whole:	Abdominal pain, moniliasis, asthenia (general feeling of weakness, tiredness)
Cardiovascular system:	(thrombo)-phlebitis
Digestive system:	SGOT increased, SGPT increased, vomiting, dyspepsia, abnormal liver function test, alkaline phosphatase increased, anorexia, flatulence, bilirubinemia
Haemic and lymphatic system:	Eosinophilia, leukopenia
Injection site reaction:	Injection site reaction
Metabolic and nutritional disorder:	Creatinin increased, BUN (urea) increased
Musculo Skeletal system:	Arthralgia (joint pain)
Nervous system:	Headache, dizziness, insomnia, agitation, confusion
Skin and appendages:	Pruritus, maculopapular rash, urticaria
Special senses:	Taste perversion
Incidence of frequency ≥ 0.01 % < 0.1 % (uncommon)	
Body as a whole:	Pain, pain in extremities, back pain, chest pain
Cardiovascular system:	Tachycardia, migraine, syncope, vasodilation (hot flushes), hypotension
Digestive system:	Moniliasis (oral), jaundice, cholestatic jaundice, pseudomembranous colitis
Haemic and lymphatic system:	Anemia, leucopenia (granulocytopenia), leucocytosis, altered prothrombin values, thrombocytopenia, thrombocytemia (thrombocytosis)
Hypersensitivity:	Allergic reaction, drug fever, anaphylactoid (anaphylactic) reaction
Metabolic disorders:	Oedema (peripheral, vascular, face), hyperglycemia
Musculo-Skeletal system:	Myalgia (muscular pain), joint disorder (joint swelling)
Nervous system:	Hallucination, sweating, paresthesia (peripheral paralgesia), anxiety, abnormal dreams (nightmares), depression, tremor (trembling), convulsion, hypesthesia
Respiratory system:	Dyspnoea, larynx oedema
Skin and appendages:	Photosensitivity reaction
Special senses:	Tinnitus, transitory deafness (especially at high frequencies), abnormal vision (visual disturbances), diplopia, chromatopsia, taste loss (impaired taste)

Urogenital system:	Acute kidney failure, kidney function abnormal, vaginal moniliasis, hematuria, crystalluria, nephritis interstitial

Incidence of frequency < 0.01%

Cardiovascular system:	Vasculitis (petechiae, haemorrhagic bullae, papules, crust formation)
Digestive system:	Moniliasis (gastrointestinal), hepatitis
Haemic and lymphatic system:	Haemolytic anemia, pancytopenia and bone marrow supression
Hypersensitivity:	Shock (anaphylactic; life threatening), pruritic rash
Metabolic and nutritional disorders:	Amylase increased, lipase increased
Nervous system:	Grand mal convulsion, abnormal (unsteady) gait
Skin and appendages	Petechia, erythema multiforme (minor), erythema nodosum

The following Adverse Reactions have been reported from post marketing surveillance.

Incidence of frequency < 0.01%

Digestive system:	Liver necrosis (very rarely progressing to life threatening hepatic failure), life threatening pseudomembranous colitis with possible fatal outcomes, pancreatitis
Haemic and lymphatic system:	Petechia (punctate skin haemorrhages), pancytopenia, agranulocytosis, marrow depression
Musculo-Skeletal system:	Tendinitis (predominantly achillo tendinitis); partial or complete tendon rupture (predominantly achilles tendon), myasthenia Exacerbation of symptoms of myasthenia gravis
Nervous system:	Psychosis, intracranial hypertension, ataxia, hyperesthesia, hypertonia, twitching
Skin and appendages:	Stevens-Johnson Syndrome, epidermal necrolysis (Lyell Syndrome), fixed eruption
Hypersensitivity:	Serum sickness like reaction
Special senses:	Parosmia (impaired smell), anosmia (usually reversible on discontinuation)

Gastrointestinal System:

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 (life threatening pseudomembranous colitis with possible fatal outcome), requiring immediate treatment. In such cases Ciprobay must be discontinued and appropriate therapy initiated (e.g. vancomycin, orally 4 x 250 mg/day)

There can be a temporary increase in transaminases, alkaline phosphatase or cholestatic jaundice, especially in patients with previous liver damage

Nervous System:

In epileptics and in patients who have suffered from previous CNS-disorders (e.g. lowered convulsion threshold, previous history of convulsion, reduced cerebral blood flow, altered brain structure or stroke),

Ciprobay should only be used where the benefits of treatment exceed the risks, since these patients are endangered because of possible central-nervous side effects.
In some instances the CNS reactions occurred after the first administration of Ciprobay already. In rare cases depression or psychosis can progress to self endangering behaviour. In these cases Ciprobay has to be discontinued and the doctor should be informed immediately.

Hypersensitivity:
In some instances, the hypersensitivity and allergic reactions already occurred after the first administration and the doctor should be informed immediately. Anaphylactic/anaphylactoid reactions in very rare instances can progress to a life threatening shock, in some instances after the first administration. In these cases Ciprobay has to be discontinued, medical treatment (e.g. treatment for shock) is required.

Musculo-Skeletal System:
At any sign of tendinitis (e. g. painfull swelling) the administration of Ciprobay should be discontinued, physical exercises be avoided, and a physician be consulted. Tendon rupture (predominantly achilles tendon) has been reported predominantly in the elderly on prior systemic treatment with glucocorticoids.

Skin and Appendages:
Ciprobay has been shown to produce photosensitivity reactions. Patients taking Ciprobay should avoid direct exposure to excessive sunlight or UV-light. Therapy should be discontinued if photosensitization (i. e. sunburn-like skin reactions) occur.

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.

Local reactions:
Phlebitis or thrombophlebitis, local irritation and pain at the site of injection have been reported with intravenous administration of Ciprobay. Intravenous infusion should be administered by slow infusion over a period of 60 minutes. These reactions are more frequent if the infusion time is 30 minutes or less, or if small veins of the hand are used. These may appear as local skin reactions which resolve rapidly upon completion of the infusion. Subsequent intravenous administration is not contraindicated unless the reactions recur or worsen.

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.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:
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 Ciprobay. Only a small amount of Ciprobay (< 10 %) is removed from the body after haemodialysis or peritoneal dialysis. Treatment should be symptomatic and supportive.

IDENTIFICATION:

CIPROBAY 250 tablets: Round, scored, convex, slightly yellowish, film-coated tablet with CIP 250 imprinted on the upper side and the Bayer cross on the lower side.

CIPROBAY 500 tablets: Oblong, scored, convex, slightly yellowish, film-coated tablet with CIP 500 imprinted on the upper side and Bayer on the lower side.

CIPROBAY 750 tablets: Oblong, scored, convex, slightly yellowish, film-coated tablet with CIP 750 imprinted on the upper side and Bayer on the lower side.

CIPROBAY IV: Clear pale yellow solution.

CIPROBAY IV Flexibag: Clear, colourless to slightly yellow solution.

CIBROBAY Suspension 5 %: White to slightly yellowish granules for reconstitution.

Microcapsules diluent: White to slightly yellowish, oily suspension with strawberry odour, occasionally may contain yellow-orange droplets and globular particles.

When reconstituted as directed, the final mixed suspension is white to slightly yellowish with a strawberry odour, occasionally may contain yellow-orange droplets and globular particles.

PRESENTATION:

CIPROBAY tablets: Blister packs of 10 tablets. 250 mg tablets also available in packs of 6.

CIPROBAY IV: 50 ml, 100 ml and 200 ml glass infusion bottles.

CIPROBAY IV Flexibag: 100ml and 200ml flexible polyvinylchloride bag with an aluminium foil overwrap.

CIPROBAY Suspension 5 %: Each trade package carton comprises:
1 brown glass bottle containing microcapsules for reconstitution.
1 white plastic bottle with suspension diluent to prepare the final mixed suspension.
1 graduated measuringspoon.

STORAGE INSTRUCTIONS:

CIPROBAY tablets: Store at or below 25 °C. Keep out of reach of children.

CIPROBAY IV: Store at or below 25 °C. Keep out of reach of children.

CIPROBAY IV: After infusion of the required dose, any remaining solution should be discarded. **CIPROBAY IV** is light-sensitive and should always be stored in the cardboard outer carton. No special precautions are, however, required during the 60 minute infusion period. In daylight conditions, efficacy is guaranteed for a period of 3 days.

CIPROBAY Suspension: The individual components viz. microcapsules and suspension diluent should not be used after the expiration dates have been reached.

Store at or below 25 °C. Keep out of reach of children.

Microcapsules diluent: Store at or below 25 °C. Protect from freezing. Store in upright position.

Keep out of reach of children.

When reconstituted as directed utilizing the individual components, the final mixed ready-to-use suspension is stable at room temperature (up to 25 °C) for 14 days. After this time the final mixed suspension should not be taken.

Keep out of reach of children.

REGISTRATION NUMBERS:

South Africa:

CIPROBAY 250:	U/20.1.1/126
CIPROBAY 500:	U/20.1.1/127
CIPROBAY 750:	U/20.1.1/128
CIPROBAY IV:	Y/20.1.1/311
CIPROBAY IV Flexibag:	32/20.1.1/0574
CIPROBAY Suspension 5 %:	31/20.1.1/0111
Diluent for Ciprobay Suspension 5 %:	31/34/0113

NAME AND BUSINESS ADDRESS OF THE APPLICANT:

Bayer (Pty) Ltd
27 Wrench Road, Isando, 1609
Registration No. 1968/011192/07

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