Dimensions: 404 mm (H) x 170 mm (W)

Folded size: 25,25 x 170 mm

Pharma Code: 289

SCHEDULING STATUS: S4

PROPRIETARY NAME (and dosage form):
CIPROGEN 250 mg (Film-coated tablets)
CIPROGEN 500 mg (Film-coated tablets)
CIPROGEN 750 mg (Film-coated tablets)

COMPOSITION:
CIPROGEN 250 mg film-coated tablet contains ciprofloxacin hydrochloride monohydrate, equivalent to 250 mg ciprofloxacin. Sugar free.
CIPROGEN 500 mg film-coated tablet contains ciprofloxacin hydrochloride monohydrate, equivalent to 500 mg ciprofloxacin. Sugar free.
CIPROGEN 750 mg film-coated tablet contains ciprofloxacin hydrochloride monohydrate, equivalent to 750 mg ciprofloxacin. Sugar free.
Excipients:
Colloidal silicon dioxide; corn starch; crospovidone; magnesium stearate; microcrystalline cellulose PH101; opadry II white Y-22-7719; pregelatinized maize starch

PHARMACOLOGICAL CLASSIFICATION:
A 20.1.1 Broad and medium spectrum antibiotics.

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

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

Organisms that exhibit varying degrees of *in vitro* sensitivity to ciprofloxacin are as follows: *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. Bacteroides, Treponema pallidum).

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 the lung, skin, fat, muscle, cartilage and bone. It is also present in the active form in the saliva, nasal and bronchial secretions, cerebrospinal fluid and the aqueous humor. Protein binding is low. 40 % to 50 % is excreted in the 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:
CIPROGEN tablets are indicated for treatment of the following infections that are caused by bacteria sensitive to ciprofloxacin:
Lower Respiratory Tract Infections caused by *Escherichia coli, Klebsiella pneumoniae, Enterobacter cloacae, Proteus mirabilis, Pseudomonas aeruginosa, Haemophilus influenzae* and *Haemophilus parainfluenzae*.
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*.
Gastrointestinal Infections: Infective diarrhoea caused by *Escherichia 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.

CONTRAINDICATIONS:
Safety during pregnancy and lactation has not been established. **CIPROGEN** is contraindicated in patients who have shown hypersensitivity to ciprofloxacin or other quinolones.

WARNINGS AND SPECIAL PRECAUTIONS:

CIPROGEN is contraindicated in children under 18 years and in growing adolescents, except where the benefit of treatment exceeds the risks. Experimental evidence indicates that species variable reversible lesions of the cartilage of weight-bearing joints have been seen in immature members of certain animal species.

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

CIPROGEN may cause crystalluria and patients receiving **CIPROGEN** should be well hydrated and excessive alkalinity of the urine should be avoided.

Disturbances in blood glucose, including both hyperglycaemia and hypoglycaemia have been reported, usually in diabetic patients receiving concomitant treatment with an oral hypoglycaemic medicine or with insulin. Cases of hypoglycaemic coma have been reported. In diabetic patients, careful monitoring of blood glucose is recommended.

SPECIAL PRECAUTIONS
Concomitant use of fluoroquinolones and ACE inhibitors/renin-angiotensin receptor blockers may precipitate acute kidney injury in patients, especially those with moderate to severe renal impairment and elderly patients. (see **CONTRAINDICATIONS**). Renal function should be assessed before initiating treatment, and monitored during treatment, with fluoroquinolones of ACE inhibitors/ renin-angiotensin receptor blockers.

Effects on ability to drive and use machines
Even when taken as prescribed, **CIPROGEN** 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.

Interactions: Concurrent administration of **CIPROGEN** 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, the plasma levels of theophylline should be monitored, and dosage adjustments made as appropriate.

CIPROGEN 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. H2-receptor blockers have no effect on the absorption of ciprofloxacin after oral administration. Administration of fenbufen (a nonsteroidal anti-inflammatory agent) with quinolones may increase the risk of central nervous system stimulation and convulsive seizures.

Transient increases in serum creatinine concentrations may occur in patients receiving cyclosporin concomitantly and monitoring of the serum creatinine is advised.

The action of warfarin may be intensified if administered together with **CIPROGEN**. The action of glibenclamide (hypoglycaemia) may be intensified if administered together with **CIPROGEN**.
Co-administration of probenecid and **CIPROGEN** increases serum concentrations of ciprofloxacin as probenecid interferes with the renal excretion of ciprofloxacin.

Metoclopramide accelerates the absorption of ciprofloxacin, resulting in a shorter time to reach C_{max}. No effect was seen on the bioavailability of ciprofloxacin.

INTERACTIONS
Concomitant use of fluoroquinolones and ACE inhibitors/renin-angiotensin receptor blockers may precipitate acute kidney injury (see **CONTRAINDICATIONS**)

In a study of volunteers treated with rifampin, moxifloxacin, or both drugs, rifampin reduced the moxifloxacin $AUC_{0\text{-}24}$ by 27 % via induction of sulfate conjugation (Weiner et al., 2007). In another study, rifapentine reduced moxifloxacin $AUC_{0\text{-}24}$ by 17 % (Dooley et al., 2008). These studies suggest that the most important cause of pharmacokinetic variability for moxifloxacin is concomitantly administered drugs for tuberculosis.

HUMAN REPRODUCTION
Safety and/or efficacy has not been established.

DOSAGE AND DIRECTIONS FOR USE:
CIPROGEN tablets should be swallowed whole with plenty of liquid and may be taken before or after meals. The dose ranges from 250 - 750 mg twice daily and the duration of treatment depends upon the severity of the infection, clinical response and bacteriological findings. Severe and complicated infections may require prolonged therapy. The usual treatment period for acute infections is 5 – 10 days. Streptococcal infections should be treated for at least 10 days because of the possibility of late complications.
Elderly people should receive doses as low as possible depending on the creatinine clearance and severity of the infection.
Lower respiratory tract infections: Mild to moderate: 250 to 500 mg twice daily; severe or complicated: 750 mg twice daily. In cystic fibrosis patients, the dosage is 7,5 to 15 mg/kg body mass/day in two divided doses.
Urinary tract infections: Acute uncomplicated cystitis and mild to moderate infections: 250 mg twice daily; severe or complicated infections: 500 mg twice daily.
Skin infections: Mild to moderate infections: 500 mg twice daily; severe or complicated infections: 750 mg twice daily.
Infectious diarrhoea: 500 mg twice daily.
Bone infections: Mild to moderate infections: 500 mg twice daily; severe or complicated infections: 750 mg twice daily. Treatment may be required for 6 weeks or longer.
Gonorrhoea: A single dose of 250 mg.

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

Dose adjustment of ciprofloxacin for patients with kidney and/or liver insufficiency	
1. Kidney insufficiency: 1.1. CL_{CR} ≥ 31 ml/min/1,73m² ≤ 60 ml/min/1,73m² 1.2. CL_{CR} ≤ 30 ml/min/1,73m² 1.3. Impaired renal function and haemodialysis	 Maximum 1000 mg/day orally. Maximum 500 mg/day orally. As in 1.2 above, on dialysis days, after dialysis.
2. Impaired renal function and CAPD: 2.1. Oral administration of **CIPROGEN** 500 mg tablet or 2 x 250 mg tablets. 2.2. For CAPD patients with peritonitis, the recommended daily dose is 500 mg 4 times daily.	
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 following side effects have been reported:
Blood and lymphatic system disorders:
Eosinophilia, leukocytopenia, granulocytopenia, anaemia, thrombocytopenia
Less frequent: leucocytosis, thrombocytosis, haemolytic anaemia, altered prothrombin values.
Metabolism and nutritional disorders:
Less frequent: Hypoglycaemia, particularly in diabetic patients.
Frequency unknown: Hyperglycaemia, hypoglycaemic coma.
Nervous system disorders:
Dizziness, headache, tiredness, nervousness, agitation, trembling, 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). These reactions may already occur after the first administration of **CIPROGEN**. **CIPROGEN** should be discontinued and a medical doctor consulted immediately.
Eye, Ear and labyrinth disorders:
Impaired taste and smell, visual disturbances (e.g. diplopia, colour vision), tinnitus, transitory impairment of hearing (high frequencies)
Cardiac disorders:
Tachycardia, hot flushes, migraine, fainting
Gastrointestinal disorders: Nausea, diarrhoea, vomiting, dyspepsia, abdominal pain, flatulence, anorexia. If severe or persistent diarrhoea occurs during or after treatment, a doctor must be consulted. This side-effect can hide a serious intestinal disease (pseudomembranous colitis) which may require immediate treatment. Treatment with **CIPROGEN** should be discontinued immediately and appropriate therapy initiated. Medicines that inhibit peristalsis should not be given.
Hypersensitivity reactions: Rashes, pruritus, drug fever, petechiae, haemorrhagic bullae, vasculitis. Erythema nodosum, erythema exsudativum multiforme, Stevens-Johnson syndrome, Lyell syndrome, interstitial nephritis, hepatitis, hepatic necrosis.
Anaphylactic/anaphylactoid reactions (facial, vascular and laryngeal oedema, dyspnoea progressing to life-threatening shock), in some instances after the first administration. In these cases, **CIPROGEN** has to be discontinued and medical treatment (e.g. treatment for shock) is required.
Other side effects: Joint pain, joint swelling. Less frequently: general feeling of weakness, muscular pains, tendosynovitis, photosensitivity, transient impairment in kidney function including transient kidney failure.
Achillotendinitis: Cases of partial or complete rupture of the Achilles tendon have been reported especially in the elderly on prior systemic treatment with glucocorticoids. At any signs of achillotendinitis (e.g. painful swelling) the administration of **CIPROGEN** should be discontinued and a physician consulted.
Long-term or repeated administration of **CIPROGEN** can lead to superinfections with resistant bacteria or yeast-like fungi.
Care is necessary in patients with impaired hepatic or renal function, glucose –6-phosphate dehydrogenase deficiency or myasthenia gravis. Exposure to strong sunlight or sunlamps should also be avoided.
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.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:
Acute, excessive overdosage may lead to reversible renal toxicity. Monitoring of renal function is recommended together with routine emergency measures and administration of magnesium and calcium containing antacids to reduce the absorption of ciprofloxacin. Less than 10 % of ciprofloxacin in the serum is removed with haemodialysis or peritoneal dialysis. Treatment is symptomatic and supportive.

IDENTIFICATION:
CIPROGEN 250 mg: White, round, biconvex, film-coated tablets with "CF" over score line, "250" on one side and "G" on the other side.
CIPROGEN 500 mg: White, biconvex, capsule shaped, film-coated tablet marked "CF" over score line, "500" on one side and "G" on the other side.
CIPROGEN 750 mg: White, biconvex, capsule shaped, film-coated tablet marked "CF" over score line, "750" on one side and "G" on the other side.

PRESENTATION:
CIPROGEN 250 mg: PVC/PVDC/aluminium blister strip containing 6 or 10 tablets packed into unit cartons. White opaque HDPP containers containing 10 or 100 tablets.
CIPROGEN 500 mg: PVC/PVDC/aluminium blister strip containing 10 tablets packed into unit cartons. White opaque HDPP containers containing 10 or 100 tablets.
CIPROGEN 750 mg: PVC/PVDC/aluminium blister strip containing 10 tablets packed into unit cartons. White opaque HDPP containers containing 10 tablets.

STORAGE INSTRUCTIONS:
Store below 25 ºC in a dry place and protect from light. KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBERS:
CIPROGEN 250 mg: 36/20.1.1/0428
CIPROGEN 500 mg: 36/20.1.1/0429
CIPROGEN 750 mg: 36/20.1.1/0427

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION:
Trinity Pharma (Pty) Ltd. 106 16th Road, Building 2, Midrand, 1686, South Africa.

DATE OF PUBLICATION OF THIS PACKAGE INSERT:
11 June 2002

TRINITY PHARMA

Tel: 010 594 5610. Email: PV@kahmagroup.co.za

F72050

SKEDULERINGSTATUS: S4

EIENDOMSNAAM (en doseervorm):
CIPROGEN 250 mg (Filmbedekte tablette)
CIPROGEN 500 mg (Filmbedekte tablette)
CIPROGEN 750 mg (Filmbedekte tablette)

SAMESTELLING:
CIPROGEN 250 mg tablet bevat siprofloksasienhidrochloriedmonohidraat, ekwivalent aan 250 mg siprofloksasien. Suikervry.
CIPROGEN 500 mg tablet bevat siprofloksasienhidrochloriedmonohidraat, ekwivalent aan 500 mg siprofloksasien. Suikervry.
CIPROGEN 750 mg tablet bevat siprofloksasienhidrochloriedmonohidraat, ekwivalent aan 750 mg siprofloksasien. Suikervry.

FARMAKOLOGIESE KLASSIFIKASIE:
A 20.1.1 Breë- en mediumspektrum antibiotika.

FARMAKOLOGIESE WERKING:
Siprofloksasien is 'n sintetiese 4-kinoloonderivaat met *in vitro* bakterisiediese aktiwiteit teen die volgende Gram-positiewe en Gram-negatiewe organismes. *In vitro* sensitiwiteit impliseer nie noodwendig *in vivo* effektiwiteit nie.

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

Organismes met wisselende grade van *in vitro* sensitiwiteit vir siprofloksasien, is die volgende: *Alcaligenes, Enterococcus faecalis, Flavobacterium, Gardnerella, Legionella, Mycobacterium fortuitum, Mycobacterium tuberculosis, Mycoplasma hominis, Streptococcus agalactiae, Chlamydia*.
Die volgende is gewoonlik weerstandig: *Enterococcus faecium, Ureaplasma urealyticum, Nocardia asteroides*. Met 'n paar uitsonderings, is anaerobe organismes matig sensitief (bv. *Peptococcus, Peptostreptococcus*), tot weerstandig (bv. *Bacteroides, Treponema pallidum*). Siprofloksasien plasmavlakke is dosisverwant en piekvlakke word 0,5 – 2 uur na orale dosering bereik. Die absolute orale biobeskikbaarheid is ongeveer 70 % met geen substansiële verlies vanweë eerstedeurgangmetabolisme nie. Verspreiding van siprofloksasien is wyd deur die liggaam en die verspreidingsvolume is hoog wat uitgebreide weefselpenetrasie aandui. Siprofloksasien is teenwoordig in die long, vel, vet, spier, kraakbeen en been. Dit is ook in aktiewe vorm teenwoordig in speeksel, neus- en brongiale sekrete, serebrospinale vog en die waterige vloeistof. Proteïenbinding is laag. Ongeveer 40 % tot 50 % word as onveranderde middel in die urien uitgeskei. Sowat 15 % van 'n enkeldosis siprofloksasien word uitgeskei as metaboliete. Uitskeiding vind primêr plaas deur die niere en meestal gedurende die eerste 12 uur na dosering. Opruiming deur die niere is ongeveer 300 ml/minuut. Die eliminasiehalfleeftyd van onveranderde siprofloksasien is 3 - 5 uur. Die eliminasiekinetika is lineêr; na herhaalde dosering met 12 uurlikse intervalle en sodra gelykvlak bereik is, kom geen akkumulasie voor nie.

INDIKASIES:
CIPROGEN Tablette is aangedui vir behandeling van die volgende infeksies veroorsaak deur bakterieë wat sensitief is vir siprofloksasien:
Onderste Lugweginfeksies veroorsaak deur *Escherichia coli, Klebsiella pneumoniae, Enterobacter cloacae, Proteus mirabilis, Pseudomonas aeruginosa, Haemophilus influenzae* en *Haemophilus parainfluenzae*.
Urienweginfeksies veroorsaak deur *Escherichia coli, Klebsiella pneumoniae, Enterobacter cloacae, Serratia marcescens, Proteus mirabilis, Providencia rettgeri, Morganella morganii, Citrobacter diversus, Citrobacter freundii, Pseudomonas aeruginosa, Staphylococcus epidermidis* en *Streptococcus faecalis*.
Vel en Sagte Weefselinfeksies veroorsaak deur *Escherichia coli, Klebsiella pneumoniae, Enterobacter cloacae, Proteus mirabilis, Proteus vulgaris, Providencia stuartii, Morganella morganii, Citrobacter freundii,, Pseudomonas aeruginosa, Staphylococcus aureus, Staphylococcus epidermidis* en *Streptococcus pyogenes*.
Gastroïntestinale Infeksies: Infektiewe diaree veroorsaak deur *Escherichia coli, Campylobacter jejuni, Shigella flexneri* en *Shigella sonnei*.
Beeninfeksies: Osteomiëlitis veroorsaak deur sensitiewe organismes.
Gonoree. Siprofloksasien is oneffektief teen *Treponema pallidum*. Tydens behandeling van *Pseudomonas aeruginosa* infeksies, moet 'n aminoglikosied saam toegedien word.

KONTRA-INDIKASIES:
Veiligheid tydens swangerskap en borsvoeding is nie vasgestel nie. **CIPROGEN** is teenaangedui by pasiënte wat hipersensitiwiteit teenoor **CIPROGEN** of ander kinolone vertoon.

WAARSKUWINGS:

CIPROGEN is teenaangedui by kinders onder 18 jaar en groeiende adolesente, behalwe waar voordele van behandeling die risiko's oortref. Eksperimentele getuienis toon aan dat, afhangende van die spesie, verskillende tipes omkeerbare letsels van die kraakbeen van gewigdraende gewrigte waargeneem is by onvolwasse diere van sekere spesies.

CIPROGEN moet versigtig gebruik word deur pasiënte met 'n geskiedenis van konvulsiewe toestande.

CIPROGEN mag kristalurie veroorsaak en pasiënte wat siprofloksasien ontvang moet goed gehidreer wees en oormatige alkaliniteit van urien moet vermy word.

Versteurings in bloedglukose insluitende beide hiperglisemie en hipoglisemie is gerapporteer, gewoonlik in diabetiese pasiënte wat meegaande behandling ontvang met ´n orale hipoglisemiese medisyne of met insulien. Gevalle van hipoglisemiese koma is gerapporteer. In diabetiese pasiënte word omsigtige monitering van bloedglukose aanbeveel.

DOSIS EN GEBRUIKSAANWYSINGS:
CIPROGEN tablette moet heel ingesluk word met baie vloeistof en mag voor of na maaltye ingeneem word. Die dosis wissel tussen 250 - 750 mg twee maal per dag en die duur van behandeling hang af van die erns van infeksie, kliniese respons en bakteriologiese bevindings. Ernstige en gekompliseerde infeksies mag verlengde terapie benodig. Die gewone behandelingsperiode vir akute infeksies is 5 - 10 dae.
Streptokokkale infeksies behoort vir ten minste 10 dae behandel te word vanweë die moontlikheid van laat komplikasies. Bejaarde pasiënte moet die laagste moontlike dosis ontvang, afhangend van die kreatinienopruiming en erns van die infeksie.
Onderste lugweginfeksies: Lig tot matig: 250 – 500 mg twee maal per dag; ernstig of gekompliseerd: 750 mg twee maal per dag. Vir sistiese fibrose is die dosis 7,5 tot 15 mg/kg liggaamsgewig/dag, in twee verdeelde doserings.
Urienweginfeksies: Akute ongekompliseerde sistitis en ligte tot matige infeksies: 250 mg twee maal per dag; ernstige of gekompliseerde infeksies: 500 mg twee maal per dag.
Velinfeksies: Ligte tot matige infeksies: 500 mg twee maal per dag; ernstige of gekompliseerde infeksies: 750 mg twee maal per dag.
Infektiewe diaree: 500 mg twee maal per dag.
Beeninfeksies: Ligte tot matige infeksies: 500 mg twee maal per dag; ernstige of gekompliseerde infeksies: 750 mg twee maal per dag. Behandeling mag benodig word vir 6 weke of langer.
Gonorree: 'n Enkele dosis van 250 mg.

Dosisaanpassing vir pasiënte met verswakte nier- en/of lewerfunksie:
By pasiënte met ingekorte nierfunksie, word die halflewe van siprofloksasien verleng en moet die dosis aangepas word. By pasiënte met veranderende nierfunksie of pasiënte met ingekorte nierfunksie of ingekorte lewerfunksie, verskaf monitering van geneesmiddelserumvlakke die mees betroubare basis vir dosisaanpassing.

Dosisaanpassing vir pasiënte met verswakte nier- en/of lewerfunksie	
1. Verswakte nierfunksie: 1.1. Kreatinienopruiming ≥ 31 ml/min/1,73m2 ≤ 60 ml/min/1,73m^2 1.2. Kreatinienopruiming ≤ 30 ml/min/1,73m^2 1.3. Ingekorte nierfunksie en hemodialise	Maksimum 1000 mg/dag oraal. Maksimum 500 mg/dag oraal. Soos vir 1.2 hierbo, op dialise dae, na die dialise.
2. Ingekorte nierfunksie en CAPD (chroniese ambulante peritoneale dialise): 2.1. Orale toediening van **CIPROGEN** 500 mg tablet of 2 x 250 mg tablette. 2.2. Vir CAPD pasiënte met peritonitis, is die aanbevole dosis 500 mg vier maal per dag.	
3. Versteurde lewerfunksie	**Geen dosisaanpassing nodig nie.**
4. Verswakte lewer- sowel as nierfunksie	Soos vir 1.1 en 1.2 hierbo.

NEWE-EFFEKTE EN SPESIALE VOORSORGMAATREËLS:
Die volgende newe-effekte is aangemeld:
Metabolisme en voedingsafwykings: *Minder dikwels:* Hipogliseimie, veral in diabetiese pasiënte. *Frekwensie onbekend:* Hiperglisemie, hipoglisemiese koma.
Gastroïntestinaal: Naarheid, diaree, braking, dispepsie, buikpyn, winderigheid, anoreksie. Indien erge of volgehoue diaree voorkom tydens of na behandeling, moet 'n dokter gespreek word. Hierdie newe-effek mag 'n ernstige dermsiekte (pseudomembraneuse kolitis) verberg, wat onmiddellike behandeling mag benodig. Siprofloksasien behandeling moet dadelik gestaak word en toepaslike terapie begin word. Geneesmiddels wat peristalse onderdruk is teenaangedui.
Senustelsel: Duiseligheid, hoofpyn, moegheid, senuweeagtigheid, agitasie, bewerigheid, slaaploosheid, perifere paralgesie, sweet, onvaste gang, konvulsies, verhoogde intrakraniale druk, angstoestande, nagmerries, verwardheid, depressie en hallusinasies. Individuele gevalle van psigotiese reaksies (wat selfs mag vorder tot selfbedreigende gedrag), is bekend. Hierdie reaksies mag reeds voorkom na die eerste toediening van **CIPROGEN**. **CIPROGEN** moet onmiddellik gestaak word en 'n dokter gespreek word.
Sensoriese organe: Verswakte smaak en reuk, visieversteurings (bv. diplopie, kleurvisie), tinnitus, verbygaande gehoorinkorting (hoë frekwensies).
Hipersensitiwiteitsreaksies: Veluitslag, pruritus, geneesmiddelkoors, petegieë, hemoragiese bullae, vaskulitis. Erythema nodosum, erythema exsudativum multiforme, Stevens-Johnson sindroom, Lyell sindroom, interstisiële nefritis, hepatitis, lewernekrose. Anafilaktiese/anafilaktoïede reaksies (edeem van gesig, bloedvate en larinks, dispnee wat tot lewensbedreigende skok vorder), in sommige gevalle na die eerste toediening. By hierdie pasiënte moet **CIPROGEN** gestaak word en mediese behandeling (bv. van skok) is noodsaaklik.
Kardiovaskulêr: Tagikardie, warm gloede, migraine, floute.
Ander newe-effekte: Gewrigspyn, gewrigswelling. *Minder algemeen:* gevoel van swakheid, spierpyne, tendosinovitis, fotosensitiwiteit, verbygaande inkorting van nierfunksie insluitend tydelike nierversaking. Achillotendinitis: Gevalle van gedeeltelike of totale skeuring van die Achilles tendon is aangemeld, veral by bejaardes of pasiënte wat vooraf met glukokortikoïede behandel is. Indien enige tekens van achillotendinitis verskyn (bv. pynlike swelling), moet **CIPROGEN** toediening gestaak word en 'n dokter geraadpleeg word. Langtermyn of herhaalde toediening van **CIPROGEN** kan lei tot superinfeksies met weerstandige bakterieë of gisagtige fungi. Wees versigtig by pasiënte met ingekorte lewer- of nierfunksie, glukose-6-fosfaatdehidrogenase tekort of myasthenia gravis. Blootstelling aan sterk sonlig of sonlampe moet ook vermy word.
Effekte op bloed en bloedkomponente: Eosinofilie, leukositopenie, granulositopenie, anemie, trombositopenie. *Selde:* leukositose, trombositose, hemolitiese anemie, veranderde protrombienwaardes.
Invloed op laboratoriumwaardes/uriensediment: Daar mag 'n tydelike verhoging wees van transaminases, alkaliese fosfatase of cholestatiese geelsug, veral by pasiënte met vorige lewerskade; tydelike toename van ureum, kreatinien of bilirubien in die serum; in enkele gevalle: hiperglisemie, kristalurie of hematurie.
Ander inligting: Selfs wanneer ingeneem soos voorgeskryf, kan **CIPROGEN** 'n persoon se reaksietyd nadelig beïnvloed, tot so 'n mate dat die vermoë om 'n motor te bestuur of masjinerie te hanteer, benadeel word. Dit geld veral as alkohol daarmee saam gebruik word.
Interaksies: Gelyktydige toediening van **CIPROGEN** met teofillien kan lei tot verhoogde plasmakonsentrasies van teofillien en verlenging van teofillien se eliminasiehalfleeftyd. Dit mag lei tot verhoogde risiko van teofillienverwante newe-effekte. Indien gesamentlike gebruik onvermydelik is, moet teofillienplasmavlakke gemonitor word en dosisaanpassings gemaak word waar toepaslik. **CIPROGEN** tablette moet ingeneem word 1 tot 2 ure voor, of ten minste 4 ure na inname van ysterpreparate, teensuurmiddels wat magnesium, aluminium, kalsium of sukralfaat bevat, omdat inmenging van absorpsie mag plaasvind. H_2 – reseptorblokkers het geen effek op die absorpsie van siprofloksasien na orale inname nie. Gelyktydige inname van fenbufen ('n nie-steroïed anti-inflammatoriese middel) met kinolone, kan die risiko van sentrale senustelselstimulasie en konvulsies verhoog. Verbygaande toename van serum kreatinien konsentrasies mag voorkom by pasiënte wat terselfdertyd siklosporien ontvang en monitering van serumkreatinien word aanbeveel. Die werking van warfarien kan versterk word wanneer saam met **CIPROGEN** geneem. Die werking van glibenklamied (hipoglukemie) kan ook versterk word deur **CIPROGEN**. Gesamentlike gebruik van probenesied en **CIPROGEN** verhoog serumkonsentrasies van siprofloksasien, omdat probenesied inmeng met renale uitskeiding van siprofloksasien. Metoklopramied versnel die absorpsie van siprofloksasien en verkort dus die tyd om C_{max} (maksimum plasmakonsentrasie) te bereik. Geen effek op die biobeskikbaarheid van siprofloksasien is waargeneem nie.

BEKENDE SIMPTOME VAN OORDOSERING EN BESONDERHEDE VAN DIE BEHANDELING DAARVAN:
Akute oormatige oordosering kan lei tot omkeerbare niertoksisiteit. Monitering van nierfunksie word aanbeveel, tesame met roetine noodmaatreëls en toediening van magnesium- en kalsiumbevattende teensuurmiddels om absorpsie van siprofloksasien te verminder. Minder as 10% van siprofloksasien in die serum word verwyder deur hemodialise of peritoneale dialise. Behandeling is simptomaties en ondersteunend.

IDENTIFIKASIE:
CIPROGEN 250 mg: Wit, ronde, bikonvekse, filmbedekte tablette.
CIPROGEN 500 mg: Wit, ronde, bikonvekse, filmbedekte tablette.
CIPROGEN 750 mg: Wit, bikonvekse, kapsulevormige, filmbedekte tablette.

AANBIEDING:
CIPROGEN 250 mg: Wit ondeursigtige HDPP houers, elk met 10 of 100 tablette.
CIPROGEN 500 mg: Wit ondeursigtige HDPP houers, elk met 10 of 100 tablette.
CIPROGEN 750 mg: Wit ondeursigtige HDPP houers, elk met 10 of 100 tablette.

BERGINGSINSTRUKSIES:
Berg benede 25 ºC in 'n droë plek en beskerm teen lig. HOU BUITE BEREIK VAN KINDERS.

REGISTRASIENOMMERS:
CIPROGEN 250 mg: 36/20.1.1/0428
CIPROGEN 500 mg: 36/20.1.1/0429
CIPROGEN 750 mg: 36/20.1.1/0427

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