APPROVED
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LOXIP P1535586

LOXIP P1535586

PROFESSIONAL INFORMATION
SCHEDULING STATUS:
SOUTH AFRICA: S4

NAMIBIA: NS2

PROPRIETARY NAME (and dosage form):

LOXIP 250 mg (Tablet)
LOXIP 500 mg (Tablet)

COMPOSITION:
LOXIP 500 mg: Each film-coated tablet contains ciprofloxacin hydrochloride equivalent to 500 mg ciprofloxacin. Sugar free.

LOXIP 250 mg: Each film-coated tablet contains ciprofloxacin hydrochloride equivalent to 250 mg ciprofloxacin. Sugar free.

The other ingredients are cellulose, microcrystalline, sodium starch glycolate, povidone; silica, colloidal anhydrous, magnesium stearate and opadry white.

Opadry white contains hypromellose, macrogol and titanium dioxide (C.I. No: 77891).

PHARMACOLOGICAL CLASSIFICATION:

A 20.1.1 Broad and medium spectrum antibiotics.

PHARMACOLOGICAL ACTION:

Pharmacodynamics

Ciprofloxacin is a synthetic fluoroquinolone antibiotic. It is bactericidal and acts by inhibiting the A subunit of DNA gyrase which is essential in the reproduction of bacterial DNA.

Micro-organisms resistant to ciprofloxacin:

Enterococcus faecium; Norcardia asteroides; Ureaplasma urealyticum; Peptostreptococcus species; *Peptococcus* species; Bacteroides; *Treponema pallidum; Staphylococcus aureus* (methicillin-resistant), *Stenotrophomonas maltophilia, Actinomyces, Listeria monocytogenes* and *Mycoplasma genitalium.*

Pharmacokinetics

After oral administration, ciprofloxacin plasma levels are dose-related and peak at 0,5 - 2 hours. The absolute bioavailability is approximately 70 %. Protein binding is 40 %. 40 to 50 % is excreted in urine as unchanged ciprofloxacin. Approximately 15 % of a single dose is eliminated as metabolites.

Elimination is primarily renal 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.

INDICATIONS:

LOXIP is indicated for the treatment of the following infections, when caused by susceptible organisms:

Lower respiratory tract infections caused by:

Enterobacter cloacae, Escherichia coli, Haemophilus influenzae, Haemophilus parainfluenzae, Klebsiella pneumoniae, Proteus mirabilis, Pseudomonas aeruginosa.

Urinary tract infections caused by:

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

Skin and soft tissue infections caused by:

Citrobacter freundii, Enterobacter cloacae, Escherichia coli, Klebsiella pneumoniae, Morganella morganii, Proteus mirabilis, Proteus vulgaris, Providencia stuartii, Pseudomonas aeruginosa, Staphylococcus aureus, Staphylococcus epidermidis, Streptococcus pyogenes.

Gastro-intestinal infections:

Infective diarrhoea caused by *Campylobacter jejuni, Escherichia coli , Shigella flexneri* and *Shigella sonnei.*

Bone Infections:

Osteomyelitis due to sensitive Gram-negative organisms.

Gonorrhoea: (except that is due to *N. gonorrhoeae*)

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

CONTRA-INDICATIONS:

LOXIP is contra-indicated in patients with a history of hypersensitivity to ciprofloxacin, any other quinolones, or any of the inactive ingredients of **LOXIP**.

Pregnancy and lactation:

LOXIP is contra-indicated in children under the age of 18 years and in growing adolescents. Experimental evidence indicates lesions of the cartilage of weight-bearing joints in immature members of certain animal species.

WARNINGS AND SPECIAL PRECAUTIONS:

LOXIP should be used in caution with patients with a history of convulsive disorders.
Crystalluria related to the use of **LOXIP** has been observed. Patients receiving **LOXIP** should be well hydrated and excessive alkalinity of the urine should be avoided.

Severe infections and/or infections due to Gram-positive or anaerobic bacteria

For the treatment of severe infections, staphylococcal infections and infections involving anaerobic bacteria, **LOXIP** should be used in combination with an appropriate antibacterial agent.

***Streptococcus pneumonia* infections**

LOXIP should not be used for treatment of pneumococcal infections due to inadequate efficacy against *Streptococcus pneumonia.*

Genital tract infections

Genital tract infections may be caused by fluoroquinolone-resistant *Neisseria gonorrhoeae* isolates. In genital tract infections thought to be due to *N. gonorrhoeae,* **LOXIP** should not be used.

Cardiac disorders

LOXIP is associated with cases of QT prolongation. In general, elderly patients may be more susceptible to **LOXIP** associated effects on the QT interval. Precaution should be taken when using **LOXIP** with concomitant medicinal products that can result in prolongation of the QT interval (e.g. class IA or III antidysrhythmics) or in patients with risk factors for torsades de pointes (e.g. known QT prolongation, uncorrected hypokalaemia).

Hypersensitivity

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

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, **LOXIP** must be discontinued and appropriate therapy initiated. Medicines that inhibit peristalsis are contra-indicated There can be a temporary increase in transaminases, alkaline phosphatase or cholestatic jaundice, especially in patients with previous liver damage.

Musculoskeletal system

At any sign of tendonitis (e.g. painful swelling) the administration of **LOXIP** should be discontinued, physical exercise should be avoided, and a medical practitioner consulted. Tendon rupture (predominantly Achilles tendon) has been reported predominantly in the elderly on prior systemic treatment with glucocorticoids and in patients with kidney or lung transplant. Close monitoring of these patients is necessary if they are prescribed **LOXIP**. The risk is still present weeks after completion of treatment.

Nervous system

In patients with epilepsy 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), **LOXIP** should only be used where the benefits of treatment exceed the risks, since these patients are vulnerable because of possible CNS side-effects.

In some instances the CNS reactions already occurred after the first administration of **LOXIP**. In these cases **LOXIP** must be discontinued and the medical practitioner informed immediately. Depression or psychosis can progress to result in self endangering behaviour.

Skin and appendages

Severe Cutaneous Adverse Reactions(SCARS) including Toxic Epidermal Necrolysis (TEN) Stevens Johnson Syndrome (SJS) and Drug Reaction with no Eosinophilia and Systemic Symptoms (DRESS), which could be life-threatening or fatal, have been reported with **LOXIP** (see **"SIDE-EFFECTS"**). At the time of prescription, patients should be advised of the signs and symptoms of severe skin reactions and closely monitored. If signs and symptoms suggestive of these reactions appear, **LOXIP** should be discontinued immediately, and an alternative treatment should be considered. If the patient have developed a serious reaction such as SJS, TEN or DRESS with use of **LOXIP**, treatment with **LOXIP** must not be restarted in this patient at any time.

Cytochrome P450

Ciprofloxacin is known to be a moderate inhibitor of the CYP 450 1A2 enzymes. Care should be taken when other medicines which are metabolised via the same enzymatic pathway (e.g. theophylline, methylxanthines, caffeine, duloxetine, clozapine) are administered concomitantly with **LOXIP**. Increased plasma concentrations associated with medicine specific side-effects may be observed due to inhibition of their metabolic clearance by **LOXIP** (see **"INTERACTIONS"**).

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 recommende Patients receiving **LOXIP** should be well hydrated and excessive alkalinity of the urine should be avoided.

Long-term or repeated administration of **LOXIP** can lead to superinfections with resistant bacteria or fungi.

Ability to Drive and Use Machines

The ability to drive a motor vehicle or operate machinery may be impaired by **LOXIP**, particularly when used in combination with alcohol.

Side-effects that may be potentially life-threatening are pancytopenia and bone marrow depression (see **"SIDE EFFECTS"**).

INTERACTIONS:

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

There is a high risk of tendonitis (see **"WARNINGS AND SPECIAL PRECAUTIONS"**).

Concurrent administration of **LOXIP** 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 toxicity. If concomitant use cannot be avoided, plasma levels of theophylline should be monitored and dosage adjustments made as appropriate.

LOXIP 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 H -receptor blockers.

Concomitant administration of the nonsteroidal anti-inflammatory drugs (NSAIDs), with quinolones such as **LOXIP** may increase the risk of central nervous system stimulation and 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 **LOXIP** and warfarin may lead to warfarin toxicity; therefore the INR should be closely monitored.

Concurrent administration of **LOXIP** and glibenclamide can potentiate the action of glibenclamide, leading to hypoglycaemia.

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

Metoclopramide accelerates the absorption of **LOXIP**, resulting in a shorter time to reach maximum plasma concentrations.

Concurrent administration of **LOXIP** with ropinirole may lead to elevated plasma concentrations of ropinirole. Monitoring for ropinirole-related side-effects and appropriate dose adjustment of ropinirole is recommended during and shortly after co-administration with **LOXIP**.

Concurrent administration of **LOXIP** with lidocaine (lignocaine) may lead to elevated plasma concentrations of lidocaine and increase in side-effects related to lidocaine also occurs.

Concurrent administration of **LOXIP** with clozapine may lead to elevated serum concentrations of clozapine and Ndesmethylclozapine. Careful monitoring of clozapine associated adverse effects and appropriate adjustment of clozapine dosage during and shortly after co-administration with **LOXIP** is advised.

Concurrent administration of **LOXIP** with sildenafil may lead to elevated serum concentrations of sildenafil. Therefore, sildenafil should be used with caution when co-administered with **LOXIP**.

PREGNANCY AND LACTATION:

Safety in pregnancy and lactation has not been established (see **"CONTRA-INDICATIONS"**)

On the basis of animal studies, it has been reported that ciprofloxacin, as in **LOXIP** may cause damage to articular cartilage in the fetus. It has also been reported to cause teratogenic effects in animals. Therefore, **LOXIP** should not be given to pregnant women.

Lactation: Ciprofloxacin is excreted in breastmilk. **LOXIP** should not be used during breastfeeding.

DOSAGE AND DIRECTIONS FOR USE:

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

LOXIP 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 cultures. 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 **LOXIP**. For severe and complicated infections more prolonged therapy may be required. In streptococcal infections the treatment must last at least 10 days.

Infections of the lower respiratory tract:

Mild to moderate:	250 - 500 mg twice daily.
Severe or complicated:	750 mg twice daily.
In cystic fibrosis patients:	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 be treated with the lowest possible dose.

DETACH BEFORE DISPENSING

PASIËNTINLIGTINGSBLAD

SUID-AFRIKA: S4

NAMIBIË: NS2

LOXIP 250 mg (Tablette)
LOXIP 500 mg (Tablette)

Lees hierdie blaadjie sorgvuldig deur voordat u begin om LOXIP te neem.
- Hou hierdie blaadjie. U mag dit moontlik weer wil lees.
- Indien u verdere vrae het, moet u asseblief u dokter of apteker raadpleeg.
- **LOXIP** is vir u persoonlik voorgeskryf en u behoort nie u medisyne met ander te deel nie. Dit mag hulle skade aandoen, ook al het hulle dieselfde simptome as u.

1. WAT BEVAT LOXIP

Die aktiewe bestanddeel is siprofloksasienhidrochloried.

LOXIP 250 mg: Elke filmbedekte tablet bevat siprofloksasienhidrochloried ekwivalent aan 250 mg siprofloksasien. Suikervry.
LOXIP 500 mg: Elke filmbedekte tablet bevat siprofloksasienhidrochloried ekwivalent aan 500 mg siprofloksasien. Suikervry.

Die ander bestanddele is mikrokristallyne sellulose, natriumstyselglikolaat, povidoon, kolloïdale anhidriese silika, magnesiumstearaat en opadry wit.

Opadry wit bevat hipromellose, makrogol en titaandioksied (C.I. No: 77891).

2. WAARVOOR WORD LOXIP GEBRUIK

LOXIP word gebruik vir die behandeling van die volgende infeksies weens vatbare organismes:
- Benede lugweginfeksies.
- Urienweginfeksies.
- Gastroïntestinale infeksies soos besmetlike diaree.
- Beeninfeksies.
- Gonoree.

3. VOORDAT U LOXIP GEBRUIK

Onder die volgende omstandighede moet u nie LOXIP gebruik nie:
- As u hipersensitief (allergies) teen siprofloksasienhidrochloried of enige ander kinolone of enige van die ander bestanddele van **LOXIP** is.
- As u swanger is of borsvoed.
- As u jonger as 18 jaar is.

Wees veral versigtig met LOXIP:
- As u 'n geskiedenis van stuiptrekkings het.
- As u kristalle in u uriene ondervind wat nierpyn of –ongemak veroorsaak wanneer u urineer. U behoort goed gehidreer te wees en oormatige alkaliniteit van die uriene te vermy wanneer u **LOXIP** gebruik.
- Langtermyn of herhaalde gebruik van **LOXIP** mag tot superinfeksies met weerstandbiedende bakterieë en swamme lei.
- As u aan 'n hartkondisie ly en/of medisyne vir u hart gebruik, sal u noukeurig deur u dokter gemonitor moet word.
- As u 'n ernstige allergiese reaksie ontwikkel wanneer u **LOXIP** gebruik moet u onmiddellik u dokter raadpleeg.
- As u erge of aanhoudende diaree gedurende of na u behandeling ondervind, behoort u so gou moontlik u dokter te raadpleeg.
- As u pynlike swelling van u tendons ondervind, behoort u enige fisiese oefening te vermy en u dokter te raadpleeg.
- U behoort direkte blootstelling aan direkte sonlig en UV-lig te vermy.
- U behoort u dokter in te lig as u enige ander medisyne gebruik.
- As u 'n diabeet is en/of as u medisyne vir u bloedsuikervlakke gebruik, sal u noukeurig deur u dokter gemonitor moet word.

Neem van LOXIP saam met kos en drank:

LOXIP behoort heel met baie vloeistof gesluk en kan met of sonder voedsel geneem word.

Swangerskap en borsvoeding:

Die veiligheid van **LOXIP** in swanger en borsvoedende vroue is nie vasgestel nie.

As u swanger is of borsvoed, moet u asseblief u dokter, apteker of gesondheidsorgbeampte vir advies raadpleeg voordat u hierdie medisyne neem.

U behoort nie **LOXIP** te gebruik as u swanger is, probeer om swanger te raak, of as u u baba borsvoed nie.

Bestuur en die gebruik van masjinerie:

Die vermoë om 'n motor te bestuur of om met masjinerie te werk, mag deur **LOXIP** beïnvloed word. Dit veral in kombinasie met alkohol.

Gebruik van ander medisyne saam met LOXIP:

As u ander medisyne op 'n gereelde basis gebruik, insluitende komplementêre of tradisionele medisyne, mag die gebruik van **LOXIP** ongewenste interaksies veroorsaak. Raadpleeg asseblief u dokter, apteker of gesondheidsorgbeampte vir advies.

Daar bestaan 'n interaksie tussen **LOXIP** en teofillien wat tipies in die behandeling van asma gebruik word, NSAIMs (bv. ibuprofen), die immuunonderdrukkende middel siklosporien, warfarien wat as bloedverdunner gebruik word, die antidiabetiese middel glibenklamied, probenesied wat vir die behandeling van jig gebruik word en metoklopramied wat vir die behandeling van naarheid gebruik word.

LOXIP behoort 1 – 2 ure voor, of ten minste 4 ure na die inname van ysterpreparate, teensuurmiddels wat magnesium, kalsium of sukralfaat bevat, aangesien inmenging met die absorpsie mag voorkom.

Lig asseblief u dokter in as u **LOXIP** gebruik. As u TB toetse ondergaan mag **LOXIP** met die toets inmeng.

4. HOE OM LOXIP TE NEEM

Neem altyd **LOXIP** presies soos deur u dokter voorgeskryf. Bevestig met u dokter of apteker as u onseker is. As u van mening is dat die effek van **LOXIP** te sterk of te swak is, raadpleeg u dokter of apteker.

Dosering en tydperk van behandeling:

Die dosisreikwydte is 250 – 750 mg twee keer per dag. Die tydperk van behandeling hang van die graad van erns van die infeksie, die kliniese respons en die bakteriologiese kulture af.

As u te veel LOXIP neem:

In die geval van oordosering moet u u dokter of apteker raadpleeg. Indien hulle nie beskikbaar is nie, kontak u naaste hospitaal of gifbeheersentrum.

As u vergeet om LOXIP te neem:

As u vergeet om 'n dosis te neem, neem dit so gou as wat u daarvan onthou, tensy dit byna tyd vir u volgende dosis is. Moenie die dosis verdubbel om vir 'n oorgeslane dosis op te maak nie.

5. MOONTLIKE NEWE-EFFEKTE

LOXIP mag newe-effekte hê.

As enige van die volgende simptome voorkom, moet u asseblief onmiddellik u dokter raadpleeg:
- Tendonskeuring of swelling van die tendon (tendonitis) – tendons is taai weefselkoorde wat die spiere aan die bene heg. Simptome van tendonprobleme mag die volgende insluit: pyn, swelling, skeure en inflammasie van die tendons, insluitende agter die enkel (achilles), skouer, hand of ander tendons.
- Myasthenia gravis ('n soort spierswakheid) – **LOXIP** mag agteruitgang van die simptome van myasthenia gravis veroorsaak, insluitende spierswakhewid, gewrigspyn, gewrigswelling en 'n algemene gevoel van swakheid.
- Erge diaree met bloeding of slym.
- As u 'n diabeet is en u het enige van hierdie simptome: moegheid, duiseligheid, hartkloppings, oormatige sweet, bewerasie en onduidelike gesig.

Die volgende simptome vereis ook dringende mediese aandag:
- Erge allergiese velreaksies, insluitende uitslag, jeuk, velbulte en sensitiwiteit teen sonlig (blase, sensasie van 'n branderige vel), klein puntbloedings onder die vel, rooiheid van die vel weens allergiese reaksies en 'n rooi uitslag veroorsaak deur hipersensitiwiteit teen medisyne, siekte of ander allergeen.
- Toename in die risiko van sonbrand.
- Erge abnormaliteite in hartritme, ongereelde hartklop.
- Afwykings van die senuweestelsel soos duiseligheid, stuiptrekkings, hallusinasies, rusteloosheid, bewerasie, angstigheid of senuweeagtigheid, verwardheid, depressie, probleme om te slaap, nagmerries, selfmoordgedagtes of –aksies. Ander newe-effekte mag die volgende insluit:
- Dubbel gesig, kleurafwykings.
- Suising in die ore, gehoorverlies, belemmerde gehoor, vertigo, gevoel van konstante beweging van self of omgewing, tolsensasie.
- Kneusing, neusbloei, tandvleisbloeding.
- Gereelde infeksies van die neus, keel, vel en ander organe.
- Bleek vel, slymvliese en naelbed, gevoel van swakheid en moegheid.
- Hoofpyn, smaakafwykings.
- Nierprobleme soos bloed in die uriene, kristalle in die uriene wat pyn met urinering veroorsaak.
- Pankreatitis (swelling en inflammasie van die pankreas) wat erge brandpyn in boonste gedeelte van die buik veroorsaak, wat dan na die rug beweeg, naarheid en braking.

FREKWENSIE ONBEKEND

Frekwensie onbekend 'n Ernstige velreaksie, bekend as DRESS (medisynereaksie met eosinofilie en sistemiese simptome, wat 'n ernstige velreaksie kan veroorsaak wat een of meer organe mag aantas), kan voorkom. Jy kan die volgende ervaar: koors, hewige uitslag, vel wat afskilfer, swelling van die gesig, geswelde limfknope, grieperige gevoel, geel vel of oë, kortasemheid, droë hoes, pyn of ongemak in die borskas, voel dors, urineer minder gereeld, minder urine.

Nie al die newe-effekte wat vir **LOXIP** aangemeld is, word in hierdie blaadjie genoem nie. As u algemene gesondheid agteruitgaan of as u enige ongewone effekte ondervind terwyl u **LOXIP** neem, moet u asseblief u dokter, apteker of gesondheidsorgbeampte vir advies raadpleeg.

6. BERGING EN WEGDOEN VAN LOXIP

Hou alle medisyne buite bereik van kinders.

Bewaar teen of benede 30 °C.

Neem alle ongebruikte medisyne na u apteker.
Moenie enige ongebruikte medisyne in die drein of riolering (bv. toilet) wegdoen nie.

7. AANBIEDING VAN LOXIP

LOXIP 250 mg:

Stolpverpakking: 6's – Elke karton bevat 'n stolpstrokie met 6 tablette.
Tablette word in helder 250 mikron PVC bedek met 60 gvm PVdc en 25 mikron gedrukte aluminiumfoelie verpak. Een stolpstrokie bevat 6 tablette.

Stolpverpakking: 10's – Elke karton bevat 'n stolpstrokie met 6 tablette.
Tablette word in helder 250 mikron PVC bedek met 60 gvm PVdc en 25 mikron gedrukte aluminiumfoelie verpak. Een stolpstrokie bevat 10 tablette.

HDPE houer: 10's – Elke houer bevat 10 tablette.
Tablette word in 'n melkwit, ondeurskynende, wye-mond, ronde 40 ml HDPE houer met 'n 33 mm PP deksel en 'n induksieseëlprop verpak. Elke houer bevat 10 tablette. *Daar is geen uitdroogmiddel in die houer nie.*

HDPE Houer: 100's – Elke houer bevat 100 tablette.
Tablette word verpak in 'n melkwit, ondeursigtige, wye bek ronde 80 ml HDPE houer met 'n 43 mm PP deksel met – induksie seëlprop verpak. Elke houer bevat 100 tablette. *Daar is geen uitdroogmiddel in die houer nie.*

LOXIP 500 mg:

Stolpverpakking: 10's – Elke karton bevat 'n stolpstrokie met 6 tablette.
Tablette word in helder 250 mikron PVC bedek met 60 gvm PVdc en 25 mikron gedrukte aluminiumfoelie verpak. Een stolpstrokie bevat 10 tablette.

HDPE houer: 10's – Elke houer bevat 10 tablette.
Tablette word in 'n melkwit, ondeurskynende, wye-mond, ronde 40 ml HDPE houer met 'n 33 mm PP deksel en 'n induksieseëlprop verpak. Elke houer bevat 10 tablette. *Daar is geen uitdroogmiddel in die houer nie.*

HDPE Houer: 100's – Elke houer bevat 100 tablette.
Tablette word verpak in 'n melkwit, ondeursigtige, wye bek ronde 140 ml HDPE houer met 'n 43 mm PP deksel met 'n induksie seëlprop verpak. Elke houer bevat 100 tablette. *Daar is geen uitdroogmiddel in die houer nie.*

8. IDENTIFIKASIE VAN LOXIP

LOXIP 250 mg:

Wit tot byna-wit, ronde filmbedekte tablette met 'n breeklyn aan die een kant en 'F' en '23' op die ander kant gedruk, met 'n breeklyn tussenin.

LOXIP 500 mg:

Wit tot byna-wit, kapsuulvormige, filmbedekte tablette met 'n breeklyn aan die een kant en 'F 22' op die ander kant gedruk.

REGISTRASIENOMMER/VERWYSINGSNOMMER:

Suid Afrika

LOXIP 250 mg (Tablette): 41/20.1.1/1052
LOXIP 500 mg (Tablette): 41/20.1.1/1053

Namibië

LOXIP 250 mg (Tablette): 10/20.1.1/0323
LOXIP 500 mg (Tablette): 10/20.1.1/0324

NAAM EN ADRES VAN DIE REGISTRASIEHOUER:

Aurogen South Africa (Edms) Bpk
Woodhill Kantoorpark, Gebou Nr.1,
Eerste Vloer Phillip Engelbrechtlaan
53, Meyersdal, Uitbr. 12,
Johannesburg,1448, Suid-Afrika

DATUM VAN PUBLIKASIE:

6 Februarie 2009

Datum van hersiening

12 September 2023

A/s: 280 x 480 mm ■ Black

AUROBINDO Packaging Development		Product Name	Component	Item Code	Date & Time
		Loxip tablets	Leaflet	P1535586	05.01.2024 & 10.50 am
		Country	Version No.	Reason Of Issue	Reviewed / Approved by
		South Africa-U3	04	Commercial	
Team Leader	Kiran	Dimensions (mm)	Colours: 01		
Initiator	Bhogi	280 x 480 mm			
Artist	Sree Designers	Pharma Code: 35586			
Additional Information: Supersede Code : P1532477 Corrections: Ranjith 05.01.2024			35586		

Impaired Renal or Liver Function:

In patients with reduced renal function, the half-life of ciprofloxacin may be prolonged. The dosage needs to be adjusted as shown below.

For patients with renal impairment and hepatic insufficiency, monitoring of medicine serum levels provides the most reliable basis for dose adjustment.

Dose adjustment of ciprofloxacin for patients with renal or hepatic impairment:

1. Kidney insufficiency:

1.1 Cl_{cr} > 31 ml/min/1,73 m^2 Max 800 mg/day intravenously.

1.2 Cl_{cr} > 30 ml/min/1,73 m^2 Max 400 mg/day intravenously.

1.3 Impaired renal function: As in 1.2 above; after dialysis and haemodialysis on dialysis days.

2. Renal impairment and CAPD (chronic ambulatory peritoneal dialysis):

2.1. Oral administration of either **LOXIP** as 500 mg tablets or 2 x 250 mg tablets or **LOXIP** suspension equivalent to 500 mg **LOXIP** is indicated.

2.2. For CAPD patients with peritonitis, the recommended daily oral dose is 500 mg four times a day.

3. Hepatic impairment: No dose adjustment.

4. Hepatic and renal impairment: As in 1.1 and 1.2 above.

SIDE-EFFECTS:

MedDRA system organ class	Frequency	Adverse reactions
Blood and the lymphatic system disorders	Frequency unknown	Eosinophilia, leucocytopaenia, granulocytopaenia, anaemia, thrombocytopenia, leucocytosis, thrombocytosis, haemolytic anaemia, altered prothrombin values, pancytopenia, bone marrow depression.
Immune system disorders	Frequency unknown	Anaphylactic/anaphylactoid reactions can occur (e.g. facial, vascular and laryngeal oedema, dyspnoea progressing to life-threatening shock), serum sickness-like reaction, in some instances after the first administration. In these cases **LOXIP** has to be discontinued and appropriate medical treatment instituted.
Metabolism and nutrition disorders	Less frequent	Hypoglycaemia, particularly in diabetic patients.
Psychiatric disorders	Less frequent	Agitation, anxiety states, confusion, disorientation, hallucinations, psychotic reactions (even progressing to self-endangering behaviour), depression, nightmares.
Nervous system disorders	Less frequent	Headache, migraine, dizziness, tiredness, nervousness and trembling, hypoaesthesia, paraesthesia, dysaesthesia, hyperaesthesia, Insomnia, peripheralparalgesia, sweating, unsteady gait, convulsions, increase in intracranial pressure, seizures, peripheral neuropathy and polyneuropathy.
Eye disorders	Less frequent	Visual disturbances (e.g. diplopia, colour vision).
Ear and labyrinth disorders	Less frequent	Tinnitus, transient impairment of hearing, vertigo, hearing loss.
Cardiac disorders	Less frequent	Tachycardia, flushes, QT prolongation, ventricular dysrhythmia, Torsades de Pointes.
Vascular disorders	Less frequent	Syncope, hypotension, vasodilatation and vasculitis.
Gastrointestinal disorders	Frequent	Impaired taste and smell, nausea, diarrhoea, vomiting, dyspepsia, abdominal pain and flatulence. The development of severe and persistent diarrhoea may indicate pseudo-membranous colitis, requiring immediate treatment. In such cases **LOXIP** must be discontinued and appropriate therapy initiated.
	Less frequent	Pancreatitis
Hepatobiliary disorders	Unknown frequency	Hepatic necrosis, very seldom progressing to hepatic failure, hepatic impairment, jaundice, hepatitis, increase in transaminases and bilirubin.
Skin and subcutaneous tissue disorders:	Unknown frequency	Rashes, pruritus, urticaria and photosensitivity (blisters, sensation of skin burning), erythema nodosum and erythema exsudativum multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis, punctate skin haemorrhages (petechiae), haemorrhagic bullae and papules with signs of vascular involvement (vasculitis)and Acute generalised exanthematous pustulosis (AGEP), Drug reaction with eosinophilia and systemic symptoms (DRESS).
Musculoskeletal, connective tissue and bone disorders	Frequency unknown	Joint pain, joint swelling, general feeling of weakness (arthralgia), and myalgia (which may be of special importance in patients with myasthenia gravis) and tendosynovitis, cases of tendon rupture and achillotendonitis, increased muscle tone and cramping.
Renal and urinary disorders	Frequency unknown	Crystalluria, interstitial nephritis, transient renal impairment including transient renal failure, and haematuria.
Investigations	Frequency unknown	Abnormal prothrombin level, increased amylase, Increased blood alkaline phosphatase, hyperglycaemia.

Post-marketing adverse reactions

Hyperglycaemia, hyperglycaemic coma.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:

In the event of acute, excessive oral over-dosage, reversible renal toxicity has been reported. Apart from routine emergency measures, it is recommended to monitor renal function and to administer magnesium- or calciumcontaining antacids which reduce the absorption of oral **LOXIP**. Only a small amount of ciprofloxacin (< 10 %) is removed from the body after haemodialysis or peritoneal dialysis.

Treatment is symptomatic and supportive.

IDENTIFICATION:

LOXIP 250 mg:

White to off-white, round shaped, film-coated tablets, with a score line on one side and debossed with 'F' and '23' with a score line in between on the other side.

LOXIP 500 mg:

White to off-white, capsule shaped, film-coated tablets, with a score line on one side and debossed with 'F 22' on theother side.

PRESENTATION:

LOXIP 250 mg:

Blister pack: 6's – Each carton contains 1 blister of 6 tablets each.

Tablets are packed in clear 250 microns PVC coated with 60 gsm PVdc and 25 microns printed aluminium foil. One blister contains 6 tablets.

Blister pack: 10's – Each carton contains 1 blister of 10 tablets each.

Tablets are packed in clear 250 microns PVC coated with 60 gsm PVdc and 25 microns printed aluminium foil. One blister contains 10 tablets.

HDPE container: 10's- Each container contains 10 tablets.

Tablets are packed in milky-white, opaque, wide mouth round 40 ml HDPE container with 33 mm PP closure with induction sealing wad. Each container contains 10 tablets. *No desiccant is included in the container.*

HDPE container: 100's – Each container contains 100 tablets.

Tablets are packed in milky-white, opaque, wide mouth round 80 ml HDPE container with 43 mm PP closure with induction sealing wad. Each container contains 100 tablets. *No dessicant is included in the container.*

LOXIP 500 mg:

Blister pack: 10's – Each carton contains 1 blister of 10 tablets each.

Tablets are packed in clear 250 microns PVC coated with 60 gsm PVdc and 25 microns printed aluminium foil. One blister contains 10 tablets.

HDPE container: 10's- Each container contains 10 tablets.

Tablets are packed in milky-white, opaque, wide mouth round 40 ml HDPE container with 33 mm PP closure with induction sealing wad. Each container contains 10 tablets. *No desiccant is included in the container.*

HDPE container: 100's – Each container contains 100 tablets.

Tablets are packed in milky-white, opaque, wide mouth round 140 ml HDPE container with 43 mm PP closure with induction sealing wad. Each container contains 100 tablets. *No desiccant is included in the container.*

STORAGE INSTRUCTIONS:

Store at or below 30 °C

STORE OUT OF REACH OF CHILDREN.

REGISTRATION NUMBER:

South Africa

LOXIP 250 mg (Tablet): 41/20.1.1/1052
LOXIP 500 mg (Tablet): 41/20.1.1/1053

Namibia

LOXIP 250 mg (Tablet): 10/20.1.1/0323
LOXIP 500 mg (Tablet): 10/20.1.1/0324

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION:

AUROGEN
MEMBER OF THE AUROBINDO PHARMA GROUP

AUROGEN SOUTH AFRICA (PTY) LTD
Woodhill Office Park, Building 1, First Floor,
53 Phillip Engelbrecht Avenue Meyersdal Ext 12, 1448,
Johannesburg, South Africa

DATE OF PUBLICATION OF THE PACKAGE INSERT:

6 February 2009

Date of revision

12 September 2023

DETACH BEFORE DISPENSING

PATIENT INFORMATION LEAFLET

SOUTH AFRICA: S4

NAMIBIA: NS2

LOXIP 250 mg (Tablet)
LOXIP 500 mg (Tablet)

Read all of this leaflet carefully before you start taking LOXIP.
- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor or your pharmacist.
- **LOXIP** has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

1. WHAT LOXIP CONTAINS

The active substance is ciprofloxacin hydrochloride.

LOXIP 250 mg: Each film-coated tablet contains ciprofloxacin hydrochloride equivalent to 250 mg ciprofloxacin. Sugar free.
LOXIP 500 mg: Each film-coated tablet contains ciprofloxacin hydrochloride equivalent to 500 mg ciprofloxacin. Sugar free.

The other ingredients are cellulose, microcrystalline, sodium starch glycolate, povidone; silica, colloidal anhydrous, magnesium stearate and opadry white.

Opadry white contains hypromellose, macrogol and titanium dioxide (C.I. No: 77891).

2. WHAT LOXIP IS USED FOR

LOXIP is used for the treatment of the following infections due to sensitive micro-organisms:

- Lower respiratory tract infections
- Urinary tract infections
- Skin and soft tissue infections
- Gastro-intestinal infections such as infective diarrhea
- Bone infections
- Gonorrhoea

3. BEFORE YOU TAKE LOXIP

Do not take LOXIP:

- If you are hypersensitive (allergic) to ciprofloxacin hydrochloride or to other quinolones or to any of the other ingredients of **LOXIP.**
- If you are pregnant or breastfeeding.
- If you are under the age of 18 years.

Take special care with LOXIP:

- If you have a history of fits.
- If you experience crystals in your urine which causes kidney pain or discomfort when passing urine. You should be well hydrated and avoid excessive alkalinity of the urine when taking **LOXIP**.
- Long-term or repeated use of **LOXIP** can lead to superinfections with resistant bacteria or fungi.
- If you have a heart condition and/or are taking medicines for your heart, you will have to be closely monitored by your doctor.
- If you have a serious allergic reaction when taking **LOXIP** you should report to your doctor immediately.
- If you experience severe and persistent diarrhoea during or after your treatment, you should consult your doctor as soon as possible.
- If you experience painful swelling of your tendons, you should avoid any physical exercise and your doctor should be consulted.
- You should avoid direct exposure to excessive sunlight and UV-light.
- You should inform your doctor if you are taking any other medicines.
- If you are diabetic and/or are taking medicines for your blood sugar levels, you will have to be closely monitored by your doctor.

Taking with food and drink:

LOXIP should be swallowed whole with plenty of liquid and can be taken with or without food.

Pregnancy and Breastfeeding:

Safety of **LOXIP** in pregnant and breastfeeding women has not been established.

If you are pregnant or breastfeeding, please consult your doctor, pharmacist or healthcare professional for advice before taking this medicine.

You should not use **LOXIP** if you are pregnant, trying to become pregnant or breastfeeding your baby.

Driving and using machinery:

The ability to drive a motor vehicle or operate machinery may be affected by **LOXIP**. This applies particularly in combination with alcohol.

Taking other medicines with LOXIP:

If you are taking other medicines on a regular basis, including complementary or traditional medicines, the use of **LOXIP** with these medicines may cause undesirable interactions. Please consult your doctor, pharmacist or other healthcare professional for advice.

LOXIP interacts with theophylline typically used in the treatment of asthma, nonsteroidal anti-inflammatory drugs (e.g. ibuprofen), the immune suppressant agent cyclosporin, warfarin used as a blood thinning agent, the antidiabetic medicine glibenclamide, probenecid used for treating gout and metoclopramide used for treating nausea.

LOXIP 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.

Please notify your doctor that you are using **LOXIP**. If you are undergoing TB tests, **LOXIP** may interfere with the test.

4. HOW TO TAKE LOXIP

Always take **LOXIP** exactly as your doctor has instructed you. You should check with your doctor or pharmacist if you are unsure. If you have the impression that the effect of **LOXIP** is too strong or too weak, talk to your doctor or pharmacist.

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 cultures.

If you take more LOXIP than you should:

In the event of overdosage, consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison control centre.

If you forget to take LOXIP:

If you forget to take a dose, take it as soon as you remember unless it is nearly time for your next dose. Do not take a double dose to make up for forgotten individual doses.

5. POSSIBLE SIDE-EFFECTS

LOXIP can have side-effects.

If any of the following symptoms occur, stop taking the **LOXIP** and tell your doctor immediately.

- Tendon rupture or swelling of the tendon (tendonitis) -Tendons are tough cords of tissue that connect muscles to bones. Symptoms of tendon problems may include: pain, swelling, tears and inflammation of tendons including the back of the ankle (achilles), shoulder, hand, or other tendon sites.
- Myasthenia gravis (a type of muscle weakness) - **LOXIP** may cause worsening of myasthenia gravis symptoms, including muscle weakness, joint pain, joint swelling and general feeling of weakness.
- Severe diarrhoea with bleeding or mucus.
- If you are diabetic and have any of these symptoms: tiredness, dizziness, palpitations, excessive sweating, trembling or shaking and blurred vision.

The following symptoms also need medical attention:

- Serious skin allergic reactions including rashes, itching skin, hives and sensitivity to sunlight (blisters, sensation of skin burning), small, pin-point bleeding under the skin, redness of the skin due to allergic reactions and a red rash caused by hypersensitivity to a medicine, disease or other allergen.
- Increased risk of sunburn.
- Severe heart rhythm abnormalities, irregular heart beat.
- Troubles associated with the nervous system such as dizziness, seizures, sense things that are not there (hallucinations), restlessness, tremors, feel anxious or nervous, confusion, depression, trouble sleeping, nightmares, suicidal thoughts or acts.

Other side-effects. that you may experience include:

- Double vision, colour disturbances.
- Ringing sound in the ears, loss of hearing, impaired hearing, vertigo, feeling of constant movement of self or surroundings; sensation of spinning.
- Bruising, nose-bleeds, bleeding gums.
- Frequent infections of the nose, throat, skin and other organs.
- Pale skin, mucosal linings and nail bed, feelings of weakness and fatigue.
- Headache, taste disorders.
- Kidney problems such blood in the urine, crystals in the urine causing pain during urination.
- Pancreatitis (swelling and inflammation of the pancreas) causing severe upper abdominal burning pain that spreads to your back, nausea and vomiting.

Frequency Unknown

A serious skin reaction may occur known as (DRESS) Drug Reaction with Eosinophilia and Systemic Symptoms which may cause a serious skin reaction that may affect one or more organs). You may experience the following fever, severe rash, peeling skin, swelling of the face, swollen lymph glands, flu-like feeling, yellow skin or eyes, shortness of breath, dry cough, chest pain or discomfort, feel thirsty, urinating less often, less urine.

Not all side-effects reported for **LOXIP** are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking **LOXIP**, please consult your doctor, pharmacist or other health care professional for advice.

6. STORING AND DISPOSING OF LOXIP

Store all medicines out of reach of children.

Store at or below 30 °C

Return all unused medicine to your pharmacist. Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

7. PRESENTATION OF LOXIP

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10. NAME AND ADDRESS OF REGISTRATION HOLDER

Aurogen South Africa (Pty) Ltd
Woodhill Office Park, Building 1, First Floor,
53 Phillip Engelbrecht Avenue Meyersdal Ext 12, 1448,
Johannesburg, South Africa

11. DATE OF PUBLICATION

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