230 mm

700 mm

SCHEDULING STATUS:
S4

1. NAME OF THE MEDICINE

LONXAVE 400 (Film-Coated Tablets)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains:
Each tablet contains 400 mg of moxifloxacin hydrochloride equivalent to 400 mg moxifloxacin.
Contains sugar (50 mg lactose monohydrate).
Excipients:
For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Brick red coloured, capsule shaped, biconvex, film-coated tablets plain surface on both the sides.

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

LONXAVE 400 is indicated for the treatment of adults (> 18 years of age) with mild to moderately severe infections caused by susceptible strains of the designated microorganisms in the conditions listed below:

- Acute bacterial sinusitis caused by *Haemophilus influenzae* or *Moraxella catarrhalis*.
- Acute bacterial exacerbation of chronic bronchitis caused by *Haemophilus influenzae, Haemophilus parainfluenzae* or *Moraxella catarrhalis*.
- Community acquired pneumonia (of mild to moderate severity) caused by *Haemophilus influenzae, Mycoplasma pneumoniae, Chlamydia pneumoniae* or *Moraxella catarrhalis*.
- Uncomplicated skin and soft tissue infections caused by *Streptococcus pyogenes*, Complicated skin and skin structure infections (including diabetic foot infections) caused by *Streptococcus pyogenes, Enterococcus faecalis, Streptococcus agalactiae, Proteus mirabilis or Enterobacter cloacae*.
- Uncomplicated pelvic inflammatory deseas (i.e. infections of female upper genital tract, including salpingitis and endometritis).
- Complicated intra-abdominal infections including polymicrobial infections such as abscesses.

4.2 Posology and method of administration

Posology

Adults
The recommended dose for **LONXAVE 400** is 400 mg once-daily for all indications.
Duration of treatment:
The duration of treatment should be determined by the severity of the indication or clinical response.
The following general recommendations for the treatment of upper and lower respiratory tract infections are made:

• Acute exacerbation of chronic bronchitis	5 days
• Community acquired pneumonia	7 - 14 days
• Acute sinusitis	10 days

The recommended duration of treatment in skin and soft tissue infections is as follows:

• Uncomplicated skin and skin structure infections	7 days
• Complicated skin and skin structure infections	7 – 21 days

The recommended durations for other infections are:

• Uncomplicated pelvic inflammatory disease	14 days
• Complicated intra-abdominal infections total treatment duration for sequential therapy (intravenous followed by oral therapy)	5 – 14 days

The recommended duration of treatment for the indication being treated should not be exceeded.

Special Populations
Elderly: No adjustment of dosage is required in the elderly.
Children: The use of **LONXAVE 400** in children and adolescents under 18 years in the growth phase is contra-indicated.
Hepatic impairment: No dosage adjustment is required in patients with mild to moderate impaired liver function (Child-Pugh A and B). No pharmacokinetic data are available for patients with severely impaired liver function (Child-Pugh C). Due to the lack of data **LONXAVE 400** is contraindicated in patients with severe hepatic impairment.
Renal impairment: No dose adjustment is required in patients with any degree of renal impairment (including creatinine clearance < 30 ml/min/1,73 m²). There is no pharmacokinetic data available in patients on dialysis treatment, or in patients with advanced renal impairment who are not on a dialysis programme. **LONXAVE 400** should therefore not be used in these patients.

Method of administration:
The tablet is swallowed whole with a glass of water. **LONXAVE 400** can be taken independent of food intake.

4.3 Contraindications:

Known hypersensitivity to moxifloxacin or to any component of the tablets or other quinolones.
Due to the lack of clinical data the use of **LONXAVE 400** is not recommended in patients with severe hepatic insufficiency (Child-Pugh C). No dosage adjustment is required in patients with mild to moderate hepatic insufficiency (Child-Pugh A and B).
Quinolones are known to distribute well into breast milk of lactating women. The use of **LONXAVE 400** in pregnancy and breastfeeding mothers is contra-indicated (see section 4.6).
LONXAVE 400 is contra-indicated in children under 18 years and in growing adolescents (except where no other suitable antimicrobial agent can be used). 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.

LONXAVE 400 is also contra-indicated in:
- Congenital or acquired QT prolongation.
- Electrolyte disturbances, particularly in uncorrected hypokalaemia.
- Clinically relevant bradycardia.
- Clinically relevant heart failure with reduced left-ventricular ejection fraction.
- Previous history of symptomatic dysrhythmias.
  - **LONXAVE 400** should not be used concurrently with other medicines that prolong the QT interval (see section 4.5).
  - Concomitant use of fluoroquinolones including **LONXAVE 400** with ACE inhibitors/Recin-Angiotensin blockers is contraindicated in patients with moderate to severe renal impairment.
  - Use of fluoroquinolones is contraindicated in patients with confirmed mitral valve and/or aortic valve regurgitation unless no safer appropriate alternative antibiotic is available, has failed or is not well tolerated

4.4 Special warnings and precautions for use

The safety and efficacy of **LONXAVE 400** in prepubertic patients, adolescents (less than 18 years of age) pregnant and lactating women have not been established (see section 4.6).

Prolongation of QTc interval and potentially QTc-prolongation-related clinical conditions
LONXAVE 400 has been shown to prolong the QT interval of the electrocardiogram in some patients. **LONXAVE 400** should be avoided in patients with known prolongation QT interval, patients with uncorrected hypokalaemia and patients receiving Class IA (e.g. quinidine, procainamide) or Class III (e.g. amiodarone, sotalol) antidysrhythmic agents, due to lack of clinical experience with **LONXAVE 400** in these patient populations (see section 4.3).
Pharmacokinetic studies between **LONXAVE 400** and other medicines that prolong the QT interval such as disopiris, erythromycin, antipsychotics and tricyclic antidepressants have not been performed. An additive effect of **LONXAVE 400** and these medicines cannot be excluded, therefore **LONXAVE 400** should not be used concurrently with these medicines.
The effect of **LONXAVE 400** on patients with congenital prolongation of the QT interval has not been studied; however it is expected that these individuals may be more susceptible to drug-induced QT prolongation. Because of limited clinical experience, **LONXAVE 400** should not be used in patients with ongoing proarrhythmic conditions, such as clinically significant bradycardia and acute myocardial ischaemia.
The magnitude of QT prolongation may increase with increasing concentrations of **LONXAVE 400** therefore the recommended dose should not be exceeded. QT prolongation may lead to an increased risk for ventricular dysrhythmias including torsade de pointes. The mean ± SD effect of moxifloxacin 400 mg on the QTc interval was 6 ± 26 ms.

Patients with myasthenia gravis
LONXAVE 400 should be used with caution in patients with myasthenia gravis because the symptoms can be exacerbated.

Effects on weight bearing joints
The oral administration of moxifloxacin caused lameness in immature dogs. Histopathological examination of the weight-bearing joints of these dogs revealed permanent lesions of the cartilage. Related group-class medicines also produce erosions of cartilage of weight bearing joints and other signs of arthropathy in immature animals of various species.

Nervous system effects
Convulsions have been reported in patients receiving quinolones such as **LONXAVE 400**. Quinolones may also cause central nervous system (CNS) events including: nervousness, agitation, insomnia, anxiety, nightmares, paranoia, dizziness, confusion, tremors, hallucinations, depression and less frequently, suicidal thoughts or acts. These reactions may occur following the first dose. If these reactions occur in patients receiving **LONXAVE 400**, **LONXAVE 400** should be discontinued and appropriate measures instituted. **LONXAVE 400** should be used with caution in patients with known or suspected CNS disorders (e.g. severe cerebral arteriosclerosis and epilepsy) or in the presence of other risk factors that may predispose to seizures or lower the seizure threshold (see section 4.8).

Peripheral neuropathy
Cases of sensory or sensorimotor polyneuropathy resulting in paraesthesias, hypoesthesias, dysaesthesias, or weakness have been reported in patients receiving quinolones including **LONXAVE 400**. Patients under treatment with **LONXAVE 400** should be advised to inform their doctor prior to continuing treatment if symptoms of neuropathy such as pain, burning, tingling, numbness, or weakness develop (see section 4.8). **LONXAVE 400** should be discontinued if the patient experiences symptoms of neuropathy in order to prevent the development of an irreversible condition.

Hypersensitivity/allergic reactions
Serious and occasionally fatal hypersensitivity (anaphylactic) reactions, some following the first dose, have been reported in patients receiving quinolone therapy such as **LONXAVE 400**. Some reactions were accompanied by cardiovascular collapse, loss of consciousness, tingling, pharyngeal or facial oedema, dyspnoea, urticaria and itching. Serious anaphylactic reactions require immediate emergency treatment with epinephrine (adrenaline). **LONXAVE 400** should be discontinued at the first appearance of a skin rash or any other sign of hypersensitivity. Oxygen, intravenous steroids and airway management, including intubation, may be administered as indicated.
Anaphylactic reactions in very rare instances can progress to a life threatening shock, in some cases after the first administration. In these cases **LONXAVE 400** has to be discontinued and medical treatment (e.g. treatment of shock) should be required.
Severe and sometimes fatal events, some due to hypersensitivity and some of uncertain aetiology, have been reported in patients receiving therapy with **LONXAVE 400**. These events may be severe and generally occur following the administration of multiple doses. Clinical manifestations may include one or more of the following: rash, fever, eosinophilia, jaundice and hepatic necrosis.

Antibiotic-associated diarrhoea including colitis
Pseudomembranous colitis has been reported with **LONXAVE 400**; therefore, it is important to consider this diagnosis in patients who present with diarrhoea subsequent to the administration of **LONXAVE 400**. Treatment with **LONXAVE 400** alters the normal flora of the colon and may permit overgrowth of Clostridia. After the diagnosis of pseudomembranous colitis has been established, therapeutic measures should be initiated. Mild cases of pseudomembranous colitis usually respond to **LONXAVE 400** discontinuation alone. In moderate to severe cases consideration should be given to management with fluids and electrolytes, protein supplementation and treatment with an antibacterial medicine clinically effective against *Clostridium difficile* colitis.

Tendon inflammation, tendon rupture
Tendon inflammation and rupture may occur with **LONXAVE 400** particularly in elderly patients and in those treated concurrently with corticosteroids. **LONXAVE 400** should be discontinued immediately if the patient experiences tendonitis with pain and inflammation or rupture of a tendon and appropriate treatment (e.g. immobilisation) must be initiated for the affected tendon.

Prevention of photosensitivity reactions
Photatoxicity has been reported in patients receiving certain quinolones; patients should be instructed to avoid excessive sunlight or artificial ultraviolet light (e.g. tanning beds) and contact a medical practitioner if sunburn-like reactions or skin eruptions occur.

Patients with pelvic inflammatory disease
For patients with complicated pelvic inflammatory disease (e.g. associated with a tubo-ovarian or pelvic abscess), for whom an intravenous treatment is considered necessary, treatment with **LONXAVE 400** is not recommended.

Severe liver disorders
Cases of fulminant hepatitis potentially leading to liver failure (including fatal cases) have been reported with **LONXAVE 400** (see section 4.8.). Patients should be advised to contact their doctor prior to continuing treatment if signs and symptoms of fulminant hepatic disease develop such as rapidly developing asthenia associated with jaundice, dark urine, bleeding tendency or hepatic encephalopathy.
Liver function tests/investigations should be performed in cases where indications of liver dysfunction occur (see section 4.3).

Serious bullous skin reactions
Cases of bullous skin reactions like Stevens-Johnson syndrome or toxic epidermal necrolysis have been reported with **LONXAVE 400** (see section 4.8). Patients should be advised to contact their doctor immediately prior to continuing treatment if skin and/or mucosal reactions occur.

Psychiatric reactions
Psychiatric reactions may occur even after the first administration of quinolones, including **LONXAVE 400**. In some cases depression or psychotic reactions have progressed to suicidal thoughts and self-injurious behaviour such as suicide attempts (see section 4.8). In the event that the patient develops these reactions, **LONXAVE 400** should be discontinued and appropriate measures instituted. Caution is recommended if **LONXAVE 400** is to be used in psychotic patients or in patients with history of psychiatric disease.

Patients with glucose-6-phosphate dehydrogenase deficiency
Patients with a family history of, or actual glucose-6-phosphate dehydrogenase deficiency are prone to haemolytic reactions when treated with quinolones. Therefore, **LONXAVE 400** should be used with caution in these patients.

Interference with biological tests
LONXAVE 400 therapy may interfere with the Mycobacterium spp. culture test by suppression of mycobacterial growth causing false negative results in samples taken from patients currently receiving **LONXAVE 400**.

Patients with MRSA infections
LONXAVE 400 is not recommended for the treatment of MRSA infections. In case of a suspected or confirmed infection due to MRSA, treatment with an appropriate antibacterial agent should be started (see section 5.1).

Concomitant use of fluoroquinolones and ACE inhibitors/renin-angiotensin receptor blockers in renal impairment and elderly patients
Concomitant use of fluoroquinolones including **LONXAVE 400** and ACE inhibitors/renin-angiotensin receptor blockers may precipitate acute kidney injury (AKI) in patients, especially those with moderate to severe renal impairment and elderly patients. (See Section 4.5). Renal function should be assessed before initiating treatment, and monitored during treatment, with **LONXAVE 400** or ACE inhibitors/renin-angiotensin receptor blockers.

Patients with mitral valve and/or aortic valve regurgitation
There is some evidence, although inconclusive, of a possible association between oral fluoroquinolone use and mitral valve and/or aortic valve regurgitation. A thorough cardiovascular examination including echocardiogram, should be performed before oral fluoroquinolones are prescribed. Fluoroquinolones should not be prescribed to patients with mitral valve and or aortic valve regurgitation (see Section 4.3)

Lactose:
LONXAVE 400 contains lactose; and should not be given to patients with known hereditary problems, or a history of galactose intolerance. Lapp-lactase deficiency or glucose-galactose malabsorption.

4.5 Interaction with other medicines and other forms of interaction

Concomitant use of LONXAVE 400 with other medicines that may prolong QT interval: An additive effect on QT interval prolongation of **LONXAVE 400** and other medicines that may prolong the QTc interval cannot be excluded. This might lead to an increased risk of ventricular arrhythmias, including torsade de pointes.
Therefore, co-administration of **LONXAVE 400** with any of the following medicines is contraindicated (see section 4.3):
- anti-dysrhythmics class IA (e.g. quinidine, hydroquinidine, disopyramide)
- anti-dysrhythmics class III (e.g. amiodarone, sotalol, dofetilide, ibutilide)
- antipsychotics (e.g. phenothiazines, pimozide, sertindole, haloperidol, sultopride)
- tricyclic antidepressives (e.g. amitriptyline, imipramine, desmipramine)
- certain antimicrobial medicines (sequinavir, sparfloxacin, erythromycin IV, erythromycin, pentamidine,
- antimalarials particularly halofantrine
- certain antihistaminics (astemizole, mizolastine)
- others (cisapride, vincamine IV, bepridil, diphemanil).

LONXAVE 400 should be used with caution in patients who are taking medication that can reduce potassium levels (e.g. loop and thiazide-type diuretics, laxatives and enemas (high doses), corticosteroids, amphotericin B) or medication that is associated with clinically significant bradycardia.

Food and dairy products: **LONXAVE 400** can be taken with or without food as the absorption of moxifloxacin is not altered by food intake.

Ranitidine: The concomitant administration with ranitidine which alters the gastric pH does not change the absorption characteristics of **LONXAVE 400** significantly.

Antacids, minerals and multivitamins: Concomitant ingestion of **LONXAVE 400** together with antacids, minerals and multivitamins may result in impaired absorption of **LONXAVE 400** due to formation of chelate complexes with the multivalent cations contained in these preparations. This may lead to plasma concentrations considerably lower than desired. Hence, antacids, anti-retroviral medicines and other preparations containing magnesium, aluminium and other minerals such as iron should be administered at least 4 hours before or 2 hours after ingestion of a **LONXAVE 400** dose.

Warfarin: Cases of increased anticoagulant activity have been reported in patients receiving oral anticoagulants concurrently with **LONXAVE 400**. International Normalised Ratio (INR) monitoring is recommended, and if necessary, the oral anticoagulant dosage should be adjusted as appropriate.

Digoxin: The pharmacokinetics of digoxin are not significantly influenced by **LONXAVE 400** (and vice versa).

Itraconazole: The pharmacokinetics of **LONXAVE 400** are not significantly altered by itraconazole. No dose adjustment is necessary for itraconazole when given with **LONXAVE 400** and vice versa.

Theophylline: No influence of **LONXAVE 400** on theophylline pharmacokinetics (and vice versa) at steady state was detected. Hence, no recommendations with respect to theophylline dosing need to be given.

Antidiabetics: Concomitant administration of **LONXAVE 400** with glibenclamide may result in a decrease of approximately 21 % in the peak plasma concentrations of glibenclamide.

Oral contraceptives: No interaction has occurred following concomitant oral administration of **LONXAVE 400** with oral contraceptives.

Calcium supplements: No interaction has occurred following concomitant oral administration of **LONXAVE 400** with calcium supplements.

Morphine: Parenteral administration of morphine does not reduce the oral bioavailability of **LONXAVE 400.**

Atenolol: The pharmacokinetics of atenolol are not significantly influenced by **LONXAVE 400.**

Medicines metabolised by Cytochrome P450 enzymes:
In vitro studies with cytochromes P450 isoenzymes (CYP) indicate that moxifloxacin does not inhibit CYP3A4, CYP2D6, CYP2C9, CYP2C19 or CYP1A2, suggesting that **LONXAVE 400** is unlikely to alter the pharmacokinetics of medicines metabolised by these enzymes (e.g. midazolam, cyclosporine, warfarin, theophylline).

Nonsteroidal anti-inflammatory drugs (NSAIDs): The concomitant administration of NSAIDs with **LONXAVE 400** may increase the risk of CNS stimulation and convulsions (see section 4.4).

Charcoal: Concomitant administration of charcoal with a dose of 400 mg **LONXAVE 400** will reduce systemic availability of the medicine by more than 80 %.

ACE inhibitors/renin-angiotensin receptor blockers: Concomitant use of fluoroquinolones including **LONXAVE 400** and ACE inhibitors/renin-angiotensin receptor blockers may precipitate acute kidney injury (see section 4.3). A potential mechanism for the observed interaction has not been identified. Most of the published reports indicate acute interstitial nephritis as the underlying cause of AKI with fluoroquinolones. Interstitial nephritis or other pathology due to a fluoroquinolone could be a trigger for ACE inhibitor-related AKI or more severe AKI leading to admission.

4.6 Fertility, pregnancy and lactation

Safety in pregnancy and lactation has not been established. The use of **LONXAVE 400** in pregnancy and breastfeeding mothers is contra-indicated (see Section 4.5).

Pregnancy
The safety of **LONXAVE 400** in human pregnancy has not been evaluated. Animal studies have shown reproductive toxicity. The potential risk for humans is unknown. Due to the experimental risk of damage by fluoroquinolones to the weight-bearing cartilage of immature animals and reversible joint injuries described in children receiving some fluoroquinolones, **LONXAVE 400** must not be used in pregnant women.

Breastfeeding
There is no data available in lactating or nursing women. Preclinical data indicate that small amounts of moxifloxacin are excreted in milk. In the absence of human data and due to the experimental risk of damage by fluoroquinolones to the weight-bearing cartilage of immature animals, breastfeeding is contraindicated during **LONXAVE 400** therapy.

Fertility: Animal studies do not indicate impairment of fertility.

4.7 Effects on ability to drive and use machines

LONXAVE 400 may cause dizziness and lightheadedness. Patients should be instructed that if they experience these symptoms they should avoid potentially hazardous tasks such as driving or operating machinery.

4.8 Undesirable effects

LONXAVE 400 can have side effects.
Apart from nausea and diarrhoea all adverse reactions were observed at frequencies below 3%.

Table 1 Tabulated summary of adverse reactions associated with LONXAVE 400

Frequency	
Infections and infestations	
Frequent:	Mycotic superinfections
Blood and lymphatic system disorders	
Less frequent:	Anaemia, leukopenia, thrombocytopenia, thrombocythemia, prolonged prothrombin time/increased INR, abnormal thromboplastin level, increased prothrombin level/decreased INR, abnormal prothrombin level/INR, blood eosinophilia.
Immune system disorders	
Less frequent:	Allergic reaction, anaphylactic/anaphylactoid reaction, allergic oedema/angioedema (including laryngeal oedema), anaphylactic/anaphylactoid shock (potentially life-threatening).
Metabolic and nutritional disorders	
Less frequent:	Hyperlipidaemia, hyperglycaemia, hypertriglyceride.
Psychiatric disorders	
Less frequent:	Anxiety reactions, psychomotor hyperactivity, agitation, emotional lability, depression (potentially culminating in self-endangering behaviour such as suicidal ideation/thoughts of suicide attempts), hallucinations.
Frequency not known:	Depersonalisation, psychotic reactions (potentially culminating in self-endangering behaviour such as suicidal ideation / thoughts of suicide attempts).
Nervous system disorders	
Frequent:	Headache, dizziness.
Less frequent:	Paraesthesia, dysaesthesia, taste disorders (including ageusia), confusion and disorientation, sleep disorders, tremor, vertigo, somnolence, hypoaesthesia, smell disorders (including anosmia), abnormal dreams, disturbed coordination (including gait disturbances due to dizziness or vertigo), which may lead to fall with injuries especially in elderly), seizures, disturbed attention, speech disorders, amnesia, peripheral neuropathy, polyneuropathy.
Eye disorders	
Less frequent:	Visual disturbances
Ear and labyrinth disorders	
Less frequent:	Tinnitus, hearing impairment including deafness.
Cardiac disorders	
Frequent:	QT prolongation.
Less frequent:	Palpitations, tachycardia, atrial fibrillation, angina pectoris, ventricular tachyarrhythmias, unspecified dysrhythmias.
Frequency not known:	Torsade de Pointes, cardiac arrest.
Vascular disorders	
Less frequent:	Vasodilatation, syncope, hypertension, hypotension.
Respiratory, thoracic and mediastinal disorders	
Less frequent:	Dyspnoea, asthma
Gastrointestinal disorders	
Frequent:	Nausea, vomiting, gastrointestinal and abdominal pain, diarrhoea.
Less frequent:	Anorexia, constipation, dyspepsia, flatulence, gastroenteritis, increased amylase, dysphagia, stomatitis, pseudomembranous colitis.
Hepato-biliary disorders	
Frequent:	Increase in transaminases.
Less frequent:	Increase in gamma-glutamyl-transferase (gGT), hepatic impairment (including LDH increase), increased bilirubin, increase in alkaline phosphatase, jaundice, hepatitis.
Frequency not known:	Fulminant hepatitis potentially leading to life-threatening liver failure.
Skin and subcutaneous tissue disorders	
Less frequent:	Pruritus, rash, urticaria, sweating.
Frequency not known:	Bullous skin reactions like Stevens-Johnson Syndrome or toxic epidermal necrolysis (potentially life-threatening), photosensitivity.
Musculoskeletal, connective tissue and bone disorders	
Less frequent:	Arthralgia, myalgia, leiconsise, increased muscle tone and cramping, arthritis, tendon rupture, exacerbation of symptoms of myasthenia gravis, rhabdomyolysis.
Renal and urinary disorders	
Less frequent:	Renal impairment, renal failure, haematuria, dysuria, interstitial nephritis.
General disorders and administrative site conditions	
Less frequent:	Feeling unwell, unspecific pain, oedema, dehydration, asthenia, malaise

Post-marketing experience
Cases of mitral valve and/or aortic valve regurgitation were reported in patients treated with oral fluoroquinolones. Due to insufficient post marketing information in the reported cases, it is unknown whether fluoroquinolone use was the causative factor or a contributory factor or played no role in the reported cases where mitral cases and/or aortic regurgitation were diagnosed.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the "6.04 Adverse Drug Reactions Reporting Form", found online under SAHPRA's publications:
https://www.sahpra.org.za/Publications/Index/9

4.9 Overdose

No specific countermeasures after accidental overdosage are recommended. General symptomatic therapy should be initiated. Concomitant administration of charcoal with a dose of 400 mg oral LONXAVE 400 will reduce systemic availability of the medicine by more than 80 %.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category A 20.1.1 broad and medium spectrum antibiotics
ATC code: J01MA14

Mechanism of action
Moxifloxacin is a fluoroquinolone antibacterial with a broad spectrum of bactericidal action.

Microbiology:
Moxifloxacin has activity against a wide range of Gram-positive and Gram-negative microorganisms *in vitro*. The bactericidal action of moxifloxacin results from inhibition of the topoisomerase II (DNA gyrase) and topoisomerase IV required for bacterial DNA replication, transcription, repair and recombination.
There is no known cross-resistance between moxifloxacin and other classes of antimicrobials.
Cross-resistance has been observed between moxifloxacin and other fluoroquinolones against Gram-negative bacteria. Gram-positive bacteria resistant to other fluoroquinolones may, however, still be susceptible to moxifloxacin.
Moxifloxacin has been shown to be active against Gram-positive and Gram-negative strains of microorganisms, both *in vitro* and in clinical infections as described under section 4.1 and section 4.2.

Resistant microorganisms
Aerobic Gram-positive microorganisms
Staphylococcus aureus (including methicillin-resistant strains (MRSA))
Streptococcus pneumoniae
Aerobic Gram-negative microorganisms
Escherichia coli
Klebsiella pneumoniae
Pseudomonas aeruginosa
Campylobacter jejuni
Salmonella
Neisseria gonorrhoae
Anaerobic Gram-positive microorganisms
Clostridium difficile
Anaerobic Gram-negative microorganisms
Bacteroides fragilis.

5.2 Pharmacokinetic properties

Pharmacokinetics in Adults
Absorption
Moxifloxacin is well absorbed after oral administration. The absolute bioavailability amounts to approximately 90 % after oral administration of a 400 mg dose. Pharmacokinetics are linear in the range of 50 to 1 200 mg single oral dose and up to 600 mg once daily dosing over 10 days. Steady state is reached within 3 days. Following a 400 mg oral dose, peak concentrations of 3,1 mg/l are reached within 0,5 to 4 h post administration. Peak and trough plasma concentrations at steady state (400 mg once daily) were 3,2 and 0,6 mg/l, respectively.

Distribution
Moxifloxacin is distributed to extravascular spaces. Exposure to moxifloxacin in terms of AUC (AUC_{∞} = 6 kg*h/L) is high; the volume of distribution at steady state amounts to Vss of approx. 2 l/kg. In saliva peak concentrations and similar to those of plasma may be reached. Due to low protein binding (approximately 45 %) high free peak concentrations > 10 x MIC are observed. In an *in vitro* and *ex vivo* experiments protein binding over a range of 0,02 to 2 mg/l resulted in a protein binding of approximately 45 % independent from the concentration of the active. Moxifloxacin is mainly bound to serum albumin. In tissues like lung (epithelial fluid, alveolar macrophages, biotic tissue), the sinuses (maxillary and ethmoid sinus, nasal polyps) and inflamed lesions (cantharide blister fluid) concentrations exceeding those of the plasma are reached.

Biotransformation
Moxifloxacin undergoes Phase II biotransformation and is excreted via renal and biliary faecal pathways as unchanged moxifloxacin as well as in form of a sulfo-compound (M1) and a glucuronide (M2). M1 and M2 are the only metabolites relevant in humans. Both are microbiologically inactive. The recovery from urine (approximately 19 % for unchanged moxifloxacin, approximately 2,5 % for M1 and approximately 14 % for M2) and faeces (approximately 25 % of unchanged moxifloxacin, approximately 36 % for M1 and no recovery for M2) totalled to approximately 96,98 % of the dose independent from the route of administration.

Elimination
Moxifloxacin is eliminated from plasma and saliva with a mean terminal half-life of approximately 12 hours. The mean apparent total body clearance following a 400 mg dose ranges from 179 to 246 ml/min. Renal clearance amounted to about 24 to 53 ml/min suggesting partial tubular reabsorption of the moxifloxacin from the kidneys. Approximately 19 % of the dose is excreted unchanged into the urine and approximately 25 % in the faeces. Approximately 2,5 % is recovered as M1 in the urine and 36 % in the faeces respectively. About 14 % is recovered as M2 in the urine.

Effects of Food on Oral Absorption
The tablet is swallowed whole with a glass of water. LONXAVE 400 can be taken independent of food intake.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Contains microcrystalline cellulose, lactose monohydrate, L-hydroxy propyl cellulose, croscarmellose sodium, polyethylene glycol, hydroxypropylmethylcellulose, magnesium stearate, titanium dioxide, purified talc, iron oxide red.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

48 months from the manufacturing date in the blister pack and strip pack.

6.4 Special precautions for storage

Store at or below 30 °C. Protect from light and moisture.
Keep the blisters in the carton until required for use.
KEEP OUT OF REACH OF CHILDREN.

6.5 Nature and contents of container

Blister Pack:
Tablets are packed in silver-metallic coloured cold form laminate, 25 µm OPA/45 µm Aluminium foil/60 µm PVC and plain silver-metallic coloured 0,025 mm aluminium foil as the lidding material.
Pack size: 5's, 10's, 25's and 30's in an outer carton.
Strip Pack:
Tablets are packed in silver-metallic coloured aluminium foil (soft tempered) laminated with low density polyethylene film as the lidding and forming material.
Pack size: 5's, 10's, 25's and 30's in an outer carton.

6.6 Special precautions for disposal of a used medicine or waste materials derived from such medicine and other handling of the product

No special requirements.
Any unused product or waste material should be disposed of in accordance with local requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Medocob Pharmaceuticals SA (Pty) Ltd
Office block 1, Bassonia Estate Office Park (East),
1 Cassonia Drive, Bassonia Rock, Ext. 12,
Alberton, South Africa.

8. REGISTRATION NUMBER(S)

48/20.1.1/0024

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

31 July 2014

10. DATE OF REVISION OF THE TEXT

12 May 2020

PATIENT INFORMATION LEAFLET

SCHEDULING STATUS:
S4

LONXAVE 400
Moxifloxacin hydrochloride 400 mg film-coated tablets
Contains sugar (50 mg lactose monohydrate)

Read all of this leaflet carefully before you start taking LONXAVE 400
- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor or your pharmacist.
- LONXAVE 400 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.

What is in this leaflet

1. What LONXAVE 400 is and what it is used for
2. What you need to know before you take LONXAVE 400 TABLETS
3. How to take LONXAVE 400 TABLETS
4. Possible side effects
5. How to store LONXAVE 400 TABLETS
6. Contents of the pack and other information

1. What LONXAVE 400 is and what it is used for

LONXAVE 400 contains moxifloxacin as the active ingredient which belongs to a group of antibiotics called fluoroquinolones. LONXAVE 400 works by killing bacteria that cause infections.
LONXAVE 400 is used in patients aged 18 years and above for treating the following bacterial infections when caused by bacteria against which moxifloxacin is active:
Infection of the sinuses, sudden worsening of long term inflammation of the airways (chronic bronchitis), infection of the lungs (pneumonia) acquired out of hospital, skin and soft tissue infections, and infections of the female upper genital tract.

2. What you need to know before you take LONXAVE 400

It is important that you tell your doctor or healthcare professional if you suffer from any of the conditions mentioned below, if you are taking LONXAVE 400 or have been prescribed LONXAVE 400.

230 mm

700 mm

Do not take LONXAVE 400:
- If you are allergic to moxifloxacin or any of the other ingredients of LONXAVE 400.
- If you have severe liver disease.
- If you are pregnant or breastfeeding.
- LONXAVE 400 should not be given to children and adolescents under 18 years.

Do not take LONXAVE 400 and inform your doctor if you were born with or have:
- any condition with abnormal heart rhythm (seen on ECG, electrical recording of the heart).
- a salt imbalance in the blood (especially low levels of potassium or magnesium in the blood).
- a very slow heart rhythm (called 'bradycardia').
- a weak heart (heart failure).
- a history of abnormal heart rhythms.

or
- If you are taking other medicines that result in abnormal ECG changes (see section 'Taking other medicines'). This is because LONXAVE 400 can cause changes on the ECG referred to as a prolongation of the QT-interval, i.e., delayed conduction of electrical signals.
- If you have kidney damage and/or taking high blood pressure medicines that belong to the class ACE inhibitors / renin-angiotensin receptor blockers (see section 'Taking other medicines'). If you have been diagnosed with mitral and/or aortic valve regurgitation (conditions in which your heart's mitral/aortic valve do not close tightly.) Mitral valve regurgitation allows blood to flow backward in your heart and aortic valve regurgitation allows some of the blood that was pumped out of your heart's main pumping chamber (left ventricle) to leak back into it.

Warnings and precautions
Inform your doctor:
- If you are taking medicines to correct the abnormal rhythm of the heart such as quinidine, procainamide, amiodarone and sotalol.
- If you suffer from myasthenia gravis (condition in which the muscles become weak and tire easily and in serious cases paralysis), taking LONXAVE 400 may worsen the symptoms of your disease.
- If you suffer from epilepsy.
- If you have or had any mental health problems.
- If you have a complicated infection of the female upper genital tract (e.g. associated with an abscess of the fallopian tubes and ovaries or of the pelvis), your doctor will prescribe an intravenous (IV) treatment and therefore treatment with LONXAVE 400 will not be appropriate.
- If you or any member of your family have glucose-6-phosphate dehydrogenase deficiency (a rare hereditary disease.). Taking LONXAVE 400 with this condition may lead to breakdown of your red blood cells.

LONXAVE 400 will not be prescribed to you if the infection you are suffering from is caused by a bacteria known as MRSA (methicillin-resistant Staphylococcus aureus).
While taking LONXAVE 400
- If you experience palpitations or irregular heart beat or fainting spells during the period of treatment, you should inform your doctor immediately.
- The risk of heart problems may increase with increase of the dose. Therefore, the recommended dosage should be followed.
- There is a chance that you may experience a severe, sudden allergic reaction (an anaphylactic reaction/shock) even with the first dose. Symptoms include tightness in the chest, feeling dizzy, feeling sick or faint, or dizziness when standing up. If so, stop taking LONXAVE 400 and seek medical advice immediately.
- LONXAVE 400 may cause a severe inflammation of the liver which could lead to life-threatening liver failure. If you suddenly feel unwell and/or are being sick and also have yellowing of the whites of the eyes, dark urine, itching of the skin, a tendency to bleed please contact your doctor before taking any more LONXAVE 400.
- If you develop a skin reaction or blistering / peeling of the skin contact your doctor immediately before you continue treatment.
- Quinolone antibiotics, including LONXAVE 400, may cause convulsions. If this happens, stop taking LONXAVE 400 and contact your doctor immediately.
- You may experience mental health problems even when taking quinolone antibiotics, including LONXAVE 400, for the first time. In some cases depression or mental health problems have led to suicidal thoughts and self-endangering behaviour such as suicide attempts. If you develop such reactions, stop taking LONXAVE 400 and inform your doctor immediately.
- Stop taking LONXAVE 400 and inform your doctor immediately if you experience symptoms of neuropathy such as pain, burning, tingling, numbness and/or weakness.
- You may develop diarrhoea whilst or after taking antibiotics including LONXAVE 400. If this becomes severe or persistent or you notice that your stool contains blood or mucus you should stop taking LONXAVE 400 immediately and consult your doctor. You should not take medicines that stop or slow down bowel movement.
- LONXAVE 400 may cause pain and inflammation of your tendons, even within 48 hours of starting treatment and up to several months after discontinuing LONXAVE 400 therapy. At the first sign of any pain or inflammation you should stop taking LONXAVE 400, rest the affected limb(s) and consult your doctor immediately. Avoid any unnecessary exercise, as this might increase the risk of a tendon rupture
- Quinolone antibiotics may make your skin become more sensitive to sunlight or UV light. You should avoid prolonged exposure to sunlight or strong sunlight and should not use a sunbed or any other UV lamp while taking LONXAVE 400.
- Inform your doctor that you are taking LONXAVE 400 if you are to take a test for TB (tuberculosis).
- Inform your doctor immediately if you are taking any high blood pressure medicines which belong to the group ACE inhibitors / renin-angiotensin receptor blockers. Use of fluoroquinolone antibiotics, including LONXAVE 400, together with ACE inhibitors / renin-angiotensin receptor blockers can cause damage to your kidneys.
- Inform your doctor immediately if you have been diagnosed with mitral and/or aortic valve regurgitation (conditions in which your heart's mitral/aortic valve do not close tightly.) Mitral valve regurgitation allows blood to flow backward in your heart and aortic valve regurgitation allows some of the blood that was pumped out of your heart's main pumping chamber (left ventricle) to leak back into it. You will be required to undergo a heart examination before you are prescribed LONXAVE 400.

Other medicines and LONXAVE 400
Always tell your healthcare professional if you are taking any other medicine. (This includes complementary or traditional medicines).

Tell your doctor if you are taking the following medicines before starting LONXAVE 400:
- medicines that belong to the group of anti-dysrhythmics (e.g. quinidine, hydroquinidine, disopyramide, procainamide, amiodarone, sotalol, dofetilide, ibutilide),
- antipsychotics (e.g. phenothiazines, pimozide, sertindole, haloperidol, sulforide).
- tricyclic antidepressants (amitriptyline, imipramine, dothiepin, trimipramine, desmopramine),
- antimicrobial medicines (IV erythromycin, saquinavir, sparfloxacin, pentamidine, amphotericin B)
- antimalarials (halofantrine)
- antihistamines (astemizole, mizolastine)
- cisapride (for heartburn and reflux), IV vincamine (increases blood flow), bepridil (for chest pain), diphemanil (for peptic ulcers)
- diuretics (water tablets), laxatives, enemas, corticosteroids, medicines used to slow the heart rate
- antacids, minerals and multi-vitamins,
- warfarin (used to thin blood),
- antidiabetics (e.g. glibenclamide),
- nonsteroidal anti-inflammatory medicines (NSAIDs).
- charcoal.
- Medicines used to treat high blood pressure that belong to the group ACE inhibitors / renin-angiotensin receptor blockers (e.g. enalapril, captopril, perindopril, losartan, irbesartan, valsartan).

LONXAVE 400 with food and drink and alcohol
LONXAVE 400 can be taken with or without food (including dairy products).

Pregnancy, breastfeeding and fertility
If you are pregnant or breast-feeding your baby while taking LONXAVE 400, please consult your doctor, pharmacist or other health care professional for advice.
The safety of LONXAVE 400 in pregnant or breastfeeding women has not been established.

Driving and using machines
Dizziness and lightheadedness may occur in some patients taking LONXAVE 400. If you experience these symptoms you should evaluate your ability to drive or to operate machinery.

LONXAVE 400 contains
LONXAVE 400 contains sugar (lactose monohydrate).
Tell your doctor if you have galactosaemia (a condition in which the body is unable to use the sugar galactose) or glucose / galactose malabsorption syndrome (a condition in which lactose (milk sugar) and other carbohydrates which contain the sugars glucose and galactose cannot be digested by the body). LONXAVE 400 contain lactose (milk sugar) and is unsuitable for patients with these disorders.

3. How to take LONXAVE 400

Do not share medicines prescribed for you with any other person.
Always take LONXAVE 400 exactly as your doctor has instructed you. You should check with your doctor or pharmacist if you are unsure. Your doctor will tell you how long your treatment with LONXAVE 400 will last. Do not stop treatment early. If you have the impression that the effect of LONXAVE 400 is too strong or too weak, talk to your doctor or pharmacist.
Take LONXAVE 400 once a day with or without food, as your doctor has prescribed.
The dose for adults for the treatment of all indications is one 400 mg tablet daily.
The tablets are to be swallowed whole with a glass of water.

The time you will take LONXAVE 400 for depends on your infection.
It is important that you complete the course of treatment even if you begin to feel better after a few days. If you stop taking LONXAVE 400 too soon your infection may not be completely cured and the infection may return or your condition may get worse. The bacteria causing your infection may become resistant to LONXAVE 400.
The recommended dose and duration of treatment should not be exceeded.

If you take more LONXAVE 400 than you should
If you have accidently taken too much LONXAVE 400, get medical help immediately by calling your nearest doctor or healthcare professional.
In the event of overdosage consult your doctor or pharmacist. If neither is available contact the nearest hospital or poison control centre

If you forgot to take LONXAVE 400
Take LONXAVE 400 as prescribed. However, if you miss a dose, resume the usual schedule of one tablet once daily.
Do not take a double dose to make up for a forgotten dose.

If you stop taking LONXAVE 400
If you stop taking this medicine too soon, you infection may not be completely cured. Talk to your doctor if you wish to stop taking your tablets before the end of the course of treatment.
If you have any further questions about this medicine, ask your doctor or pharmacist.

4. Possible side effects

LONXAVE 400 can have side effects.
Not all the side effects reported for LONXAVE 400 are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking LONXAVE 400, please consult your doctor, pharmacist or healthcare professional for advice.
If any of the following happens, stop taking LONXAVE 400 and tell your doctor immediately or go to the casualty department at your nearest hospital:
- hives; difficulty breathing; swelling of your face, lips, tongue, or throat.

Tell your doctor immediately or go to the casualty department at your nearest hospital if you notice any of the following:
- psychiatric symptoms including confusion, severe depression, suicidal thoughts, aggression, extreme fear, hallucinations, or unusual behaviour.
- fever with a severe blistering, peeling and red skin rash or any severe skin reaction.
- seizures (have a "fit" or convulsion).
- nausea, stomach pain, loss of appetite, dark urine, clay-coloured stools jaundice (yellowing of the skin or eyes).

These are all serious side effects. You may need urgent medical attention
Tell your doctor if you notice any of the following side-effects or if any of these symptoms are bothersome or do not go away:
- weight gain or weight loss
- dizziness
- numbness, tingling, pins and needles
- tremor (shake)
- difficulty concentrating
- drowsiness
- difficulty falling asleep
- unusual dreams
- headache
- disturbances of co-ordination and balance
- forgetfulness
- confusion
- abnormally happy mood
- blurred vision
- ringing in the ears
- sexuality
- palpitations (rapid irregular action of heart)
- increased rate of heart beat
- asthma
- nausea, vomiting
- diarrhoea or constipation
- stomach pain
- indigestion
- upset stomach
- increased appetite
- taste disturbances
- skin rash
- itching
- increased sweating
- eczema
- loss of hair
- acne
- changes in skin colour
- muscle or joint pain
- impotence (loss of male sexual ability); increased and decreased sexual drive (libido)
- fatigue or lack of energy
- hot flushes
- flu-like symptoms
- generally feeling unwell
- pain
- changes in shape or location of body fat (especially in your arms, legs, face, neck, breasts, and waist)
- heart murmur

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

Reporting of side effects
If you get side effects, talk to your doctor or pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects to SAHPRA via the "6.94 Adverse Drug Reaction Reporting Form", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8. By reporting side effects, you can help provide more information on the safety of LONXAVE 400.

5. How to store LONXAVE 400

Store all medicines out of reach of children.
Store at or below 30 °C.
Keep well closed and protect from light.
Do not store in a bathroom.
Do not use after the expiry date stated on the label / carton / bottle.
Any expired or outdated medicines and unused medicines can be returned to your nearest pharmacy.
Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

6. Contents of pack and other information

What LONXAVE 400 contains
- The active substance is 400 mg moxifloxacin as moxifloxacin hydrochloride.

The other ingredients are:
microcrystalline cellulose, lactose monohydrate, L-hydroxy propyl cellulose, croscarmellose sodium, polyethylene glycol, hydroxypropyl methylcellulose, magnesium stearate, titanium dioxide, purified talc, iron oxide red.

What LONXAVE 400 looks like and contents of the pack
Brick red coloured, capsule shaped, biconvex, film-coated tablets plain surface on both the sides.

Blister Pack:
Tablets are packed in silver-metallic coloured cold form laminate, 25 µm OPA/45 µm Aluminium foil/60 µm PVC and plain silver-metallic coloured 0.023 mm aluminium foil as the lidding material.
Pack size: 5's, 10's, 28's and 30's in an outer carton.

Strip Pack:
Tablets are packed in silver-metallic coloured aluminium foil (soft tempered) laminated with low density polyethylene film as the lidding and forming material.
Pack size: 5's, 10's, 28's and 30's in an outer carton.

Holder of Certificate of Registration and Manufacturer
MACLEODS PHARMACEUTICALS SA (PTY) LTD
Office block 1, Bassonia Estate Office Park (East),
1 Dunsoole Drive, Bassonia Rock, Ext. 12,
Alberton, South Africa.

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INLIGTINGSBLAD VIR PASIËNTE

SKEDULERINGSTATUS
S4

LONXAVE 400
Moksifloksasiensalsindrochloried 400 mg filmbedekte tablette
Bevat suiker (50 mg laktosemonohidraat)

Lees die hele bisaldjie voordat u begin om LONXAVE 400 te neem
- Hou hierdie bisaldjie. U mag dit moontlik weer wil lees.
- Indien u enige verdere vrae het, moet u asseblief u dokter of apteker raadpleeg.
- LONXAVE 400 is vir u persoonlik voorgeskryf en u behoort nie u medisyne met ander mense te deel nie. Dit mag hulle slade aandoen, selfs al toon hulle dieselfde simptome as u.

Wat is in hierdie bisaldjie
1. Wat LONXAVE 400 is en waarvoor dit gebruik word.
2. Wat u behoort te weet voordat u LONXAVE 400 neem.
3. Hoe om LONXAVE 400 te neem.
4. Moontlike newe-effekte.
5. Hoe om LONXAVE 400 op te berg.
6. Inhoud van die pak en ander inligting.

1. Wat is LONXAVE 400 en waarvoor word dit gebruik

LONXAVE 400 bevat moksifloksasien as die aktewe bestanddeel wat aan die groep antibiotika wat as fluorokinolone bekend staan, behoort. **LONXAVE 400** werk deur bakterieë wat infeksies veroorsaak, dood te maak.

LONXAVE 400 word gebruik vir pasiënte van **18 jaar** oud en ouer vir die behandeling van die volgende bakteriese infeksies, wanneer dit deur bakterieë wat vir moksifloksasien vatbaar is, veroorsaak word:

Infeksie van die sinusse, akutiewe asterualgang van langtermyn inflammasie van die lugweë (chroniese bronchitis), infeksies van die longe (pneumonie) wat buite die hospitaal opgedoen is, vel- en sagteweefselinfeksies en infeksies van die bioonste gedeeltes van die vroulike geslagsteelsel

2. Wat u behoort te weet voordat u LONXAVE 400 neem

Dit is belangrik om u dokter of professionele gesondheidswerker in kennis te stel as u LONXAVE 400 neem of as dit aan u voorgeskryf is, as u aan enige van die kondisies hieronder ly.

Moenie LONXAVE 400 neem nie:
- As u allergies teen moksifloksasien of enige van die ander bestanddele van **LONXAVE 400** is.
- As u aan enige lewersiekte ly
- As u swanger is of u baba borsvoed.
- LONXAVE 400 behoort nie aan kinders en adolessente jonger as 18 jaar oud toegedien te word nie.

Moenie **LONXAVE 400** neem as u aan enige van die volgende kondisies ly of as u daarmee gebore is nie:
- Enige kondisie met abnormale hartritme (sien op EKG, elektriese opname van die hart)
- 'n soutwanbalans in die bloed (veral lae vlakke van kalium of magnesium in die bloed)
- 'n Baie stadige hartslerap (bradikardie)
- 'n Swak hart (hartversaking)
- 'n Geskiedenis van abnormale hartritmes

of
- As u ander medisyne neem wat tot abnormale EKG-veranderinge lei (sien afdeling Neem van ander medisyne). Dit is omdat LONXAVE 400 veranderings in die EKG wat as verlenging van die QT-interval bekend staan) kan veroorsaak, d.i. vertraging van die elektriese impulse in die hart).
- As u aan nierbeskadiging ly en/of medisyne vir hoë bloeddruk wat aan die klas ACE-inhibeerders / renien-angiotensien reseptorblokkeerders behoort, gebruik. Sien afdeling Neem van ander medisyne).

As u met mitrale- en/of aortaldsregurgitering gediagnoseer is (toestawes waartydens u hart se mitrale- en aortaklep nie deeglik sluit nie). Mitralsklepregurgitering laat toe dat die bloed terugvloei na die hart, terwyl aortaklepregurgitering sommige van die bloed wat uit u hart se hoof pompkamer (linker ventrikel) gepomp word, daarheen terugvloei.

Waarskuwings en voorsorgmaatreëls
Stel u dokter in kennis:
- As u medisyne neem om die abnormale ritme van u hart reg te stel, soos kinidien, prokaïenamied, amiodaron en sotalol.
- As u aan myasthenia gravis ly (n kondisie waar die spiere swak en maklik moeg word en in ernstige gevalle verlam raak), mag die neem van LONXAVE 400 die simptome van u siekte vererger.
- As u aan epilepsie ly.
- As u enige geestesgesondheidsprobleme gehad het.
- As u aan 'n gekompliseerde infeksie van die bovonste gedeelte van die vroulike geslagskanaal (geassosieer met 'n abses van die fallopiese buise en ovaria, of van die pelvis, sal u dokter 'n intravenuse (IV) behandeling instel en daarom sal behandeling met LONXAVE 400 nie van toepassing wees nie.
- As u of enige lid van u familie aan glukose-6-fosfaat dehidrogeneasekort (n seldsame voorkomende overerflike siekte) ly. Die neem van LONXAVE 400 met hierdie kondisie mag tot afbraak van u rooibloedselle lei.
- LONXAVE 400 sal nie aan u voorgeskryf word as die infeksie wat aan u ly deur bakterieë wat as MRSA (metisillienweerstandbiedende Staphylococcus aureus) bekend staan, veroorsaak word nie.

Terwyl u LONXAVE 400 gebruik.
- As u hartkloppings of ongewoonlike hartslag of floute gedurende die periode van behandeling ondervind, moet u onmiddellik u dokter in kennis stel
- Die risiko van hartprobleme mag met 'n toename in die dosis toeneem. Daarom moet die voorgeskrewe dosis gevolg word.
- Daar bestaan 'n kans dat u 'n erge, skielike allergiese reaksie ('n anafilaktiese reaksie/skok) mag ondervind, selfs met die eerste dosis. Simptome sluit in beklemde bors, duiseligheid, naarheid of floute, of duiseligheid wanneer u opstaan. In, indien dit gebeur, staak die gebruik van LONXAVE 400 en kry onmiddellik mediese advies.
- LONXAVE 400 mag erge inflammasie van die lewer veroorsaak wat tot lewensbedreigende lewerversaking mag lei. As u ewe skielik ongesteld voel en/of naar word en u oë en vel rasit geel, urien verdonker, velkuis, 'n neiging om te bloei, moet u asseblief u dokter raadpleeg voordat u enigsins verder LONXAVE 400 neem.
- As u 'n velreaksie of blaarvorming/skilvlerting van die vel ondervind, moet u onmiddellik u dokter raadpleeg voordat u met die behandeling voortgaan.
- Kinolooantibiotika, insluitende LONXAVE 400, mag stuipaanvalle veroorsaak. As dit gebeur, moet u ophou om LONXAVE 400 te neem en onmiddellik u dokter raadpleeg.
- U mag geestelike gesondheidsprobleme ondervind, selfs wanneer kinoloonantibiotika, insluitende LONXAVE 400 vir die eerste keer gebruik word. In sommige gevalle het depressie of geestelike gesondheidsprobleme tot selfmoordidees en selfbeskadigingsgedrag, soos poging tot selfmoord gelei. As u sulke reaksies ontwikkel, moet u met die gebruik van LONXAVE 400 ophou en onmiddellik u dokter raadpleeg.
- Staak die gebruik van LONXAVE 400 onmiddellik as u simptome van neuropatie soos pyn, brandergheid, prikkeling, gevoelloosheid en/of swakheid ondervind.
- U mag diarree ontwikkel terwyl of nadat u antibiotika, insluitende LONXAVE 400 neem. Indien dit erg of aanhoudende raak, of u kom agter dat daar bloed in die stoelgang is, behoort u met die gebruik van LONXAVE 400 te staak en onmiddellik u dokter raadpleeg. U behoort nie medisyne te gebruik wat die dermbeweging stop of vertraag nie.
- LONXAVE 400 mag pyn en inflammasie van die tendons veroorsaak, selfs binne 48 uur na die begin van behandeling tot selfs as stilte maande na staking van LONXAVE 400. Met die eerste teken van enige pyn of inflammasie behoort u met die gebruik van LONXAVE 400 op te hou, rus die aangetaste ledemate en raadpleeg onmiddellik u dokter. Vermy enige onnodige oefening aangesien dit die risiko van lendenskeuring mag verhoog.
- Kinoloonantibiotika mag veroorsaak dat u vel meer sensitief teen sonlig of UV-lig raak. Vermy verlengde blootstelling aan sonlig of sterk sonlig en u behoort nie 'n sonbed of ander UV-lamp te gebruik terwyl u LONXAVE 400 neem nie.
- Stel u dokter in kennis indien u LONXAVE 400 neem as u 'n TB-toets moet ondergaan.
- Stel u dokter onmiddellik in kennis as u enige medisyne vir hoë bloeddruk wat aan die ACE-inhibeerders / renien-angiotensien reseptorblokkeerders behoort, neem. Die gebruik van fluoorkinolee antibiotika, insluitende LONXAVE 400, saam met ACE-inhibeerders / renien-angiotensien reseptorblokkeerders kan nierbeskadiging veroorsaak.
- Stel u dokter onmiddellik in kennis as u met mitrale- en/of aortaldsregurgitering gediagnoseer is (toestawes waartydens u hart se mitrale- en aortaklep nie deeglik sluit nie). Mitralsklepregurgitering laat toe dat die bloed terugvloei na die hart, terwyl aortaklepregurgitering sommige van die bloed wat uit u hart se hoof pompkamer (linker ventrikel) gepomp is, daarheen terugvloei. U mag 'n hartondersoek ondergaan voordat u met LONXAVE 400 voorgeskryf word.

Ander medisyne en LONXAVE 400
Stel altyd u professionele gesondheidswerker in kennis as u enige ander medisyne neem (dit sluit komplementêre en tradisionele medisyne in).
Stel u dokter in kennis as u die volgende medisyne neem voordat u begin om **LONXAVE 400** te gebruik:
- medisyne wat aan die groep van antiaritmiemiddels behoort (bv. kinidien, hidrokinidien, disopiramied, prokaïenamied, amiodaron, sotalol, dofetilied, ibutilied),
- antipsigotika (bv. fenotiasiene, pimosied, sertindool, haloperidol, sulforied),
- trisikliese antidepressante (bv. amitriptilien, imipramien, dotiepien, trimipramien, desipramien),
- antimikrobiese medisyne (IV eritromisien, saksinavir, sparfloksasien, pentamidien, amfotericien B),
- antimalariamiddels (halofantrien),
- antihistamiene (astemisool, misolastien),
- kisapried (vir sooibrand en refluks), IV vinkamien, (verhoog die bloedvloei), bepridiel (vir borspyn), difemaniel (vir maagsuurlope)
- diuretika (waterpilletjies), lakseermiddels, enemas, kortikosteroïede, medisyne om die hartiempo te vertraag,
- teensuurmiddels, minerale en multi-vitamiene.
- warfarien (gebruik om die bloed te verdun),
- antidiabetiese middels (bv. glibenklamied)
- nie-steroïed anti-inflammatoriese middels (NSAIMs),
- houtskool.
- medisyne wat gebruik word om hoë bloeddruk te behandel wat aan die klas ACE-inhibeerders / renien-angiotensien reseptorblokkeerders behoort (bv. enalapriel, kaptopriel, perindopriel, losartan, irbesartan, valsartan).

LONXAVE 400 met voedsel, vloeistof en alkohol
LONXAVE 400 kan met of sonder voedsel geneem word (insluitende suiwelprodukte).

Swangerskap, borsvoeding en vrugbaarheid
As u swanger is of u borsvoed u baba terwyl u LONXAVE 400 gebruik, moet u asseblief u dokter, apteker of ander professionele gesondheidswerker vir advies raadpleeg. Die veiligheid van **LONXAVE 400** in swangerskap en borsvoedende vrouens is nie vasgestel nie.

Bestuur en die gebruik van masjinerie
Duiseligheid en ligkoptigheid mag in sommige pasiënte wat LONXAVE 400 neem, voorkom. As u hierdie simptome ondervind, behoort u u vermoë om te bestuur of om met masjinerie te werk, te evalueer.

LONXAVE 400 bevat
LONXAVE 400 bevat suiker (laktosemonohidraat).
Stel u dokter in kennis as u aan galaktosemie (n kondisie waarin die liggaam nie in staat is om die suiker galaktose te gebruik nie) of glukose-/galaktose waarabsorpsiesindroom (n kondisie waarin die liggaam nie in staat is om laktose (melksuiker) en ander koolhidrate wat die suikers glukose en galaktose bevat wat nie deur die liggaam gemetaboliseer kan word nie). LONXAVE 400 bevat laktose (melksuiker) en is nie geskik vir gebruik in hierdie pasiënte nie.

3. Hoe om LONXAVE 400 te neem

Moenie medisyne wat aan u voorgeskryf is met enigiemand anders deel nie.

Neem altyd LONXAVE 400 presies soos deur u dokter voorgeskryf. Bevestig met u dokter of apteker as u onseker is. U dokter sal u in kennis stel oor hoe lank die behandeling met LONXAVE 400 sal duur. Moenie te vroeg met die behandeling ophou nie. Indien u van mening is dat die effek van LONXAVE 400 te sterk of te swak is, moet u u dokter of apteker raadpleeg.

Neem LONXAVE 400 een keer per dag met of sonder voedsel, soos deur u dokter voorgeskryf.

Die dosis vir volwassenes vir die behandeling van al die indikasies is een 400 mg tablet per dag. Die tablet moet heel met 'n glas water ingeslik word.

Die tyd wanneer u LONXAVE 400 moet neem sal van u infeksie afhang.

Dit is belangrik dat u die kursus van behandeling voltooi, selfs al voel u na 'n paar dae reeds beter. As u te vroeg met LONXAVE 400 ophou, mag die infeksie nie heeltemal genees wees nie en terugkeer of erger word. Die bakterieë wat u infeksie veroorsaak mag weerstand teen LONXAVE 400 ontwikkel.

Die aanbevole dosis en duurte van behandeling behoort nie oorskry te word nie.

As u te veel LONXAVE 400 neem
As u per ongeluk te veel LONXAVE 400 geneem het, moet u onmiddellik mediese hulp ontvang deur u naaste dokter of professionele gesondheidsorgverskaffer te kontak.

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

As u vergeet het om LONXAVE 400 te neem
Neem LONXAVE 400 soos een u voorgeskryf. As u egter 'n dosis oorslaan, gaan met die normale skedule van een tablet voort.

Moenie die dosis verdubbel om vir 'n oorgeslaande dosis op te maak nie.

As u ophou om LONXAVE 400 te neem
Indien u te vroeg met hierdie medisyne ophou, mag die infeksie nie volledig genees nie. Raadpleeg u dokter as u vóór die einde van die kursus met die tablette wil ophou.

Raadpleeg u dokter of apteker as u enige verdere vrae oor hierdie medisyne het.

4. Moontlike newe-effekte

LONXAVE 400 mag newe-effekte hê.
Nie al die newe-effekte wat vir LONXAVE 400 aangeneld is, word in hierdie bisaldjie genoem nie. Indien u algemene gesondheid agteruitgaan of u ondervind enige abnormale effekte terwyl u LONXAVE 400 neem, moet u asseblief u dokter, apteker of professionele gesondheidswerker vir advies raadpleeg.

Indien enige van die volgende gebeur, moet u met LONXAVE 400 ophou en onmiddellik u dokter raadpleeg of na die naaste hospitaal gaan:
- Uitslane, moeilik met asemhaling, swelling van u gesig, lippe, long of keel.

Stel onmiddellik u dokter in kennis of gaan na die naaste hospitaal indien u enige van die volgende waarneem:
- Psigiatriese probleme, insluitende verwardheid, erge depressie, selfmoordidees, aggressie, uitermatige angs, hallusinasies of abnormale gedrag.
- Koors met erge blaasvorming, afskilfering en rooi velutslag of enige ernstige velreaksie.
- Stuipaanvalle.
- Naarheid, maagpyn verlies aan eetlus, donker urien, kleigekleurde stoelgang, geelsug (geel verkleuring van die vel of oë).

Hierdie is slimal erge newe-effekte. U het moontlik dringende mediese hulp nodig.

Stel u dokter in kennis as u enige van die volgende newe-effekte waarneem of as enige van hierdie simptome kwelland of nie verdwyn nie:
- Massatoename of -verlies.
- Duiseligheid.
- Gevoelloosheid, prikkeling, spalde en naaldjie.
- Bewerstelo.
- Moeite om te konsentreer.
- Lomerigheid.
- Moeite om aan die slaap te raak.
- Abnormale drome.
- Hoofpyn
- Afwykinge van kordrinasie en balans.
- Vergeetagtigheid.
- Verwardheid.
- Abnormale gemoel van lewensvlus.
- Onduidelike gesig.
- Suisering oe die ore.
- Sinusitis.
- Hartkloppings (vinnige, ongereelde hartslag).
- Toename in hartiempo.
- Asma.
- Naarheid, braking.
- Diarree of hardlywigheid.
- Maagpyn.
- Indigestie.
- Omgeskrapte maag.
- Toename in eetlus.
- Smaakafwykinge.
- Velluitslag.
- Jeuk.
- Toename in sweet.
- Ekseem.
- Haarverlies
- Aknee.
- Veranderinge in velkleur.
- Spier- of gewrigspyn.
- Impotensie (verlies aan manlike seksuele vermoë), toename of afname in seksdrang (libido).
- Moegheid of tekort aan energie.
- Hitegloede.
- Griepagtige simptome.
- Algemene gevoel van ongesteldheid.
- Pyn.
- Veranderinge in die vorm en plasing van liggaamsvet (veral in u arms, bene, gesig, nek, borste en heupe).
- Hartgeruis.

As u enige newe-effekte waarneem wat nie in hierdie bisaldjie genoem word nie, moet u asseblief u dokter of apteker raadpleeg.

Aanmelding van newe-effekte
As u enige newe-effekte ondervind moet u u dokter, apteker of verpleegster/verpleër raadpleeg. U kan ook newe-effekte aan SAHPRA via die "6.94 Adverse Drug Reaction Reporting Form" aan te meld, wat aanlyn onder SAHPRA se publikasies gevind kan word: https://www.sahpra.org.za/Publications/Index/8. Deur newe-effekte aan te meld, kan u help om meer inligting oor die veiligheid van LONXAVE 400 te verskaf.

5. Hoe om LONXAVE 400 op te berg

Bewaar alle medisyne buite bereik van kinders.
Bewaar teen of benaie 30 °C.
Hou dig toe en beskerm teen lig.
Moet nie in die badkamer bêre nie.
Moet nie na die vervaldatum op die etiket/fles/bottel gebruik nie.
Enige vervalde of ou medisyne kan nie u naaste apteek teruggeneem word.
Moet nie ongebruikte medisyne in die riolering (bv. toilet) weggdoen nie.

6. Inhoud van die pak en ander inligting

Wat LONXAVE 400 bevat
- Die aktiewe bestanddeel is moksifloksasien 400 mg as moksifloksasienhidrochloried.

Die ander onskilmee bestanddele is; mikrokristallyne sellulose, laktosemonohidraat, L-hidroksipropiel-sellulose, Natriumkruiskarmellose, poliëtileenglikol, hidroksiepropielmetielsellulose, magnesiumstearaat, titaandioksied, gesuiwerde talk, rooi yster oksied.

Hoe lyk LONXAVE 400 en die inhoud van die verpakking
Baksteenrooogekleurde, kapsulevormige, bikonvekse, filmbedekte tablette met 'n gladde oppervlak aan beide kante.

Blisterverpakking:
Tablette word in silwer-metaalgekleurde kouevorm laminaat verpak. OPA/45 µm Aluminiumblaaie/ 60 µm PVC en silwer-metaalgekleurde 0,025 aluminium foelie as die deklaagmateriaal
Pakgrootte: 5's, 10's, 28's en 30's in 'n buitenste karton.

Strookverpakking
Tablette word in silwer metaalgekleurde aluminiumfoelie (sag getemper), strooibare, gelamineer met lae-digtheid polieteen film as deklaags- en vormingsmateriaal verpak
Pakgrootte: 5's, 10's, 28's en 30's in 'n buitenste karton.

Houer van die registrasiesertifikaat en vervaardiger
Macleods Pharmaceuticals SA (Edms.) Bpk,
Kantoorblok 1
Bassonia Estate Office Park (Oos)
Castoriaryklaan 1
Bassonia Rock uitbr. 12
Alberton
Suid-Afrika

Registrasienommer/verwysingsnommer
48/20.1.1/0024

Vorige hersiening van hierdie bisaldjie
Datum van registrasie: 31 Julie 2014

Hersieningsdatum:
12 Mei 2020

PM0194770S

PACKAGING RESEARCH & DEVELOPMENT

Restricted Circulation

(Front Page)

ARTWORK / PRINTPROOF APPROVAL FORM

Note : Change in text format.

1. Product: LONXAVE 400 (Moxifloxacin Tablets 400 mg)	
2. Country: South Africa	3. Packaging component: Professional Package insert
4. No. of Colours: 1 Colour	5. Pantone Shade No.: Black
6. Specification: 40 gsm bible paper	
7. Machine Layout No.: NA	8. Dimensions: 700 (L) x 230 (H) mm
9. Design / Style: NA	10. Item code No.: PM01947705
11. Artwork has been made: Actual Size	12. Pharma code No.: Front - 27931 mini
13. Barcode/NDC no: NA	14. Supersedes Item code No: PM01947704
15. Revision no: 04	16. File Name :E:\ANDA Regulatory\South Africa\Moxifloxacin\Active Pharma\PM\Moxifloxacin PI & PIL Common PM01947705.cdr
Approved By:	17. Location: Daman

PRD	M.A. HOLDER	MEDICAL/RAD	QC	PRODN	QA
04-12-21	Vanita Rajool	04/12/21	04/12/21	06/12/21	06/12/21

Note: 1. To follow overleaf checklist for approval of Artwork / Print proof.

Instructions to Vendor :

1. Before processing, please ensure First pull out / Commercial supply should match with approved Artwork with respect to Design, Size, Fonts & Text.
2. Print proof to represent full printing area with Station Numbers.

FRM/CQA/021/04-01

Reason for revision :	Item code	Artwork Release Date	Artwork Implementation Date
1) New Artwork for South Africa	PM01947701	08/09/15	03/09/15
2) New presentation added & Brand name change	PM01947702	1/11/17	25/11/17
3) Address change & Revision date removed	PM01947703	02/06/18	13/07/18
4) Change in text matter, format and size.	PM01947704	10/03/21	Not Implemented
5) Change in text format.	PM01947705		