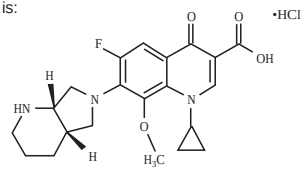
MOXIGET™

(Moxifloxacin HCL Tablets 400mg)

Tablets 400mg

DESCRIPTION
MOXIGET (Moxifloxacin) is a new oral 8-methoxyfluroquinolone antibacterial agent. Chemically, moxifloxacin is a monohydrate salt of 1-cyclopropyl-7-[(S, S)-2, 8-diazabicyclo [4.3.0] non-8-yl]-6-flouro-8-methoxy-1, 4-dihydro-4-oxo-3 quinolone carboxylic acid. The molecular formula is $C_{21}H_{24}FN_3O_4$•HCl and the structural formula is:



Moxifloxacin HCl

Moxiget (Moxifloxacin) Tablet 400mg is a pink, oblong shaped film coated tablets engraved “Getz” on one side and break line on the other side.

QUALITATIVE & QUANTITATIVE COMPOSITION
MOXIGET (Moxifloxacin) is available for oral administration as:

MOXIGET Tablets 400mg
Each film-coated tablet contains:
Moxifloxacin hydrochloride Ph. Eur. equivalent to Moxifloxacin …400mg

CLINICAL PHARMACOLOGY
Mechanism of Action
Moxifloxacin is bactericidal against a range of Gram-positive and Gram-negative organisms. Such activity arises through the inhibition of DNA gyrase (topoisomerase II) and topoisomerase IV, which bacteria require for DNA replication, transcription, repair, and recombination. Moxifloxacin contains the C8-methoxy moiety that augments its antibacterial activity and reduces the possibility of Gram-positive mutations. Because the 8-fluroquinolones use a different mechanism of action than do the aminoglycosides, beta-lactams, macrolides, or tetracyclines, there has been no cross resistance between the quinolones and these antimicrobial agents.

Microbiology:
Aerobic Gram-positive micro-organisms:
Staphylococcus aureus (methicillin-susceptible)
Streptococcus pneumoniae, Streptococcus pyogenes
Streptococcus epidermidis (methicillin-susceptible)
Streptococcus anginosus

Aerobic Gram-negative micro-organisms:
Haemophilus influenzae
Haemophilus parainfluenzae
Klebsiella pneumoniae
Moraxella catarrhalis
Enterobacter cloacae
Escherichia coli
Proteus mirabilis

Anaerobic micro-organisms:
Fusobacterium species
Prevotella species
Peptostreptococcus species

Others:
Chlamydia pneumoniae
Mycoplasma pneumoniae
Legionella pneumophila
Mycobacterium leprae
Mycobacterium tuberculosis

Pharmacokinetics
Moxifloxacin is readily absorbed from the gastrointestinal tract with an absolute bioavailability of about 90%. It is widely distributed throughout the body tissues and is approximately 50% bound to plasma proteins. Moxifloxacin has an elimination half life of approximately 12 hours, allowing once daily dosing. It is metabolised principally via sulphate and glucuronide conjugation. About 45% of the drug is excreted in the urine and the faeces as unchanged drug. The sulphate conjugate is excreted primarily in the faeces and the glucuronide exclusively in the urine.

THERAPEUTIC INDICATIONS
Moxiget (Moxifloxacin) Tablets 400mg is indicated in combination with other antituberculosis agents for the treatment of tuberculosis caused by *Mycobacterium tuberculosis*.

Moxiget (Moxifloxacin) Tablets 400mg is only indicated as a second-line antimycobacterial drug when use of first line drugs is not appropriate due to resistance or intolerance.

DOSAGE AND ADMINISTRATION
Moxiget (Moxifloxacin) Tablets 400mg may be taken without regard to food.

Adults, adolescents and children weighing at least 33kg:
The dose of Moxiget (Moxifloxacin) Tablets 400mg is one tablet once daily.

Children: Moxiget (Moxifloxacin) Tablets 400mg is not recommended for use in children with a body weight below 33kg, as recommended dose adjustments cannot be made.

Special Population.

Renal impairment:
No adjustment of dosage is required in patients with impaired renal function or in patients on chronic dialysis, including hemodialysis and continuous ambulatory peritoneal dialysis.

Hepatic impairment:
No dosage adjustment is recommended in hepatic insufficiency.

Elderly:
No dosage adjustment is required in the elderly.

ADVERSE REACTIONS
Moxifloxacin was usually well tolerated. Most adverse reactions were mild to moderate. The most common adverse reactions were nausea and diarrhea.

Common:
Headache, dizziness, abdominal pain, vomiting, QT prolongation in patients with hypokalemia, increase in transaminases, superinfection due to resistant bacteria.

Uncommon:
Anorexia, constipation, dyspepsia, flatulence, gastritis, increase amylase, QT prolongation, palpitations, tachycardia, artrial fibrillation, angina pectoris, dyspnea, hepatic impairment, increased bilirubin, increase gamma glutarryl transferase, increase in blood alkaline phosphatase, pruritis rash, urticaria, dry skin, arthralgia, myalgia, dehydration, visual disturbances, anxiety reactions, psychomotor hyperactivity, taste disorder, paresthesia/dysesthesia, confusion, disorientation, hyperlipidemia, allergic reaction, anaemia, leucopenia, neutropenia, thrombocytopenia.

Rare:
Dysphagia, pseudomembranous colitis, ventricular tachyarrhythmias, syncope, hypertension, hypotension, vasodilatation, tinnitus, hypoesthesia, smell disorder, abnormal dreams, disturbed coordination, seizures, disturbed attention, speech disorders, amnesia, anaphylaxis, allergic edema/angioedema, hyperglycaemia, hyperuricemia, emotional liability, depression, hallucination, prothrombin time prolonged.

CONTRAINDICATIONS
Moxifloxacin is contraindicated in patients:
– With hypersensitivity to moxifloxacin or other quinolones and any components of this medication.
– Less than 18 years of age.
– Pregnancy and lactation.
– With history of tendon disease/disorder related to quinolone treatment.
– With impaired liver function and in patients with transaminases >5 fold ULN.
– With congenital or documented acquired QT prolongation.
– With electrolyte disturbances, particularly in uncorrected hypokalaemia.
– With clinically relevant bradycardia.
– With clinically relevant heart failure with reduced left-ventricular ejection fraction.
– With previous history of symptomatic arrhythmias.
– Receiving Class IA (e.g. quinidine, procainamide) or Class III (amiodarone, sotalol) antiarrhythmic agents or other drugs that prolong the QT interval.

WARNINGS AND PRECAUTIONS:
Prolongation of QTc interval and potentially QTc-prolongation-related clinical conditions
Moxifloxacin has been shown to prolong the QTc interval on the electrocardiogram in some patients. Moxifloxacin should be used

with caution in patients with ongoing proarrhythmic conditions (especially women and elderly patients), such as acute myocardial ischemia or QT prolongation as this may lead to an increased risk for ventricular arrhythmias (including torsade de pointes) and cardiac arrest. If signs of cardiac arrhythmia occur during treatment with moxifloxacin, treatment should be stopped and an ECG should be performed.

Hypersensitivity / allergic reactions
Hypersensitivity and allergic reactions have been reported for fluoroquinolones including moxifloxacin after first administration.

Severe liver reactions
Cases of fulminant hepatitis potentially leading to liver failure (including fatal cases) have been reported with moxifloxacin. 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.

Serious bullous skin reactions
Cases of bullous skin reactions like Stevens-Johnson syndrome or toxic epidermal necrolysis have been reported with moxifloxacin. Patients should be advised to contact their doctor or health care provider immediately prior to continuing treatment if skin and/or mucosal reactions occur.

Prevention of photosensitivity reactions
Quinolones have been shown to cause photosensitivity reactions in patients. Patients should be advised to avoid exposure to either UV irradiation or extensive and/or strong sunlight during treatment with moxifloxacin.

Psychiatric reactions
Psychiatric reactions may occur even after the first administration of quinolones, including moxifloxacin. In very rare cases depression or psychotic reactions have progressed to suicidal thoughts and self-endangering behaviour such as suicide attempts. In the event that the patient develops these reactions, moxifloxacin should be discontinued and appropriate measures instituted. Caution is recommended if moxifloxacin is to be used in psychotic patients or in patients with history of psychiatric disease

Tendon rupture, tendon inflammation
Tendon inflammation and rupture may occur with quinolone therapy including moxifloxacin, particularly in elderly patients and in those treated concurrently with corticosteroids. At the first sign of pain or inflammation, patients should discontinue treatment with moxifloxacin, rest the affected limb(s) and consult their doctor or health care provider immediately in order to initiate appropriate treatment (e.g. immobilisation) for the affected tendon.

Vision disorders
If vision becomes impaired or any effects on the eyes are experienced, an eye specialist should be consulted immediately.

Antibiotic-associated diarrhea including colitis
Antibiotic-associated diarrhea (AAD) and antibiotic-associated colitis (AAC), including pseudomembranous colitis and Clostridium difficile-associated diarrhea, has been reported in association with the use of broad spectrum antibiotics including moxifloxacin and may range in severity from mild diarrhea to fatal colitis.If AAD or AAC is suspected or confirmed, ongoing treatment with antibacterial agents, including moxifloxacin, should be discontinued and adequate therapeutic measures should be initiated immediately.

Peripheral neuropathy
Cases of sensory or sensorimotor polyneuropathy resulting in paraesthesias, hypoaesthesias, dysaesthesias, or weakness have been reported in patients receiving quinolones.

Pediatric population
Moxifloxacin should only be used in children and adolescents with *M. Tuberculosis* infection if the benefit is considered to exceed the risk and there are no treatment alternatives.

Patients with pre-existing impaired liver function
Due to metabolic disturbances associated with hepatic insufficiency, which may lead to QT prolongation, moxifloxacin should be used with caution in patients with impaired liver function.

Patients predisposed to seizures
Quinolones are known to trigger seizures. They should be used with caution in patients with CNS disorders or in the presence of other risk factors which may predispose to seizures or lower the seizure threshold. In case of seizures, treatment with moxifloxacin should be discontinued and appropriate measures instituted.

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

Patients with galactose intolerance Lapp lactase deficiency or glucose-galactose malabsorption,
Moxiget (Moxifloxacin) Tablets 400mg contains a small amount of lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption may experience symptoms of intolerance.

Drug Interactions
- Moxifloxacin should be taken at least 4 hours before or 8 hours after antacids containing magnesium, calcium or aluminium, as well as sucralfate, metal cations such as iron, and multivitamin preparations with zinc or didanosine.
- Medication that can reduce potassium levels should be used with caution in patients receiving moxifloxacin.
- Concomitant administration of *charcoal* with an oral dose of 400mg moxifloxacin leads to a pronounced prevention of drug absorption and a reduced systemic availability of the drug by more than 80%. Therefore, the concomitant use of these two drugs is not recommended (except for overdose cases).
- The prothrombin time, International Normalized Ratio (INR), or other suitable anticoagulation tests should be closely monitored if a quinolone is administered concomitantly with *warfarin* or its *derivatives*.
- Concomitant administration of *NSAIDs* with quinolones may increase the risks of CNS stimulation and convulsions.

STORAGE
Store below 30°C.
Protect from sunlight and moisture.
The expiration date refers to the product correctly stored at the required conditions.

HOW SUPPLIED
MOXIGET (Moxifloxacin) Tablets 400mg are available in blister pack of 5's.

Keep out of reach of children.

To be sold on prescription of a registered medical practitioner only.

Please read the contents carefully before use.
This package insert is continually updated from time to time.

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