Summary of product characteristics

1. Name of drug product

MOXIGET (MOXIFLOXACIN) IV INFUSION 400 mg/250 mL

2. Qualitative and quantitative composition

Each vial of 250ml solution for infusion contains:
Moxifloxacin hydrochloride Ph. Eur. equivalent to Moxifloxacin.....400mg

Excipient with known effect:
250 ml of solution for infusion contains 884.6mg sodium

3. Pharmaceutical form

Light yellow clear liquid filled in clear glass USP type II vial with blue color flip off seal having FLIP OFF embossed on top and grey color rubber stopper.

4. Clinical particulars

4.1 Indications

MOXIGET (Moxifloxacin) IV is indicated for

- Community acquired pneumonia (CAP)
- Complicated skin and skin structure infections (cSSSI).

Moxifloxacin should be used only when it is considered inappropriate to use antibacterial agents that are commonly recommended for the initial treatment of these infections.

4.2 Posology and method of administration

The recommended dose is 400 mg Moxifloxacin, infused once daily Initial intravenous treatment may be followed by oral treatment with Moxifloxacin 400 mg tablets, when clinically indicated

Renal /hepatic impairment
No adjustment of dosage is required in patients with mild to severely impaired renal function or in patients on chronic dialysis i.e. haemodialysis and continuous ambulatory peritoneal dialysis No adjustment of dosage is required in the elderly and in patients with low bodyweight.

Paediatric population
Moxifloxacin is contraindicated in children and growing adolescents. Efficacy and safety of moxifloxacin in children and adolescents have not been established

Method of administration
For intravenous use; constant infusion over 60 minutes
If medically indicated the solution for infusion can be administered via a T-tube, together with compatible infusion solutions

4.3 Contra-indications

Moxifloxacin is contraindicated in

- Patients with a history of hypersensitivity to moxifloxacin or any member of the quinolones class of antimicrobial agents.
- Pediatric patients, adolescents (less than 18 years of age).
- Patients with a history of tendon disease/disorder related to quinolone treatment
- Congenital or documented 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 arrhythmias
- Pregnant and lactating women.
- Moxifloxacin should be avoided in patients with known prolongation of the QT interval.

4.4 Special warnings and special precautions for use

- Moxifloxacin should be avoided in patients who have experienced serious adverse reactions in the past when using quinolone or fluoroquinolone containing products. Treatment of these patients with moxifloxacin should only be initiated in the absence of alternative treatment options and after careful benefit/risk assessment.

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. The magnitude of QT prolongation may increase with increasing plasma concentrations due to rapid intravenous infusion. Therefore, the duration of infusion should not be less than the recommended 60 minutes and the intravenous dose of 400 mg once a day should not be exceeded.
- Treatment with moxifloxacin should be stopped if signs or symptoms that may be associated with cardiac arrhythmia occur during treatment, with or without ECG findings.
- Moxifloxacin should be used with caution in patients with any condition pre-disposing to cardiac arrhythmias (e.g. acute myocardial ischaemia) because they may have an increased riskof developing ventricular arrhythmias (incl. torsade de pointes) and cardiac arrest.
- Moxifloxacin should be used with caution in patients who are taking medications that can reduce potassium levels.
- Moxifloxacin should be used with caution in patients who are taking medications associated with clinically significant bradycardia.
- Female patients and elderly patients may be more sensitive to the effects of QTc-prolonging medications such as moxifloxacin and therefore special caution is required.

Hypersensitivity/allergic reactions
Hypersensitivity and allergic reactions have been reported for fluoroquinolones including moxifloxacin after first administration. Anaphylactic reactions can progress to a life-threatening shock, even after the first administration. In cases of clinical manifestations of severe hypersensitivity reactions moxifloxacin should be discontinued and suitable treatment (e.g., treatment for shock) initiated.

Severe liver disorders
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 (see section 4.8). Patients should be advised to contact their doctor immediately prior to continuing treatment if skin and/or mucosal reactions occur.

Patients predisposed to seizures
Quinolones are known to trigger seizures. Use should be 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.

Prolonged, disabling and potentially irreversible serious adverse drug reactions
Very rare cases of prolonged (continuing months or years), disabling and potentially irreversible serious adverse drug reactions affecting different, sometimes multiple, body systems (musculoskeletal, nervous, psychiatric and senses) have been reported in patients receiving quinolones and fluoroquinolones irrespective of their age and pre-existing risk factors. Moxifloxacin should be discontinued immediately at the first signs or symptoms of any serious adverse reaction and patients should be advised to contact their prescriber for advice.

Peripheral neuropathy
Cases of sensory or sensorimotor polyneuropathy resulting in paraesthesia, hypoaesthesia, dysaesthesia, or weakness have been reported in patients receiving quinolones and fluoroquinolones. Patients under treatment with moxifloxacin should be advised to inform their doctor prior to continuing treatment if symptoms of neuropathy such as pain, burning, tingling, numbness, or weakness develop in order to prevent the development of a potentially irreversible condition.

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-injurious 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.

Antibiotic-associated diarrhoea incl. colitis
Antibiotic-associated diarrhoea (AAD) and antibiotic-associated colitis (AAC), including pseudomembranous colitis and Clostridium difficile-associated diarrhoea, has been reported in association with the use of broad spectrum antibiotics including moxifloxacin and may range in severity from mild diarrhoea to fatal colitis. Therefore it is important to consider this diagnosis in patients who develop serious diarrhoea during or after the use of moxifloxacin. 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. Furthermore, appropriate infection control measures should be undertaken to reduce the risk of transmission. Drugs inhibiting peristalsis are contraindicated in patients who develop serious diarrhoea.

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

Tendinitis and tendon rupture
Tendinitis and tendon rupture (especially but not limited to Achilles tendon), sometimes bilateral, may occur as early as within 48 hours of starting treatment with quinolones and fluoroquinolones and have been reported to occur even up to several months after discontinuation of treatment. The risk of tendinitis and tendon rupture is increased in older patients, patients with renal impairment, patients with solid organ transplants, and those treated concurrently with corticosteroids. Therefore, concomitant use of corticosteroids should be avoided. At the first sign of tendinitis (e.g. painful swelling, inflammation) the treatment with moxifloxacin should be discontinued and alternative treatment should be considered. The affected limb(s) should be appropriately treated (e.g. immobilisation). Corticosteroids should not be used if signs of tendinopathy occur.

Aortic aneurysm and dissection
Epidemiologic studies report an increased risk of aortic aneurysm and dissection after intake of fluoroquinolones, particularly in the older population. Therefore, fluoroquinolones should only be used after careful benefit-risk assessment and after consideration of other therapeutic options in patients with positive family history of aneurysm disease, or in patients diagnosed with pre-existing aortic aneurysm and/or dissection, or in presence of other risk factors or conditions predisposing for aortic aneurysm and dissection (e.g. Marfan syndrome, vascular Ehlers-Danlos syndrome, Takayasu arteritis, giant cell arteritis, Behcet´s disease, hypertension, known atherosclerosis). In case of sudden abdominal, chest or back pain, patients should be advised to immediately consult a physician in an emergency department.

Patients with renal impairment
Elderly patients with renal disorders should use moxifloxacin with caution if they are unable to maintain adequate fluid intake, because dehydration may increase the risk of renal failure.

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

Dysglycemia
As with all fluoroquinolones, disturbances in blood glucose, including both hypoglycemia and hyperglycemia have been reported with moxifloxacin (see section 4.8). In moxifloxacin-treated patients, dysglycemia occurred predominantly in elderly diabetic patients receiving concomitant treatment with an oral hypoglycemic agent (e.g. sulfonylurea) or with insulin. Cases of hypoglycaemic coma have been reported. In diabetic patients, careful monitoring of blood glucose is recommended.

Prevention of photosensitivity reactions
Quinolones have been shown to cause photosensitivity reactions in patients. However, studies have shown that moxifloxacin has a lower risk to induce photosensitivity. Nevertheless patients should be advised to avoid exposure to either UV irradiation or extensive and/or strongsunlight during treatment with moxifloxacin.

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, moxifloxacin should beused with caution in these patients.

Peri-arterial tissue inflammation
Moxifloxacin solution for infusion is for intravenous administration only. Intra-arterial administration should be avoided since preclinical studies demonstrated peri-arterial tissue inflammation following infusion by this route.

Patients with special cSSSI
Clinical efficacy of moxifloxacin in the treatment of severe burn infections, fasciitis and diabetic foot infections with osteomyelitis has not been established.

Patients on sodium diet
This medicinal product contains 787 mg (approximately 34 mmol) sodium per bottle with 250ml solution for infusion, equivalent to 39.35% of the WHO recommended maximum daily intake of 2g sodium for an adult.

Interference with biological tests
Moxifloxacin 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 moxifloxacin.

Patients with MRSA infections
Moxifloxacin 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

Paediatric population

Due to adverse effects on the cartilage in juvenile animals the use of moxifloxacin in children and adolescents < 18 years is contraindicated.

4.5 Interaction with other medicaments and other forms of interactionInteractions with medicinal products:

- Anti-arrhythmics class IA (e.g. quinidine, hydroquinidine, disopyramide
- Anti-arrhythmics class III (e.g. amiodarone, sotalol, dofetilide, ibutilide)
- Antipsychotics (e.g. phenothiazines, pimozide, sertindole, haloperidol, sultopride)
- Tricyclic antidepressive agents
- Antimicrobial agents (saquinavir, sparfloxacin, erythromycin IV, pentamidine, antimalarials particularly halofantrine)
- Antihistaminics (terfenadine, astemizole, mizolastine)
- Others (cisapride, vincamine IV, bepridil, diphemanil).

Changes in INR

A large number of cases showing an increase in oral anticoagulant activity have been reported in patients receiving antibacterial agents, especially fluoroquinolones, macrolides, tetracyclines, cotrimoxazole and some cephalosporins. The infectious and inflammatory conditions, age and general status of the patient appear to be risk factors. Under these circumstances, it is difficult to evaluate whether the infection or the treatment caused the INR (international normalised ratio) disorder. A precautionary measure would be to more frequently monitor the INR. If necessary, theoral anticoagulant dosage should be adjusted as appropriate.

Interaction with food

Moxifloxacin has no clinically relevant interaction with food including dairy products.

4.6 Use in Pregnancy and LactationPregnancy

The safety of moxifloxacin 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, moxifloxacin must not be used in pregnant women.

Breast-feeding

There is no data available in lactating or nursing women. Preclinical data indicate that small amounts of moxifloxacin are secreted 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, breast-feeding is contraindicated during moxifloxacin therapy.

Fertility

Animal studies do not indicate impairment of fertility.

4.7 Effects on ability to drive and operate machines

No studies on the effects of moxifloxacin on the ability to drive and use machines have been performed. However, fluoroquinolones including moxifloxacin may result in an impairment of the patient's ability to drive or operate machinery due to CNS reactions (e.g. dizziness; acute, transient loss of vision) or acute and short lasting loss of consciousness (syncope). Patients shouldbe advised to see how they react to moxifloxacin before driving or operating machinery.

4.8 Undesirable effects

Following are the adverse effects reported with moxifloxacin

Common:
Increased gamma-glutamyl-transferase

Uncommon:
Ventricular tachyarrhythmias, hypotension, oedema, antibiotic-associated colitis (incl. pseudomembranous colitis, in very rare cases associated with life-threatening complications, see section 4.4), seizures incl. grand mal convulsions, hallucination, renal impairment (incl. increase in BUN and creatinine), renal failure.

There have been very rare cases of the following side effects reported following treatment with other fluoroquinolones, which might possibly also occur during treatment with moxifloxacin: increased intracranial pressure (including pseudotumor cerebri), hypernatraemia, hypercalcaemia, haemolytic anaemia, rhabdomyolysis, photosensitivity reactions.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme,

4.9 Overdose

No specific countermeasures after accidental overdose are recommended. In the event of overdose,symptomatic treatment should be implemented. ECG monitoring should be undertaken, because ofthe possibility of QT interval prolongation. Concomitant administration of charcoal with a dose of 400 mg oral or intravenous moxifloxacin will reduce systemic availability of the drug by more than 80% or 20% respectively. The use of charcoal early during absorption may be useful to prevent excessive increase in the systemic exposure to moxifloxacin in cases of oral overdose.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic propertiesMechanism of Action

Moxifloxacin inhibits bacterial type II topoisomerases (DNA gyrase and topoisomerase IV) that are required for bacterial DNA replication, transcription and repair.

Microbiology:
Spectrum of moxifloxacin is broad and it is active against most strains of the following micro-organisms in both in vitro and in vivo.

Aerobic Gram-positive micro-organisms:
Staphylococcus aureus (including methicillin-susceptible strains)
Streptococcus pneumoniae (penicillin-susceptible strains only)
Streptococcus pyogenes
Streptococcus anginosus
Streptococcus constellatus
Gardnerella vaginalis
Streptococcus milleri
Streptococcus mitior
Streptococcus agalactiae
Streptococcus dysgalactiae
Staphylococcus cohnii
Staphylococcus epidermidis
Staphylococcus haemolyticus
Staphylococcus hominis
Staphylococcus saprophyticusStaphylococcus simulans Corynebacterium diphtheriae
*Enterococcus faecalis** (Vancomycin, gentamicin susceptible strains only)

Aerobic Gram-negative micro-organisms:
Haemophilus influenzae
Haemophilus parainfluenzae
Klebsiella pneumoniae
Moraxella catarrhalis (including -lactamase negative and positive strains)
Enterobacter cloacae
Escherichia coli
Proteus mirabilis
Klebsiella pneumoniae
Bordetella pertussis
Klebsiella oxytoca
Enterobacter aerogenes
Enterobacter agglomerans

Enterobacter intermedius
Enterobacter sakazakii
Proteus vulgaris
Morganella morganii
Providencia rettgeri
Providencia stuartii

Atypicals
Chlamydia pneumoniae
Chlamydia trachomatis
Mycoplasma
pneumoniaeMycoplasma
hominis Mycoplasma
genitalum Legionella
pneumophila Coxiella
burnetti

Anaerobic micro-organisms:
Bacteroides distasonis
Bacteroides eggerthii
Bacteroides fragilis
Bacteroides ovatus
Bacteroides thetaiotaomicron
Bacteroides uniformis
Fusobacterium spp.
Peptostreptococcus
spp.
Porphyromonas spp.
Porphyromonas anaerobius Porphyromonas asaccharolyticus Porphyromonas magnus
Prevotella spp.
Propionibacterium spp.
Clostridium perfringens
Clostridium ramosum

5.2 Pharmacokinetic propertiesAbsorption

After a single 400 mg intravenous 1 hour infusion peak plasma concentrations of approximately 4.1 mg/l were observed at the end of the infusion corresponding to a mean increase of approximately 26% relative to those seen after oral administration (3.1 mg/l). The AUC value of approximately 39 mg•h/l after i.v. administration is only slightly higher than that observed after oral administration (35 mg•h/l) in accordance with the absolute bioavailability of approximately 91%.

Distribution

Moxifloxacin is distributed to extravascular spaces rapidly. The steady-state volume of distribution (Vss) is approximately 2 l/kg. In vitro and ex vivo experiments showed a protein binding of

approximately 40 - 42% independent of the concentration of the drug. Moxifloxacin is mainly bound to serum albumin.
Maximum concentrations of 5.4 mg/kg and 20.7 mg/l (geometric mean) were reached in bronchial mucosa and epithelial lining fluid, respectively, 2.2 h after an oral dose. The corresponding peak concentration in alveolar macrophages amounted to 56.7 mg/kg. In skin blister fluid concentrationsof 1.75 mg/l were observed 10 h after intravenous administration. In the interstitial fluid unbound concentration time profiles similar to those in plasma were found with unbound peak concentrations of 1.0 mg/l (geometric mean) reached approximately 1.8 h after an intravenousdose.

Biotransformation
Moxifloxacin undergoes Phase II biotransformation and is excreted via renal (approximately 40%) and biliary/faecal (approximately 60%) pathways as unchanged drug as well as in the form of a sulpho-compound (M1) and a glucuronide (M2). M1 and M2 are the only metabolites relevant in humans, both are microbiologically inactive.

Excretion
Moxifloxacin is eliminated from plasma 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. Following a 400 mg intravenous infusion recovery of unchanged drug from urine was approximately 22% and from faeces approximately 26%. Recovery of the dose (unchanged drug and metabolites) totalled to approximately 98% after intravenous administration of the drug. Renal clearance amounted to about 24 - 53 ml/min suggesting partial tubular reabsorption of the drug from the kidneys. Concomitant administration of moxifloxacin with ranitidine or probenecid did not alter renal clearance of the parent drug.

6. Pharmaceutical particulars

6.1 List of excipients

- Sodium Chloride
- Hydrochloric Acid
- Sodium Hydroxide
- Water for injection

6.2 Incompatibilities
Not applicable.

6.3 Shelf-life
2 years
The expiration date refers to the product correctly stored in the required conditions.

6.4 Special precautions for storage

- Do not store above 30^{O}C.
- Do not refrigerate or freeze. (Product precipitates upon refrigeration which re-dissolves at roomtemperature)
- Protect from sunlight.
- Store in the carton until time of use.

6.5 Nature and contents of container

MOXIGET I.V Infusion is packed in USP glass type II bottle with a package insert in a unit carton.
Unit pack size is 1x250ml vial.

6.6 Instructions for use/handling

- Once the infusion vial has been opened, the infusion solution must be used within 60 minutes.
- Keep in the pack until required.
- To be dispensed on medical prescription only
- Keep out of reach of children.

7. Marketing authorisation holder

Getz Pharma (Private) Limited
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Tel: (92-21) 5063100-03
Fax: (92-21) 5060141

8. Product registration number

TAN 21 HM 0479

9. Date of first authorisation/renewal of the authorisation

Date of first authorization: November 26, 2021
Date of latest renewal: N/A

10. Date of revision of the text

April, 2022