Bosch

For Medical Professional only

AVELIN

Solution for IV Infusion

400mg/250ml Infusion

(Moxifloxacin HCl U.S.P.)

(Product Specs.: Bosch)

ایوی لِن

۴۰۰ ملی گرام/ ۲۵۰ ملی لیٹر انفیوژن

(موکسی فلاکساسن ہائیڈروکلورائیڈ یو۔ایس۔پی)

DESCRIPTION:
Avelin (moxifloxacin hydrochloride) is a synthetic broad spectrum antibacterial agent. Moxifloxacin, a fluoroquinolone, is available as the monohydrochloride salt of 1-cyclopropyl-7-[(S,S)-2,8diazabicyclo[4.3.0] non-8-yl]-6-fluoro-8-methoxy-1,4-dihydro-4-oxo-3 quinoline carboxylic acid. It is a slightly yellow to yellow crystalline substance with a molecular weight of 437.9. Its empirical formula is $C_{21}H_{24}FN_3O_4$ *HCl

PHARMACOLOGICAL PROPERTIES
Pharmacodynamic properties
Pharmacotherapeutic group: Quinolone antibacterials, fluoroquinolones, ATC code: J01MA14

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

MICROBIOLOGY:
The prevalence of acquired resistance may vary geographically and with time for selected species and local information of resistance is desirable, particularly when treating severe infections.

Aerobic Gram-positive micro-organism:
Staphylococcus aureus, Streptococcus agalactiae
Streptococcus milleri group (S. anginosus, S. constellatus and S. intermedius), Streptococcus pneumonia, Streptococcus pyogenes, Streptococcus viridans group (S. viridans, S. mutans, S. mitis, S. sanguinis, S. salivarius, S. thermophilus)

Aerobic Gram-negative micro-organisms: Acinetobacter baumanii, Haemophilus influenza, Legionella pneumophila, Moraxella (Branhamella) catarrhalis

Other micro-organism:
Chlamydophila (Chlamydia) pneumonia, Coxiella burnetii, Mycoplasma pneumoniae

Pharmacokinetic Properties:
Absorption:
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%. In patients, there is no need for age or gender related dose adjustment on intravenous moxifloxacin. Pharmacokinetics are linear in the range of 50 - 1200 mg single oral dose, up to 600 mg single intravenous dose and up to 600 mg once daily dosing over 10 days.

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 concentrations of 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 intravenous dose.

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) totaled 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.

Renal impairment
The pharmacokinetic properties of moxifloxacin are not significantly different in patients with renal impairment (including creatinine clearance > 20 ml/min/1.73 m2). As renal function decreases, concentrations of the M2 metabolite (glucuronide) increase by up to a factor of 2.5 (with a creatinine clearance of < 30 ml/min/1.73 m2).

Hepatic impairment
Impaired liver function was associated with higher exposure to M1 in plasma, whereas exposure to parent drug was comparable to exposure in healthy volunteers. There is insufficient experience in the clinical use of moxifloxacin in patients with impaired liver function.

CLINICAL PARTICULARS:
Therapeutic indications
Avelin is indicated for the treatment of:
- 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.

Consideration should be given to official guidance on the appropriate use of antibacterial agents.

DOSAGE AND 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. There is insufficient data in patients with impaired liver function.

Other special populations
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; infusion over 60 minutes.
If medically indicated the solution for infusion can be administered via a T-tube, together with compatible infusion solutions

CONTRAINDICATION:
- Hypersensitivity to moxifloxacin, other quinolones or to any of the excipients.
- Patients below 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

WARNINGS AND PRECAUTIONS:
The use of 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
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 risk of 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. 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
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 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.

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 .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. 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.

Aortic aneurysm and dissection
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.

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. 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 strong sunlight 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 be used with caution in these patients.

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.

INTERACTION WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTION:
Interactions with medicinal products
An additive effect on QT interval prolongation of moxifloxacin and other medicinal products 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 moxifloxacin with any of the following medicinal products is contraindicated:
- 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
- certain antimicrobial agents (saquinavir, sparfloxacin, erythromycin IV, pentamidine, antimalarials particularly halofantrine)
- certain antihistaminics (terfenadine, astemizole, mizolastine)
- others (cisapride, vincamine IV, bepridil, diphemanil).

Moxifloxacin 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.

USE IN PREGNANCY AND LACTATION:
Pregnancy: Pregnancy Category C. Because no adequate or well-controlled studies have been conducted in pregnant women, Avelin should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Lactation: Moxifloxacin is excreted in the breast milk of rats. Moxifloxacin may also be excreted in human milk. Because of the potential for serious adverse reactions in infants who are nursing from mothers taking Avelin, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

ADVERSE EFFECTS:
The following adverse effects have been observed with Moxifloxacin therapy.

Common: Superinfections due to resistant bacteria or fungi e.g. oral and vaginal candidiasis, Headache,Dizziness, QT prolongation in patients with, hypokalaemia, Nausea, Vomiting, Gastrointestinal and abdominal pains, Diarrhoea, Increase in transaminases, Injection and infusion site reactions

Uncommon: Anaemia, Leucopenia(s), Neutropenia, Thrombocytopenia, Thrombocythemia, Blood eosinophilia, Prothrombin time prolonged/ INR increased, Hyperlipidemia, Anxiety reactions,Psychomotor hyperactivity/ agitation, Par- and Dysaesthesia, Taste disorders, Confusion and disorientation,Sleep disorders (predominantly insomnia), Tremor, Vertigo, Somnolence, Visual disturbances incl. diplopia and blurred vision, Palpitations, Tachycardia, Atrial fibrillation, Angina pectoris, Vasodilatation, Dyspnea, Decreased appetite and food intake, Constipation, Dyspepsia, Flatulence, Gastritis, Increased amylase, Increased bilirubin, Increased gamma-glutamyl-transferase, Increase in blood alkaline phosphatase, Pruritus, Rash, Urticaria, Dry skin, Arthralgia, Myalgia, Dehydration, Sweating.

Not known: Anaphylaxis incl. very rarely life-threatening shock, Allergic oedema/ angioedema, Hyperglycemia, Hyperuricemia, Emotional lability, Hypoaesthesia, Smell disorders (incl. anosmia),Abnormal dreams, Disturbed attention, Speech disorders, Amnesia, Photophobia, Tinnitus, Hearing impairment incl. deafness, Ventricular tachyarrhythmias, Syncope, Hypertension, Hypotension, Dysphagia, Stomatitis, Jaundice, Tendonitis, Muscle cramp,Muscle twitching,Muscle weakness, Renal impairment (incl. increase in BUN and creatinine),Renal failure.

Rare: Prothrombin level increased/ INR decreased, Agranulocytosis, Hypoglycemia, Depersonalization, Psychotic reactions, Hyperaesthesia, Transient loss of vision, Uveitis and bilateral acute iris transillumination, Unspecified arrhythmias, Cardiac arrest, Vasculitis, Fulminant hepatitis potentially leading to life-threatening liver failure, Bullous skin reactions like Stevens-Johnson syndrome or toxic epidermal necrolysis, Arthritis, Muscle rigidity, Exacerbation of symptoms of myasthenia gravis

OVERDOSAGE:
No specific countermeasures after accidental overdose are recommended. In the event of overdose, symptomatic treatment should be implemented. ECG monitoring should be undertaken, because of the 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.

PHARMACEUTICAL PARTICULARS
Special precautions for disposal and other handling
This product is for single use only. Any unused solution should be discarded.
The following co-infusions were found to be compatible with moxifloxacin 400 mg solution for infusion:

Water for injections, Sodium chloride 0.9%, Sodium chloride 1 molar, Glucose 5%/10%/40%, Xylitol 20%, Ringer's solution, Compound Sodium Lactate Solution (Hartmann's Solution, Ringer-Lactate Solution).
Moxifloxacin solution for infusion should not be co-infused with other drugs.
Do not use if there are any visible particulate matter or if the solution is cloudy.
At cool storage temperatures precipitation may occur, which will re-dissolve at room temperature.

INCOMPATIBILITIES
The following solutions are incompatible with moxifloxacin solution for infusion:
Sodium chloride 10% and 20% solutions
Sodium bicarbonate 4.2% and 8.4% solutions
This medicinal product must not be mixed with other medicinal products

PRESENTATION:
Avelin (Moxifloxacin hydrochloride) is supplied as Intravenous infusion in ready to use 250mL bottle containing 400 mg of moxifloxacin.

DIRECTIONS:
Protect from heat & sunlight, store at 25°C excursions permitted between 15°C-30°C.
At cool storage temperature precipitation may occur, which will redissolve at room temperature.
The expiration date refer to the product correctly stored at the required condition.
Do not use if bottle is leaking, solution is cloudy or contains foreign matter.
Keep out of the reach of children.
To be sold on prescription of a registered medical practitioner only.

ہدایات :

دھوپ اور گرمی سے محفوظ ۲۵ ڈگری سینٹی گریڈ درجہ حرارت پر رکھیں۔
کم درجہ حرارت پر عارضی Precipitation نمودار ہوسکتا ہے
جو کمرے کے درجہ حرارت پر دوبارہ حل ہوجائیگا۔
بوتل لیک ہو یا اس میں کوئی غیر حل پذیر شئے نظر آئے تو ہرگز استعمال نہ کریں۔
بچوں کی پہنچ سے دور رکھیں۔
صرف مستند ڈاکٹر کے نسخے پر فروخت کے لئے۔

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ISO 9001:2015 Certified Company