STAXIN
(MOXIFLOXACIN)

TABLETS
INFUSION

COMPOSITION
TABLETS:
Each film coated tablet contains: Moxifloxacin (as HCl) (USP).....400mg
INFUSION:
Each 250ml contains: Moxifloxacin (as HCl) (USP).....400mg

DESCRIPTION
STAXIN (moxifloxacin hydrochloride) 400mg Tablets & Infusion is a synthetic broad spectrum antibacterial agent for oral & intravenous administration. Moxifloxacin, a fluoroquinolone, is available as the monohydrochloride salt of 1-cyclopropyl-7-[(S,S)- 2,8-diazabicyclo[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.
Moxifloxacin has in vitro activity against a wide range of Gram-positive and Gram-negative organisms, anaerobes, acid fast bacteria and atypicals e.g. Mycoplasma spp. Chlamydia spp. and Legionella spp.
Moxifloxacin is effective against β-lactam and macrolide resistant bacteria. Studies in animal models of infection have demonstrated high in vivo activity. Moxifloxacin has been shown to be active against most strains of the following microorganisms, both in vitro and in clinical infections.

GRAM-POSITIVE MICROORGANISMS
- Staphylococcus aureus (including methicillin-sensitive strains)
- Streptococcus pneumoniae, (including penicillin and macrolide resistant strains)
- Streptococcus pyogenes (group A)

GRAM-NEGATIVE MICROORGANISMS
- Haemophilus influenzae, (including β-lactamase negative & positive strains)
- Haemophilus parainfluenzae
- Klebsiella pneumoniae
- Moraxella catarrhalis (including β-lactamase negative and positive strains)
- Escherichia coli
- Enterobacter cloacae

ATYPICALS
Chlamydia pneumoniae and Mycoplasma pneumoniae.
According to in vitro studies, the following organisms are sensitive to Moxifloxacin, however, the safety and effectiveness of Moxifloxacin in treating clinical infections due to these microorganisms has not been established in adequate and well controlled clinical trials.

GRAM-POSITIVE MICROORGANISMS
- o Streptococcus milleri
- o Streptococcus agalactiae
- o Staphylococcus cohnii
- o Staphylococcus epidermidis (including methicillin sensitive strain)
- o Staphylococcus haemolyticus
- o Staphylococcus saprophyticus
- o Corynebacterium diphtheriae
- o Streptococcus mitior
- o Streptococcus dysgalactiae
- o Staphylococcus hominis
- o Staphylococcus simulans

GRAM-NEGATIVE MICROORGANISMS
- o Bordetella pertussis
- o Enterobactor aerogenes
- o Enterobactor intermedius
- o Proteus mirabilis
- o Morganella morganii
- o Providencia stuartii
- o Klebsiella oxytoca
- o Enterobactor agglomerans
- o Enterobactor sakazaki
- o Proteus vulgaris
- o Providencia rettgeri

ANAEROBES
- o Bacteroides distasonis
- o Bacteroides fragilis
- o Bacteroides thetaiotaomicron
- o Fusobacterium spp
- o Porphyromonas anaerobius
- o Porphyromonas asaccharolyticus
- o Prevotella spp
- o Clostridium perfringens
- o Bacteroides eggerthii
- o Bacteroides ovatus
- o Bacteroides uniformis
- o Porphyromonas spp
- o Porphyromonas magnus
- o Propionibacterium spp
- o Clostridium ramosum

ATYPICALS
Legionella pneumophila
Caxiella burnettii

MECHANISM OF ACTION
The bactericidal actions results from the interference with topoisomerases II and IV. Topoisomerases are essential enzymes which control DNA topology and assist in DNA replication, repair and transcription. Moxifloxacin exhibits concentration dependent bactericidal killing. Minimum bactericidal concentrations are generally similar to minimum inhibitory concentrations.
Resistance mechanisms which inactivate penicillins, cephalosporins, aminoglycosides, macrolides and tetracyclines do not interfere with the antibacterial activity of Moxifloxacin. There is no cross resistance between Moxifloxacin and these agents. Plasmid-mediated resistance has not been observed to date. A very low overall frequency of resistance was demonstrated (10^{-7} - 10^{-10}). In vitro studies have demonstrated that resistance to Moxifloxacin develops slowly by multiple step mutations. Serial exposure of organisms to sub-MIC concentrations of Moxifloxacin showed only a small increase in MIC values. Cross-resistance has been observed. However some Gram-positive and anaerobic organisms resistant to other quinolones are susceptible to Moxifloxacin.

INDICATIONS
Staxin (Moxifloxacin) is indicated for the treatments of adults (>18 years of age) with upper and lower respiratory tract infections such as
Acute sinusitis, Acute exacerbation of chronic bronchitis, Community acquired pneumonia and skin & soft tissue infections.

CONTRA-INDICATIONS
Known hypersensitivity to any components of the tablets / infusion or other quinolones. Staxin tablets are contra-indicated in children, growing adolescents and pregnant women. Quinolones are known to distribute well into breast milk of lactating women. Preclinical evidence indicates that small amounts of Moxifloxacin may be secreted in human milk. There is no data available in lactating or nursing women. Therefore the use of Moxifloxacin in lactating mothers is contra-indicated.

SPECIAL WARNINGS AND SPECIAL PRECAUTIONS FOR USE
Seizures may occur with quinolones therapy. Moxifloxacin should be used with caution in patients with known or suspected CNS disorders which may predispose to seizures or lower the seizures threshold. As no pharmacokinetic / pharmacodynamic data are available in severe hepatic impairment (Child Pugh C) the use of Moxifloxacin in this patient group is not recommended.
Moxifloxacin, as with some other quinolones and macrolides, has been shown to prolong the QT interval of the electrocardiogram in some patients. The drug should be avoided in patients with known prolongation of the QT interval, patients with uncorrected hypokalemia and patients receiving class IA (e.g. quinidine, procainamide) or class III (e.g, amiodarone, sotalol) anti arrhythmic agents, due to lack of clinical experience with the drug in these patient populations. The magnitude of QT prolongation may increase with increasing concentration of the drug. Therefore, the recommended dose should not be exceeded. Tendon inflammation and rupture may occur with quinolone therapy, particularly in elderly patients and in those treated concurrently with corticosteroids. At the first sign of pain or inflammation, patient should discontinue treatment and rest the affected limb(s). Tendon ruptures have not been reported in clinical trials with Moxifloxacin.
Pseudomemberanous colitis has been reported with the use of broad-spectrum antibiotics; therefore it is important to consider this diagnosis in patients who develop serious diarrhoea in association with antibiotic use. In this clinical situation adequate therapeutic measures should be initiated. No case of pseudomembranous colitis was observed in the clinical trial programme. In some instances, the hypersensitivity and allergic reactions already occurred after the first administration and the doctor should be informed immediately. Anaphylactic reactions in very rare instances can progress to a life threatening shock, in some instances after the first administration. In these cases Moxifloxacin has to be discontinued and medical treatment (e.g, treatment for shock) is required.

UNDESIRABLE EFFECTS
In Moxifloxacin clinical trials the majority of adverse drug reactions (ADRs) were described as mild to moderate (over 90%). The discontinuation rate of Moxifloxacin treated patients due to ADRs was 3.8%. The most common adverse drug reactions (relationship defined as probable, possible or not assessable) based on all clinical studies with Moxifloxacin are listed below:

INCIDENCE OF FREQUENCY >1 %<10%
Body as whole: Abdominal pain, headache. Injection site reaction (e.g. edema / hypersensitivity / inflammation / pain).
Digestive system: Nausea, diarrhoea, vomiting, dyspepsia abnormal liver

function test.
Special senses: Taste prevention.
Nervous system: Dizziness.
Cardiovascular system: QT prolongation in patients with concomitant hypokalemia.

INCIDENCE OF FREQUENCY >0.1 %<1 %
Body as whole: Asthenia, moniliasis, pain, back pain, lab test abnormal, malaise, chest pain, allergic reaction, leg pain.
Cardiovascular system: Tachycardia, peripheral edema, hypertension, palpitation, QT prolongation.
Digestive system: Nausea, dry mouth, vomiting, flatulence, constipation, oral moniliasis, anorexia, stomatitis, gastrointestinal disorder, glossitis, GT increase.
Hemic and lymphatic system: Leucopenia, prothrombin decrease, eosinophilia, thrombocytopenia, thrombopenia, anemia.
Metabolic and nutritional: Amylase increased Musculoskeletal system: arthralgia, myalgia.
Nervous system: Insomnia, vertigo, nervousness, somnolence, anxiety, tremor, parasthesia, confusion, depression
Skin and appendages: Rash, pruritus, sweating, urticaria Special sense: amblyopia
Urogenital system: Vaginal moniliasis, vaginitis

INCIDENCE OF FREQUENCY >0.01% <0.1 %>
Body as a whole: Pelvic pain, face edema
Cardiovascular system: Hypotension, vasodilatation
Digestive system: Gastritis, tongue discoloration, dysphagia / jaundice, diarrhoea (Clostridium difficile)
Hemic and Lymphatic System: Thromboplastin decrease, prothrombin increase
Metabolic and nutritional: Hyperglycemia, hyperlipemia, hyperurecemia
Musculoskeletal: Arthritis, tendon disorder.
Nervous system: Hallucinations, depersonalization, hypertonia, in coordination, agitation, amnesia, aphasia, emotional liability, sleep disorders, speech disorders, hypesthesia, abnormal dreams, confusion.
Respiratory system: Asthma, dyspnea
Skin and appendages: Rash (maculapapular, purpuric, pustular)
Special senses: Tinnitus, abnormal vision, taste loss, parosmia
Urogenital system: Kidney function abnormal Incidence of frequency <0.01%
Hypersensitivity: Anaphylactic reaction, shock (anaphylactic, possibly life threatening)

INTERACTION WITH OTHER MEDICAMENTS AND OTHER FORMS OF INTERACTION
FOOD AND DAIRY PRODUCTS: Absorption of Moxifloxacin was not altered by food intake.
RANITIDINE: the concomitant administration with ranitidine did not change the absorption characteristics of Moxifloxacin significantly. Absorption parameters (C max, T max, AUC) were very similar indicating absence of an influence of gastric pH on Moxifloxacin uptake from the gastrointestinal tract.
ANTACIDS, MINERALS AND MULTI-VITAMINS: concomitant ingestion of Moxifloxacin together with antacids, minerals and multi-vitamins may result in impaired absorption of the drug 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 drugs 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 an oral Moxifloxacin dose.
WARFARIN: No interaction during concomitant treatment with warfarin on prothrombin time and other coagulation parameters has been observed.
DIGOXIN, THEOPHYLLINE, PROBENECID: The pharmecokinetics of digoxin, theophylline and probenecid are not significantly influenced by Moxifloxacin (and vice versa).
ANTIDIABETICS: No clinically relevant interaction was seen between glibenclamide and Moxifloxacin.
PHOTOSENSITIVITY: phototoxicity has been reported with other quinolones. However, a study in human volunteers concluded that Moxifloxacin has no measurable phototoxic potential.

OVERDOSE
Only limited data on overdose are available. Single doses of up to 1200 mg and multiple doses of 600 mg over 10 days were administered to healthy subjects without any significant undesirable effects. In the event of over-dosage it is recommended that appropriate supportive care should be instituted as dictated by the patient's clinical status. The use of charcol early during absorption after oral administration may be useful to prevent excessive increase of systemic exposure to Moxifloxacin. After intravenous drug administration charcoal only slightly reduces systemic exposure (approx. 20%) and is of limited use in case of intravenous overdosing.

DOSAGE AND ADMINISTRATION
RANGE OF DOSE: The recommended dose for Moxifloxacin is (400mg) once-daily for all indications.

DURATION OF TREATMENT
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, 10 days Acute sinusitis, 7 days.
The recommended duration of treatment in skin & soft tissue infections is 7 days. Therapy may be initial intravenous administration, followed by oral tablet administration when clinically indicated.
Staxin (Moxifloxacin) 400mg tablets have been studied in clinical trials for up to 14 days treatment.
Staxin infusion solution has been studied in clinical trials for up to 14 days treatment.
ELDERLY: No adjustment of dosage is required in the elderly.
CHILDREN: The use of Moxifloxacin in children and adolescents in the growth phase is not recommended.
HEPATIC IMPAIRMENT: No dosage adjustment is required in patients with slightly impaired liver function (Child Pugh A,B). No pharmacokinetic data is available for patients with severely impaired liver fupctjon (Child Pugh C).
RENAL IMPAIRMENT: No dose adjustment is required in patients with any degree of renal impairment (including creatinine clearance <30ml/min/1.73m^2). There is no pharmacokinetic data available in patients on dialysis treatment.
INTERETHNIC DIFFERENCES: No adjustment of dosage is required in ethnic groups.
NOTES:
INCOMPATIBILITIES
The following co-infusions were found to be incompatible with Moxifloxacin infusion solution:

Sodium Chloride	10%
Sodium Chloride	20%
Sodium Hydrogen Carbonate	4.2%
Sodium Hydrogen Carbonate	8.4%

INSTRUCTIONS
FOR TABLETS: Protect from heat, light and moisture. Store below 30°C. Keep out of the reach of children. To be sold on the prescription of a registered medical practitioner only.
FOR IV INFUSION: Store at 25°C. Do not store below 8°C. At cool storage temperature precipitation may occur, which will re-dissolve at room temperature. Keep all medicines out of the reach of children. To be sold on the prescription of a registered medical practitioner only.

PRESENTATION
STAXIN Tablets 400mg: Alu-Alu pack of 1x5 tablets.
STAXIN IV Infusion 400mg is available in 1 x 250ml bottle.

سٹیکسن (موکسی فلوکساسن)

ٹیبلیٹس / انفیوژن

ہدایات:

برائے ٹیبلیٹس

دھوپ، نمی اور گرمی سے بچائیں۔ 30° سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔

برائے آئی وی اِنفیوژن

25° سینٹی گریڈ پر رکھیں۔ 8° سینٹی گریڈ سے کم درجہ حرارت پر سٹور نہ کریں۔ کم درجہ حرارت پر حل پذیر اشیاء علیحدہ ہوسکتی ہیں جو کہ معتدل درجہ حرارت پر دوبارہ حل ہوجاتی ہیں۔ تمام دوائیں بچوں کی پہنچ سے دُور رکھیں۔ صرف مستند ڈاکٹر کے نسخہ پر فروخت کریں۔

نوٹ: وائل کے لیک ہونے، دھندلا ہونے یا اس میں غیر حل پذیر ذرات نظر آنے کی صورت میں ہرگز استعمال نہ کریں۔ آئی وی اِنفیوژن مریض کے جسم میں 60 منٹ کے دوران داخل کیا جائے۔

Manufactured by:
STANDPHARM PAKISTAN (PVT) LTD
20 Km Ferozepur Road Lahore, Pakistan.