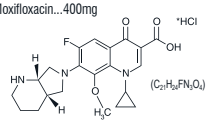
Danmox 400mg
(Moxifloxacin) Tablets U.S.P.

QUALITATIVE AND QUANTITATIVE COMPOSITION:
Danmox 400mg Tablets U.S.P.
Each film-coated tablet contains:
Moxifloxacin HCl U.S.P. eq. to Moxifloxacin...400mg

Structure of Moxifloxacin:



WARNING: SERIOUS ADVERSE REACTIONS INCLUDING TENDINITIS, TENDON RUPTURE, PERIPHERAL NEUROPATHY, CENTRAI NERVOUS SYTEM EFFECTS and EXACERBATION OF MYASTHENIA GRAVIS.

- Fluoroquinolones, including Danmox, have been associated with disabling and potentially irreversible serious adverse reactions that have occurred together, including:
  - Tendinitis and tendon rupture.
  - Peripheral neuropathy.
  - Central nervous system effects.

Discontinue Danmox immediately and avoid the use of fluoroquinolones, including Danmox, in patients who experience any of these serious adverse reactions.

- Fluoroquinolones, including Danmox may exacerbate muscle weakness in patients with myasthenia gravis. Avoid Danmox in patients with known history of myasthenia gravis.
- Because fluoroquinolones, including Danmox, have been associated with serious adverse reactions, reserve Danmox for use in patients who have no alternative treatment options for the following indications:
  - Acute bacterial sinusitis [see Indications and Usage.
  - Acute bacterial exacerbation of chronic bronchitis

DESCRIPTION: Danmox (Moxifloxacin Hydrochloride) is a synthetic broad spectrum antibacterial agent & is available as Danmox Tablets for oral administration. Danmox (Moxifloxacin hydrochloride) is a fluoroquinolone, available as the monohydrochloride salt. Chemically moxifloxacin hydrochloride is 1-cyclopropyl-7-[(S,S)-2,8 diazabicyclo non-8-yl] -6-fluoro-8-methoxy-1,4-dihydro-4-oxo-quinoline-3-carboxylic acid.

CLINICAL PHARMACOLOGY: Mechanism of Action: Moxifloxacin is a broad-spectrum antibiotic that is active against both Gram-positive and Gram-negative bacteria. It functions by inhibiting DNA gyrase, a type II topoisomerase, and topoisomerase IV, enzymes necessary to separate bacterial DNA, thereby inhibiting cell division.

PHARMACOKINETIC

Absorption: Moxifloxacin, given as an oral tablet, is well absorbed from the gastrointestinal tract. The absolute bioavailability of moxifloxacin is approximately 90 percent. Co-administration with a high fat meal (i.e., 500 calories from fat) does not affect the absorption of moxifloxacin. Plasma concentrations increase proportionately with dose up to the highest dose tested (1200 mg single oral dose). The mean (± SD) elimination half-life from plasma is 12 ± 1.3 hours; steady-state is achieved after at least three days with a 400 mg once daily regimen.

The mean (± SD) Cmax and AUC values following single dose of 400mg moxifloxacin given orally is summarized below.

	Cmax (mg/L)	AUC (mg•h/L)	Half-life (hr)
SINGLE DOSE ORAL			
Healthy (n = 372)	3.1 ± 1	36.1 ± 9.1	11.5 - 15.6*

Moxifloxacin Concentrations (mean ± SD) in Tissues and the Corresponding Plasma Concentrations after a Single 400mg Oral dose.

Tissue or Fluid	Plasma concentration (ug/ML	Tissue or Fluid Concentration (ug/ML or ug/g)	Tissue Plasma Ratio
SINGLE DOSE ORAL			
Alveolar Macrophages	3.3 ± 0.7	61.8 ± 27.3	21.2 ± 10
Bronchial Mucosa	3.3 ± 0.7	5.5 ± 1.3	1.7 ± 0.3
Epithelial Lining Fluid	3.3 ± 0.7	24.4 ± 14.7	8.7 ± 6.1

Distribution: Moxifloxacin is approximately 30-50% bound to serum proteins, independent of drug concentration. Moxifloxacin is widely distributed throughout the body, with tissue concentrations often exceeding plasma concentrations. Moxifloxacin has been detected in the saliva, nasal and bronchial secretions, mucosa of the sinuses, skin blister fluid, subcutaneous tissue, skeletal muscle and abdominal tissues and fluids following oral administration of 400 mg.

Metabolism: Approximately 52% of an oral dose of moxifloxacin is metabolized via glucuronide and sulfate conjugation. The cytochrome P450 system is not involved in moxifloxacin metabolism and is not affected by moxifloxacin. The sulfate conjugate (M1) accounts for approximately 38% of the dose and is eliminated primarily in the feces. Approximately 14% of an oral dose is converted to a glucuronide conjugate (M2), which is excreted exclusively in the urine. Peak plasma concentrations of M2 are approximately 40% those of the parent drug, while plasma concentrations of M1 are generally less than 10% those of moxifloxacin.

Excretion: Approximately 45% of an oral dose of moxifloxacin is excreted as unchanged drug (~20% in urine and ~25% in feces). A total of 96% ± 4% of an oral dose is excreted as either unchanged drug or known metabolites.

INDICATION AND DOSAGE:

Infection	Daily Dose	Duration
Acute Bacterial Sinusitis	OD 400mg	10 days
Acute exacerbation of chronic obstructive pulmonary disease including bronchitis	OD 400mg	5 days
Community Acquired Pneumonia	OD 400mg	7-14 days
Uncomplicated Skin and Skin Structure Infections	OD 400mg	7 days
Complicated Skin and Skin Structure Infections	OD 400mg	7 – 21 days
Complicated Intra-Abdominal Infections	OD 400mg	5-14 days

SIDE EFFECTS: Clinical efficacy trials enrolled over 9,200 moxifloxacin orally treated patients, of whom over 8,600 patients received the 400 mg dose. Most adverse events reported in moxifloxacin trials were described as mild to moderate in severity and required no treatment. Moxifloxacin was discontinued due to adverse reactions thought to be drug-related in 2.9% of orally treated patients nausea (6%), diarrhea (5%), dizziness (2%). Additional clinically relevant uncommon events, judged that occurred in greater than or equal to 0.1% and less than 2% of moxifloxacin.

BODY AS A WHOLE: Abdominal pain, headache, asthenia, dehydration (secondary to diarrhea or reduced fluid intake), injection site reaction (including phlebitis), malaise, moniliasis, pain, allergic reaction.
CARDIOVASCULAR: Cardiac arrhythmia (not otherwise specified), tachycardia, palpitation, vasodilation, QT interval prolonged.
COMMON SIDE EFFECTS: Nausea, diarrhea, dizziness, lightheadedness, headache, weakness, or trouble sleeping may occur. If any of these effects persist or worsen, tell your doctor or pharmacist promptly.
CONTRAINDICATIONS: Moxifloxacin is contraindicated in persons with a history of hypersensitivity to moxifloxacin or any member of the quinolone class of antimicrobial agents.

PRECAUTIONS: Pediatric Use Safety and effectiveness in pediatric patients and adolescents less than 18 years of age have not been established. Moxifloxacin causes arthropathy in juvenile animals. The pharmacokinetics of moxifloxacin in pediatric subjects have not been studied.
GENERAL: Quinolones may cause central nervous system (CNS) events, including: nervousness, agitation, insomnia, anxiety, nightmares or paranoia. Moderate to severe photosensitivity/phototoxicity reactions, the latter of which may manifest as exaggerated sunburn reactions (e.g., burning, erythema, exudation, vesicles, blistering, edema) involving areas exposed to light (typically the face, "V" area of the neck, extensor surfaces of the forearms, dorsa of the hands), can be associated with the use of quinolone antibiotics after sun or UV light exposure. Therefore, excessive exposure to these sources of light should be avoided. Drug therapy should be discontinued if phototoxicity occurs. **NURSING MOTHERS:** 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 moxifloxacin, 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.

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

DRUG INTERACTIONS: Antacids, Sucralfate, Metal Cations, Multivitamins: Quinolones form chelates with alkaline earth and transition metal cations. Oral administration of quinolones with antacids containing aluminum or magnesium, with sucralfate, with metal cations such as iron, or with multivitamins containing iron or zinc, or with formulations containing divalent and trivalent cations such as didanosine may substantially interfere with the absorption of quinolones, resulting in systemic concentrations considerably lower than desired. Therefore, moxifloxacin should be taken at least 4 hours before or 8 hours after these agents.This drug should not be used with the following medications because very serious interactions may occur: strontium, certain drugs that affect the heart rhythm (antiarrhythmics that may cause QT prolongation such as amiodarone, dofetilide, quinidine, procainamide, sotalol). The potential for pharmacokinetic drug interactions between moxifloxacin and itraconazole, theophylline, warfarin, digoxin, atenolol, probenecid, morphine, oral contraceptives, ranitidine, glyburide, calcium, iron, and antacids has been evaluated. There was no clinically significant effect of moxifloxacin on itraconazole, theophylline, warfarin, digoxin, atenolol, oral contraceptives, or glyburide kinetics. Itraconazole, theophylline, warfarin, digoxin, probenecid, morphine, ranitidine, and calcium did not significantly affect the pharmacokinetics of moxifloxacin. These results and the data from in vitro studies suggest that moxifloxacin is unlikely to significantly alter the metabolic clearance of drugs metabolized by CYP3A4, CYP2D6, CYP2C9, CYP2C19, or CYP1A2 enzymes. As with all other quinolones, iron and antacids significantly reduced bioavailability of moxifloxacin.

QT PROLONGATION: Moxifloxacin 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) antiarrhythmic agents, due to the lack of clinical experience with the drug in these patient populations.

RENAL INSUFFICIENCY: The pharmacokinetic parameters of moxifloxacin are not significantly altered in mild, moderate, severe, or end-stage renal disease. No dosage adjustment is necessary in patients with renal impairment, including those patients requiring hemodialysis (HD) or continuous ambulatory peritoneal dialysis (CAPD).
HEPATIC INSUFFICIENCY: No dosage adjustment is recommended for mild, moderate, or severe hepatic insufficiency (Child-Pugh Classes A, B, or C). However, due to metabolic disturbances associated with hepatic insufficiency, which may lead to QT prolongation, moxifloxacin should be used with caution in these patients.

PHOTOSENSITIVITY POTENTIAL: A study of the skin response to ultraviolet (UVA and UVB) and visible radiation conducted in 32 healthy volunteers (8 per group) demonstrated that moxifloxacin does not show phototoxicity in comparison to placebo. The minimum erythematous dose (MED) was measured before and after treatment with moxifloxacin (200 mg or 400 mg once daily), lomefloxacin (400 mg once daily), or placebo. In this study, the MED measured for both doses of moxifloxacin were not significantly different from placebo, while lomefloxacin significantly lowered the MED.

OVERDOSE: Single oral overdoses up to 2.8 g were not associated with any serious adverse events. In the event of acute overdose, the stomach should be emptied and adequate hydration maintained. ECG monitoring is recommended due to the possibility of QT interval prolongation. The patient should be carefully observed and given supportive treatment. The administration of activated charcoal as soon as possible after oral overdose may prevent excessive increase of systemic moxifloxacin exposure. About 3% and 9% of the dose of moxifloxacin, as well as about 2% and 4.5% of its glucuronide metabolite are removed by continuous ambulatory peritoneal dialysis and hemodialysis, respectively.

WARNING: This medication may rarely cause tendon damage (e.g., tendinitis, tendon rupture) during or after treatment. Your risk for tendon problems is greater if you are over 60 years of age, if you are taking corticosteroids (such as prednisone), or if you have had a kidney, heart or lung transplant. Stop exercising, rest, and seek immediate medical attention if you develop joint/muscle/tendon pain or swelling.

MISSED DOSE: If you miss a dose, take it as soon as you remember. If it is near the time of the next dose, skip the missed dose and resume your usual dosing schedule. Do not double the dose to catch up.

INSTRUCTIONS: Dosage as directed by the physician. Store below 30°C. Protect from heat, light and moisture. Keep all medicines out of the reach of children. To be sold on the prescription of a registered medical practitioner only.

PRESENTAION: Danmox (Moxifloxacin) 400mg tablets U.S.P. are available in Alu-Alu bilster pack of 1x5's tablets with leaf insert.

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