Danmox

400mg/250mL
I.V. INFUSION

(Moxifloxacin)

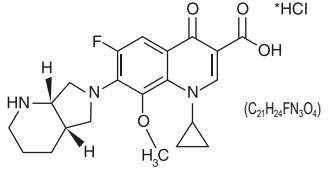
QUALITATIVE AND QUANTITATIVE COMPOSITION

Danmox Infusion 400mg/250mL
Each mL contains Moxifloxacin HCl U.S.P. eq. to
Moxifloxacin 1.6mg

WARNING: Fluoroquinolones, including Danmox Infusion, are associated with an increased risk of tendinitis and tendon rupture in all ages. This risk is further increased in older patients usually over 60 years of age, in patients taking corticosteroid drugs, and in patients with kidney, heart or lung transplants.

DRUG DESCRIPTION:

Danmox (Moxifloxacin) is a synthetic broad spectrum antibacterial agent for oral and intravenous administration. Moxifloxacin, a fluoroquinolone, is available as the monohydrochloride salt, its chemical structure is as follows:



CLINICAL PHARMACOLOGY

Mechanism of action: For fluoroquinolones, including moxifloxacin, is different from that of macrolides, beta-lactams, aminoglycosides, or tetracyclines; therefore, microorganisms resistant to these classes of drugs may be susceptible to moxifloxacin and other fluoroquinolones. There is no known cross-resistance between moxifloxacin and other classes of antimicrobials.

Pharmacodynamics: Moxifloxacin has in vitro activity against a wide range of Gram-positive and Gram-negative microorganisms. The bactericidal action of moxifloxacin results from inhibition of the topoisomerase II (DNA gyrase) and topoisomerase IV required for bacterial DNA replication, transcription, repair, and recombination. It appears that the C8-methoxy moiety contributes to enhanced activity and lower selection of resistant mutants of Gram-positive bacteria compared to the C8-H moiety. The presence of the bulky bicycloamine substituent at the C-7 position prevents active efflux, associated with the NorA or pmrA genes seen in certain Gram-positive bacteria.

Pharmacokinetics

Absorption: Moxifloxacin, given as I.V Infusion, is well absorbed from the gastrointestinal tract. The absolute bioavailability of moxifloxacin is approximately 90 percent. Co-administration with a high fat meal (that is, 500 calories from fat) does not affect the absorption of moxifloxacin.
Consumption of 1 cup of yogurt with moxifloxacin does not significantly affect the extent or rate of systemic absorption (AUC).

Excretion: Approximately 45% of an intravenous dose of moxifloxacin is excreted as unchanged drug (~20% in urine and ~25% in feces).

Mean (± SD) Cmax and AUC values following single and multiple doses of 400 mg moxifloxacin given by 1 hour I.V. infusion

Single Dose I.V.	Cmax (mg/L)	AUC (mg•h/L)	Half-life (hr)
Healthy (n = 56)	3.9 ± 0.9	39.3 ± 8.6	8.2-15.4

INDICATIONS

Acute Bacterial Sinusitis: Danmox is indicated for the treatment of Acute Bacterial Sinusitis caused *by Streptococcus pneumoniae, Haemophilus influenzae, or Moraxella catarrhalis.*

Acute Bacterial Exacerbation of Chronic Bronchitis: Danmox is indicated for the treatment of Acute Bacterial Exacerbation of Chronic Bronchitis caused by *Streptococcus pneumoniae, Haemophilus influenzae, Haemophilus parainfluenzae, Klebsiella pneumoniae, methicillin-susceptible Staphylococcus aureus, or Moraxella catarrhalis.*

Community Acquired Pneumonia: Danmox is indicated for the treatment of Community Acquired Pneumonia caused by *Streptococcus pneumoniae (including multi-drug resistant isolates*), Haemophilus influenzae, Moraxella catarrhalis, methicillin-susceptible Staphylococcus aureus, Klebsiella pneumoniae, Mycoplasma pneumoniae, or Chlamydophila pneumoniae.*

** MDRSP, Multi-drug resistant Streptococcus pneumoniae includes isolates previously known as PRSP (Penicillin resistant S. pneumoniae),* and are isolates resistant to two or more of the following antibiotics: penicillin (minimum inhibitory concentrations [MIC] ≥ 2 mcg/mL), 2nd generation cephalosporins (for example, cefuroxime), macrolides, tetracyclines, and trimethoprim/sulfamethoxazole.

Uncomplicated Skin and Skin Structure Infections: Danmox is indicated for the treatment of Uncomplicated Skin and Skin Structure Infections caused by methicillin susceptible *Staphylococcus aureus or Streptococcus pyogenes.*

Complicated Skin and Skin Structure Infections: Danmox is indicated for the treatment of Complicated Skin and Skin Structure Infections caused by *methicillinsusceptible Staphylococcus aureus, Escherichia coli, Klebsiella pneumoniae, or Enterobacter cloacae.*

Complicated Intra-Abdominal Infections: Danmox is indicated for the treatment of Complicated Intra-Abdominal Infections including polymicrobial infections such as abscess caused by *Escherichia coli, Bacteroides fragilis, Streptococcus anginosus, Streptococcus constellatus, Enterococcus faecalis, Proteus mirabilis, Clostridium perfringens, Bacteroides thetaiotaomicron, or Peptostreptococcus species.*

DOSAGE AND ADMINISTRATION

Dosage in Adult Patients
The duration of therapy depends on the type of infection as described below.
By intravenous infusion over 60 minutes, community acquired pneumonia, complicated skin and soft-tissue infections, 400mg once daily Note Recommended duration of treatment is 7–14 days for community-acquired pneumonia, 5–10 days in exacerbations of chronic bronchitis, 7 days in sinusitis, 14 days in pelvic inflammatory disease, 7–21 days for complicated skin and soft-tissue infections.

Administration Instructions
Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.
Danmox IV should be administered by INTRAVENOUS infusion only. It is not intended for intra-arterial, intramuscular, intrathecal, intraperitoneal, or subcutaneous administration.
Danmox IV should be administered by intravenous infusion over a period of 60 minutes by direct infusion or through a Y-type intravenous infusion set.
Caution: rapid or bolus intravenous infusion must be avoided.

SIDE-EFFECTS:

Gastritis, flatulence, constipation, arrhythmias, palpitation, angina, vasodilatation, hyperlipidaemia, sweating; rarely oedema,
hypertension, syncope, dysphagia, abnormal dreams, incoordination, amnesia, peripheral neuropathy, hyperglycaemia, hyperuricaemia, myopathy, stomatitis; very rarely rhabdomyolysis, potentially life-threatening hepatic failure; on intravenous infusion, pain and phlebitis at injection site.

INTERACTIONS:

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

USE IN SPECIFIC POPULATIONS

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.

Nursing Mothers:
There is no data available in lactating or nursing women.
Moxifloxacin may be excreted in human milk.

Pediatric Use:
Safety and effectiveness in pediatric patients and adolescents less than 18 years of age have not been established.
Hepatic impairment: Avoid in severe impairment.
Renal Impairment: The pharmacokinetic properties of moxifloxacin are not significantly different in patients with renal impairment.

OVERDOSE:

ECG monitoring is recommended due to the possibility of QT interval prolongation. The patient should be carefully observed and given supportive treatment. 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.
Single oral Moxifloxacin doses of 2000, 500, and 1500 mg/kg were lethal to rats, mice, and cynomolgus monkeys, respectively. The minimum lethal intravenous dose in mice and rats was 100 mg/kg. Adverse clinical signs included CNS and gastrointestinal effects such as decreased activity, somnolence, tremor, convulsions, vomiting and diarrhea.

CONTRAINDICATIONS:

Danmox is contraindicated in persons with a history of hypersensitivity to moxifloxacin or any member of the quinolone class of antimicrobial agents.
Moxifloxacin is contra-indicated in patients with risk factors for QT interval prolongation (e.g. electrolyte disturbances, acute myocardial infarction, heart failure with reduced left ventricular ejection fraction, bradycardia, congenital long QT syndrome, concomitant use with other drugs known to prolong the QT interval, history of symptomatic arrhythmias) and the other quinolones should be used with caution in these patients.
The CSM has warned that quinolones may induce convulsions in patients with or without a history of convulsions; taking NSAIDs at the same time may also induce them.

Tendon damage: Tendon damage (including rupture) has been reported rarely in patients receiving quinolones. Tendon rupture may occur within 48 hours of starting treatment; cases have also been reported several months after stopping a quinolone. Healthcare professionals are reminded that:

- quinolones are contra-indicated in patients with a history of tendon disorders related to quinolone use;
- patients over 60 years of age are more prone to tendon damage;
- the risk of tendon damage is increased by the concomitant use of corticosteroids;
- if tendinitis is suspected, the quinolone should be discontinued immediatly.

INSTRUCTIONS:

Dosage as directed by the physician. Store below 30°C. Protect from heat & light. It should not be refrigerated. Avoid freezing and injection should not be used if container is leaking, solution is cloudy or it contains un-dissolved particles. Keep all medicines out of the reach of children.

PRESENTATION:

Danmox (Moxifloxacin) 400mg/250mL I.V. Infusion is available in 250mL glass vial with leaf insert.

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