

VHA Pharmacy Benefits Management (PBM)-Medical Advisory Panel (MAP) Criteria for Non-Formulary Use of Alatrofloxacin/Trovafloxacin

I. Indications for VA Patients

Trovafloxacin should be reserved for use **only** in the treatment of patients who meet **ALL** of the following criteria:

- A. Have at least one of the following infections, judged to be serious and life- or limb- threatening:
- Nosocomial pneumonia
 - Community acquired pneumonia
 - Complicated intra-abdominal infections (including post-surgical)
 - Gynecologic and pelvic infections
 - Complicated skin and skin structure infections, including diabetic foot infections
- B. Receive initial therapy through an in-patient health care facility.
- C. The treating physician believes that, even given the possibility of serious liver injury, the benefit to the patient outweighs the potential risk.

II. Dosage and Administration

Infection type	Dose and Regimen	Duration ^a
Complicated intra-abdominal	300mg IV ^b then 200mg PO ^c QD ^d	7-14 days
Complicated SSSI ^e	200mg IV then 200mg PO QD	10-14 days
Gynecologic/pelvic infections	300mg IV then 200mg PO QD	7-14 days
Nosocomial pneumonia	300mg IV then 200mg PO QD	10-14 days

^a total duration of therapy, both PO and IV

^b IV=intravenous

^c PO=by mouth

^d QD=daily

^e SSSI=skin and skin structure infection

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Dosing of alatrofloxacin/trovafloxacin must be adjusted in patients with chronic hepatic disease. Approximately 5% of a dose is excreted unchanged in the urine, therefore a dosing adjustment in renal failure is not required.

Indicated dose in normal hepatic function	Chronic hepatic disease dose
300 mg IV	200mg IV
200mg IV	100mg IV
200mg PO	100mg PO

III. Warnings

- A. Severe liver toxicity has been reported with use of this drug. Acute liver failure has occurred, resulting in the need for liver transplant and/or death. No single factor appears to predict the development of toxicity. Cases have occurred early in therapy as well as after 14 days of therapy.
- B. Cross-resistance among fluoroquinolone agents is documented for S. aureus, P. aeruginosa and enteric gram-negative rods. Trovafloxacin should be reserved for cases where other therapeutic options have failed. This should be documented with antimicrobial sensitivities and culture results.
- C. Alatrofloxacin is only for IV use. It is not to be administered IM, intraperitoneal or SC. Alatrofloxacin is not compatible with 0.9% sodium chloride.
- D. Trovafloxacin is contraindicated in pregnancy, lactation and in children.
- E. Patients treated with agents of this class may experience phototoxicity reactions.

IV. Monitoring Parameters

A. Drug Interactions

- 1. Decreased absorption of trovafloxacin has been reported with the use of sucralfate, ferrous sulfate, magnesium and aluminum containing antacids and omeprazole.
- 2. Trovafloxacin has not been shown to effect theophylline, digoxin or warfarin pharmacokinetics/pharmacodynamics.
- 3. Although food delays the t_{max} and C_{max} of trovafloxacin, the bioavailability remains unchanged.

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4. Co-administration of intravenous morphine decreases the absorption of oral trovafloxacin. Dosing should be separated by 2 hours in the fasted state and 4 hours in the fed state.

B. Clinical Parameters

1. Trovafloxacin should be discontinued if the patient experiences any sign of liver dysfunction including, fatigue, anorexia, jaundice, severe stomach pain with nausea and vomiting, or dark urine.
2. Liver function tests may be preformed; however, they do not consistently predict the development of liver toxicity with trovafloxacin.

V. Outcomes

To date, alatrofloxacin/trovafloxacin does not have published trials demonstrating an effect on clinical outcomes.