



NATIONAL PBM BULLETIN

January 13, 2016

DEPARTMENT OF VETERANS AFFAIRS
PHARMACY BENEFITS MANAGEMENT SERVICES (PBM), MEDICAL ADVISORY PANEL (MAP),
VISN PHARMACIST EXECUTIVES (VPEs), AND THE CENTER FOR MEDICAL SAFETY (VA MedSAFE)

NOXAFIL (POSACONAZOLE):

DOSING ERRORS WHEN SWITCHING BETWEEN DIFFERENT ORAL FORMULATIONS

I. ISSUE

Due to reports of dosing errors when switching between the two oral formulations of Noxafil (posaconazole), the patient information and outer carton have been revised to indicate that the oral formulations cannot be directly substituted for each other due to differences in how each formulation is dosed.

II. BACKGROUND

Noxafil (posaconazole) is available in two oral formulations that cannot be directly substituted for one another due to differences in bioavailability. The delayed-release tablet has a higher bioavailability than the oral suspension. The dose and frequency of administration for this agent depend on the particular formulation used and the indication for use.

III. DISCUSSION

FDA has received eleven reports of the wrong oral formulation of the delayed-release tablet formulation of Noxafil (posaconazole) being prescribed and/or dispensed to patients since its approval in 2013. In one instance, an underdose occurred when the delayed-release tablet formulation was directly replaced with the oral suspension for the prophylaxis of invasive *Aspergillus* and *Candida* infection. The patient was reported to have later died from a stroke related to an invasive *Aspergillus* infection. The other ten case reports described overdoses when patients switched from Noxafil (posaconazole) oral suspension to the delayed-release tablets in the same dose and frequency of administration as the oral suspension. Some of these patients reported nausea and vomiting, and one patient presented to a hospital with these adverse reactions and was found to have a low serum potassium level.

Within the VA, there was one case of dosing confusion with posaconazole reported in 2014, where a patient received an excessive dose of two 200 mg tablets by mouth four times a day for lung transplant. The patient experienced tremor and chills and also had an elevated FK506 level secondary to the error.

IV. PROVIDER CONSIDERATIONS/RECOMMENDATIONS

FDA recommends that:

- Prescribers should specify the dosage form, strength, and frequency on all prescriptions they write for Noxafil.
- Pharmacists should request clarification from prescribers when the dosage form, strength, or frequency is not specified.
- Prescribers should follow the specific dosing instructions for each formulation.

Dosage for Noxafil Delayed-Release Tablets

Indication	Dose and Duration of Therapy
Prophylaxis of invasive <i>Aspergillus</i> and <i>Candida</i> infections	<u>Loading Dose:</u> 300 mg (three 100 mg delayed-release tablets) twice a day on the first day. <u>Maintenance Dose:</u> 300 mg (three 100 mg delayed-release tablets) once a day, starting on the second day. Duration of therapy is based on recovery from neutropenia or immunosuppression.

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NOXAFIL (POSACONAZOLE): DOSING ERRORS WHEN SWITCHING BETWEEN DIFFERENT ORAL FORMULATIONS *(continued from page 1)*

Dosage for Noxafil Oral Suspension

Indication	Dose and Duration of Therapy
Prophylaxis of invasive <i>Aspergillus</i> and <i>Candida</i> infections	200 mg (5 mL) three times a day. The duration of therapy is based on recovery from neutropenia or immunosuppression.
Oropharyngeal Candidiasis	<u>Loading Dose:</u> 100 mg (2.5 mL) twice a day on the first day. <u>Maintenance Dose:</u> 100 mg (2.5 mL) once a day for 13 days.
Oropharyngeal Candidiasis Refractory to Itraconazole and/or Fluconazole	400 mg (10 mL) twice a day. Duration of therapy should be based on the severity of the patient's underlying disease and clinical response.

Providers should continue to report any adverse reactions with the use of Noxafil (posaconazole) by entering the information into CPRS' Allergies/ Adverse Reactions field and/or via local reporting mechanisms. Adverse events should also be reported, as appropriate, to the VA ADERS program and FDA MedWatch. MedWatch reports can be completed and faxed to the FDA through VA ADERS (https://vaww.cmop.med.va.gov/MedSafe_Portal/ select VA ADERS Launch).

V. REFERENCES

FDA Drug Safety Communication: FDA cautions about dosing errors when switching between different oral formulations of antifungal Noxafil (posaconazole); label changes approved. <http://www.fda.gov/Drugs/DrugSafety/ucm479352.htm> . (Accessed 01/07/2016).

ACTIONS

- **Facility Director** (or physician designee): Forward this document to the Facility Chief of Staff (COS).
- **Facility COS and Chief Nurse Executives:** Forward this document to all appropriate providers and health care staff (e.g., **primary care providers, infectious disease specialists, and pharmacists, including contract providers, etc.**). In addition, forward to the Associate Chief of Staff (ACOS) for Research and Development (R&D). Forward to other VA employees as deemed appropriate.
- **ACOS for R&D:** Forward this document to Principal Investigators (PIs) who have authority to practice at the facility and to your respective Institutional Review Board (IRB).