



## Therapeutic Class Review<sup>SM</sup>

### Antifungals – Posaconazole (Noxafil<sup>®</sup>)

April 2007

**New Product for Review:**

posaconazole (Noxafil<sup>®</sup>) [Schering-Plough]

**Dossier Provided by Manufacturer: Yes**

**Dossier Evaluation: 3**

- 1- dossier w/missing components
- 2- all components present, except pharmacoeconomic model
- 3- all components present (comprehensive)

**Available Therapeutic Alternatives:**

Preferred/Formulary	Non-Preferred/Non-Formulary
fluconazole (Diflucan <sup>®</sup> ) [Pfizer]	posaconazole (Noxafil <sup>®</sup> ) [Schering-Plough]
itraconazole* (Sporanox <sup>®</sup> ) [Janssen]	
voriconazole (Vfend <sup>®</sup> ) [Pfizer]	
Covered Under Medical Benefit	
miconazole (Mycamine <sup>®</sup> ) [Astellas Pharma]	
caspofungin (Cancidas <sup>®</sup> ) [Merck]	
amphotericin B liposome (Ambisome <sup>®</sup> ) [Fujisawa]	
amphotericin B (Fungizone <sup>®</sup> ) [generics]	

\* Covered with prior authorization

**Executive Summary**

- Transplant and oncology patients have compromised immune systems, placing them at risk for invasive fungal infections, which are associated with significant morbidity and mortality.
- The most common fungal infections affecting these populations are *Candida* and *Aspergillus*.
- Current FDA labeling for available antifungal options:

Drug	Aspergillus		Oral Candidiasis	
	Prophylaxis	Treatment	Prophylaxis	Treatment
Fluconazole (Diflucan <sup>®</sup> )				X
Itraconazole (Sporanox <sup>®</sup> )		X		X
Posaconazole (Noxafil <sup>®</sup> )	X		X	X
Voriconazole (Vfend <sup>®</sup> )		X		X

- In clinical practice, fluconazole and itraconazole have been used for antifungal prophylaxis in transplant and oncology patients.
- When given in combination with cyclosporine, posaconazole (Noxafil), like other azole antifungal agents, is associated with drug interactions (some of which have been fatal).
- Potential off-label uses of posaconazole (Noxafil) include abdominal candidiasis, zygomycosis, coccidioidomycosis, and salvage therapy for other invasive fungal infections.

### Evidence

- All of the available evidence for posaconazole (Noxafil) in the treatment and prevention of fungal infections is uncertain (Grade U) or not useful (Grade X).
  - No reliable conclusions can be drawn from these trials.
  - Available evidence is not helpful in determining the superiority of posaconazole (Noxafil) over existing formulary/preferred antifungal agents.
- Nausea was the most common side effect reported during clinical trials, occurring in up to 38% of patients.

### Considerations in subpopulations

- *Pediatrics*: Safety and efficacy in pediatric patients (<13 years old) have not been established. A total of 28 pediatric patients ages 8 through 17 were treated with posaconazole (Noxafil) in clinical trials.
- *Geriatrics*: No differences in efficacy and safety of posaconazole (Noxafil) were noted between older ( $\geq 65$  years of age) and younger patients. Out of 605 patients randomized to posaconazole (Noxafil) in prophylaxis trials, 63 (10%) were 65 years of age or older.
- *Race, ethnicity*: No adjustment in the dosage of posaconazole (Noxafil) is necessary.
- *Gender*: No adjustment in the dosage of posaconazole (Noxafil) is necessary.

### Conclusion

- Posaconazole (Noxafil) is non-preferred/non-formulary because:

- There is no reliable evidence of posaconazole (Noxafil) efficacy in the treatment of oropharyngeal candidiasis or prophylaxis of invasive fungal infections.
- There is no consensus on the value of Aspergillus prophylaxis in clinical practice.

## Products

Drug Products	FDA approval <sup>a</sup>	Patent Expiration(s) <sup>c</sup>	FDA approved indications	Usual Dose/Route	Cost <sup>b</sup>	Potential Off-label Uses <sup>d</sup>
fluconazole (Diflucan <sup>®</sup> ) <sup>1</sup>	1/1990	N/A	<ol style="list-style-type: none"> <li>1. Bone marrow transplant - Candidiasis; Prophylaxis</li> <li>2. Candidal vulvovaginitis</li> <li>3. Candidiasis</li> <li>4. Candidiasis of mouth and esophagus</li> <li>5. Candidiasis of urogenital site</li> <li>6. Cryptococcal meningitis</li> </ol>	200 mg – 400 mg po/iv daily	PO: \$33 - \$66  IV: \$743 - \$1,485  Prophylaxis (PO): \$ 66  Treatment: \$33 - \$1,485	Asthma, prophylaxis for candidiasis, coccidioidomycosis, cryptococcosis, cutaneous leishmaniasis, deep mycosis, disseminated sporotrichosis, eye infection, febrile neutropenia, histoplasmosis, aspergillosis pneumonia, P. marneffeii, onychomycosis, perforated tympanic membrane, septic shock, tinea
itraconazole (Sporanox <sup>®</sup> ) <sup>2</sup>	9/1992	2014 – 2019 <sup>e</sup>	<ol style="list-style-type: none"> <li>1. Aspergillosis</li> <li>2. Blastomycosis</li> <li>3. Candidiasis of mouth and esophagus</li> <li>4. Febrile neutropenia</li> <li>5. Histoplasmosis</li> <li>6. Onychomycosis due to dermatophyte</li> </ol>	200 mg – 400 mg po/iv daily	PO: \$489 - \$979  IV: \$7,062	Allescheriosis, aspergillosis prophylaxis, candidal vulvovaginitis, chromomycosis, coccidioidomycosis, cryptococcosis, cutaneous leishmaniasis, fungal keratitis, disseminated C. trichoides, Penicillium marneffeii, invasive fungal infection prophylaxis, mycetoma, superficial tinea, yellow nails, paracoccidioidomycosis, sporotrichosis, phaeohyphomycosis
posaconazole (Noxafil <sup>®</sup> ) <sup>3</sup>	9/2006	9/2011	<ol style="list-style-type: none"> <li>1. Disseminated candidiasis in severely immunocompromised patients; Prophylaxis</li> <li>2. Infection due to Aspergillus species in severely immunocompromised patients; Prophylaxis</li> <li>3. Oropharyngeal candidiasis</li> </ol>	100 mg – 800 mg daily (in divided doses)	PO: \$429 - \$3,420  Prophylaxis \$2580  Treatment \$870 - \$3420	Fusarium infection, mycosis, disseminated zygomycosis, disseminated phaeohyphomycosis, mycotic keratitis

## Products (Continued)

Drug Products	FDA approval <sup>a</sup>	Patent Expiration(s) <sup>c</sup>	FDA approved indications	Usual Dose/Route	Cost <sup>b</sup>	Potential Off-label Uses <sup>d</sup>
voriconazole (Vfend®) <sup>4</sup>	5/2002	5/2007	<ol style="list-style-type: none"> <li>1. Aspergillosis, Invasive</li> <li>2. Candidal septicemia</li> <li>3. Candidiasis of the esophagus</li> <li>4. Disseminated candidiasis, of the skin and infections in abdomen, kidney, bladder wall, and wounds</li> <li>5. Mycosis, Serious infections due to <i>Scedosporium apiospermum</i> and <i>Fusarium</i> spp. including <i>Fusarium solani</i></li> </ol>	100 mg – 300 mg po/iv q12h  (Dose based on 75 kg person)	PO: \$1,160 - \$3,480  IV: \$7,240 – \$14,479	Febrile neutropenia, fungal keratitis, hyalohyphomycosis

<sup>a</sup> Date applies to approval date for the original brand name medication where there are now generics available.

<sup>b</sup> Cost estimate based on AWP (average wholesale price) listed in First Data Bank or MAC (maximum allowable cost) as of December 2006 for 30 days of therapy.

<sup>c</sup> Based on patents listed in Orange Book as of April 4, 2007.

<sup>d</sup> As listed in © 1974 - 2007 Thomson MICROMEDEX database or as referenced.

<sup>e</sup> Sporanox molecule patent has expired. Current patent refers to oral formulation.

## References

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