

Clinical Pharmacy Program Guidelines for Azole Antifungals

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| Program | Prior Authorization |
| Medication | Sporanox (itraconazole) capsules, Sporanox (itraconazole) oral solution, Onmel (itraconazole) tablets, Vfend (voriconazole) tablets, Noxafil (posaconazole) tablets, Noxafil (posaconazole) oral suspension, Cresemba (isavuconazonium) capsules |
| Issue Date | 6/2009 |
| Pharmacy and Therapeutics Approval Date | 7/2017 |
| Effective Date | 9/2017 |

1. Background:

Drug Name: Sporanox (itraconazole) capsules

Indications

Blastomycosis

Indicated for the treatment of the following fungal infection in immunocompromised and non-immunocompromised patients: Blastomycosis, pulmonary and extrapulmonary

Histoplasmosis

Indicated for the treatment of the following fungal infection in immunocompromised and non-immunocompromised patients: Histoplasmosis, including chronic cavitary pulmonary disease and disseminated, nonmeningeal histoplasmosis

Aspergillosis

Indicated for the treatment of the following fungal infection in immunocompromised and non-immunocompromised patients: Aspergillosis, pulmonary and extrapulmonary, in patients who are intolerant of or refractory to amphotericin B therapy

Onychomycosis of the toenail

Indicated for the treatment of the following fungal infection in non-immunocompromised patients: Onychomycosis of the toenail, with or without fingernail involvement, due to dermatophytes (Tinea unguium)

Onychomycosis of the fingernail

Indicated for the treatment of the following fungal infection in non-immunocompromised patients: Onychomycosis of the fingernail due to dermatophytes (Tinea unguium)

Drug Name: Sporanox (itraconazole) oral solution

Indications

Oropharyngeal and esophageal candidiasis

Indicated for the treatment of oropharyngeal and esophageal candidiasis.

Drug Name: Onmel (itraconazole)

Indications

Onychomycosis of the toenail

Indicated for the treatment of onychomycosis of the toenail due to *Trichophyton rubrum* or *T. Mentagrophytes* in non-immunocompromised patients. Prior to initiating treatment, appropriate nail specimens for laboratory testing (KOH preparation, fungal culture, or nail biopsy) should be obtained to confirm the diagnosis of onychomycosis.

Drug Name: Vfend (voriconazole)

Indications

Invasive aspergillosis

Indicated for use in patients 12 years of age and older in the treatment of invasive aspergillosis. In clinical trials, the majority of isolates recovered were *Aspergillus fumigatus*. There was a small number of cases of culture-proven disease due to species of *Aspergillus* other than *A. fumigatus*. Specimens for fungal culture and other relevant laboratory studies (including histopathology) should be obtained prior to therapy to isolate and identify causative organism(s). Therapy may be instituted before the results of the cultures and other laboratory studies are known; however, once these results become available, anti-infective therapy should be adjusted accordingly.

Candidemia and other Candida infections

Indicated for use in patients 12 years of age and older in the treatment of candidemia in non-neutropenic patients and the following *Candida* infections: disseminated infections in skin and infections in abdomen, kidney, bladder wall, and wounds. Specimens for fungal culture and other relevant laboratory studies (including histopathology) should be obtained prior to therapy to isolate and identify causative organism(s). Therapy may be instituted before the results of the cultures and other laboratory studies are known; however, once these results become available, anti-infective therapy should be adjusted accordingly.

Esophageal candidiasis

Indicated for use in patients 12 years of age and older in the treatment of esophageal candidiasis. Specimens for fungal culture and other relevant laboratory studies (including histopathology) should be obtained prior to therapy to isolate and identify causative organism(s). Therapy may be instituted before the results of the cultures and other laboratory studies are known; however, once these results become available, anti-infective therapy should be adjusted accordingly.

Serious fungal infections

Indicated for use in patients 12 years of age and older in the treatment of serious fungal infections caused by *Scedosporium apiospermum* (asexual form of *Pseudallescheria boydii*) and *Fusarium* spp. including *Fusarium solani*, in patients intolerant of, or refractory to, other therapy. Specimens for fungal culture and other relevant laboratory studies (including histopathology) should be obtained prior to therapy to isolate and identify causative organism(s). Therapy may be instituted before the results of the cultures and other laboratory studies are known; however, once these results become available, anti-infective therapy should be adjusted accordingly.

Drug Name: Noxafil (posaconazole) tablets

Indications

Prophylaxis of Invasive Aspergillus and Candida Infections

Indicated for prophylaxis of invasive *Aspergillus* and *Candida* infections in patients, 13 years of age and older, who are at high risk of developing these infections due to being severely immunocompromised, such as hematopoietic stem cell transplant (HSCT) recipients with graft-versus-host disease (GVHD) or those with hematologic malignancies with prolonged neutropenia from chemotherapy.

Drug Name: Noxafil (posaconazole) suspension

Indications

Prophylaxis of invasive Aspergillus and Candida infections

Indicated for use in the following situations: Prophylaxis of invasive *Aspergillus* and *Candida* infections in patients, 13 years of age and older, who are at high risk of developing these infections due to being severely immunocompromised, such as hematopoietic stem cell transplant (HSCT) recipients with graft-versus-host disease (GVHD) or those with hematologic malignancies with prolonged neutropenia from chemotherapy.

Treatment of oropharyngeal candidiasis

Indicated for treatment of oropharyngeal candidiasis, including oropharyngeal candidiasis refractory to itraconazole and/or fluconazole.

Drug Name: Cresemba (isavuconazonium)

Indications

Treatment of invasive aspergillosis and invasive mucormycosis

Indicated for patients 18 years of age and older for the treatment of invasive mucormycosis and

invasive aspergillosis. Specimens for fungal culture and other relevant laboratory studies (including histopathology) to isolate and identify causative organism(s) should be obtained prior to initiating antifungal therapy. Therapy may be instituted before the results of the cultures and other laboratory studies are known. However, once these results become available, antifungal therapy should be adjusted accordingly.

2. Coverage Criteria:

A. Itraconazole Capsules –Systemic Fungal Infections

1. Diagnosis of one of the following fungal infections:

- Blastomycosis
- Histoplasmosis
- Aspergillosis

Authorization will be issued for 12 months.

B. Itraconazole Capsules –Onychomycosis Fingernails

1. Initial Authorization

a. Diagnosis of fingernail onychomycosis confirmed by one of the following:

- KOH test
- Fungal culture
- Nail biopsy

Authorization will be issued for 2 months.

2. Reauthorization

a. Three months have elapsed since completion of initial therapy for fingernail onychomycosis

-AND-

b. Documentation of positive clinical response to therapy

Authorization will be issued for 2 months.

C. Itraconazole Capsules –Onychomycosis Toenails

1. Initial Authorization

a. Diagnosis of toenail onychomycosis confirmed by one of the following:

- KOH test
- Fungal culture
- Nail biopsy

Authorization will be issued for 3 months.

2. Reauthorization

a. Nine months have elapsed since completion of initial therapy for toenail onychomycosis

-AND-

b. Documentation of positive clinical response to therapy

Authorization will be issued for 3 months.

D. Sporanox Oral Solution

1. One of the following diagnoses:

- Oropharyngeal candidiasis
- Esophageal candidiasis

Authorization will be issued for 12 months.

E. Onmel

1. Initial Authorization

a. Diagnosis of toenail onychomycosis due to *Trichophyton rubrum* or *T. Mentagrophytes* confirmed by one of the following:

- KOH test
- Fungal culture
- Nail biopsy

-AND-

b. History of failure to generic itraconazole

Authorization will be issued for 3 months.

2. Reauthorization

a. Nine months have elapsed since completion of initial therapy for toenail onychomycosis

-AND-

b. Documentation of positive clinical response to therapy

Authorization will be issued for 3 months.

F. Voriconazole Tablets

1. One of the following diagnoses:

a. Invasive aspergillosis including *Aspergillus fumigatus*

-OR-

b. All of the following:

- (1) Candidemia
- (2) Patient is non-neutropenic
- (3) History of failure, contraindication, intolerance, or resistance to Diflucan (fluconazole)

-OR-

c. Both of the following:

(1) One of the following:

- Candida infection in the abdomen
- Candida infection in the kidney
- Candida infection in the bladder wall
- Candida infection in wounds
- Disseminated Candida infections in skin
- Esophageal candidiasis

-AND-

(2) History of failure, contraindication, intolerance, or resistance to Diflucan (fluconazole)

-OR-

d. *Scedosporium apiospermum* infection (asexual form of *Pseudallescheria boydii*)

-OR-

e. *Fusarium* spp. infection including *Fusarium solani*, in patients intolerant of, refractory to, other therapy.

Authorization will be issued for 12 months.

G. Noxafil Tablets

1. Used as prophylaxis of invasive fungal infections caused by one of the following:

- Aspergillus
- Candida

-AND-

2. One of the following conditions:

a. Patient is at high risk of infections due to severe immunosuppression from one of the following conditions:

- Hematopoietic stem cell transplant (HSCT) with graft-versus-host disease (GVHD)
- Hematologic malignancies with prolonged neutropenia from chemotherapy [eg, acute myeloid leukemia (AML), myelodysplastic syndromes (MDS)]

-OR-

b. Patient has a prior fungal infection requiring secondary prophylaxis

Authorization will be issued for 12 months.

H. Noxafil Suspension –Prophylaxis of Aspergillus or Candida Infections

1. Used as prophylaxis of invasive fungal infections caused by one of the following:

- Aspergillus
- Candida

-AND-

2. One of the following conditions:

a. Patient is at high risk of infections due to severe immunosuppression from one of the following conditions:

- Hematopoietic stem cell transplant (HSCT) with graft-versus-host disease (GVHD)
- Hematologic malignancies with prolonged neutropenia from chemotherapy [eg, acute myeloid leukemia (AML), myelodysplastic syndromes (MDS)]

-OR-

b. Patient has a prior fungal infection requiring secondary prophylaxis

Authorization will be issued for 12 months.

I. Noxafil Suspension –Oropharyngeal Candidiasis (OPC)

1. Diagnosis of oropharyngeal candidiasis (OPC)

-AND-

2. History of failure, contraindication, or intolerance to one of the following:

- Diflucan (fluconazole)
- Sporanox (itraconazole)

Authorization will be issued for 12 months

J. Cresemba

1. **One** of the following:

a. **Both** of the following:

(1) Diagnosis of invasive aspergillosis

-AND-

(2) History of failure, contraindication, or intolerance to voriconazole

-OR-

b. Diagnosis of invasive mucormycosis

Authorization will be issued for 3 months.

3. References:

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| Program | Prior Authorization –Azole Antifungals |
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| Change Control | |
| Date | Change |
| June 2009 | Itraconazole: Criteria taken from previously approved AmeriChoice policy. Added coverage for pulmonary coccidioidomycosis (Valley Fever). Policy |

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| | reformatted. |
| Sept 2010 | New Policy - Voriconazole |
| Dec 2010 | Annual Review - Itraconazole |
| June 2011 | Annual Review - Voriconazole |
| Dec 2011 | Annual Review - Itraconazole No clinical changes. Updated references. |
| June 2012 | VORICONAZOLE: Expanded diagnoses in section III.A.1, diagnoses that do not require a preferred alternative trial. Created new section III.A.3 for separate diagnoses where voriconazole is recommended as second line therapy, only one preferred alternative trial is required |
| June 2012 | ITRACONAZOLE Annual Review. Removed requirement for trial and failure of amphoterecin B for the following diagnoses: aspergillosis, blastomycosis, and empiric therapy of febrile neutropenia. |
| March 2013 | Itraconazole and Voriconazole criteria combined into a single policy, Azole antifungals. Added criteria for posaconazole, ketoconazole and other non-preferred itraconazole products (pulse pack). Thorough update of all criteria. |
| June 2015 | Removed Sporanox pulse pack from Itraconazole Onychomycosis criteria because Sporanox pulse pack is non-preferred and itraconazole is the preferred drug list option. Reauthorization criteria for onychomycosis for itraconazole capsules and Onmel were revised to no longer require confirmation of diagnosis by KOH test, fungal culture, or nail biopsy (per consult with ORx medical director). Removed the off-label criteria for febrile neutropenia, histoplasmosis, and aspergillosis for Sporanox oral solution. Voriconazole tablet section: <ul style="list-style-type: none"> • Removed off-label criteria for oropharyngeal candidiasis and candidemia in neutropenic patients • Removed voriconazole criteria for fungal infections due to contaminated steroid injections. These criteria were added in association with The New England Compounding Center's meningitis outbreak in 2012 and are no longer current |

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| | <p>Ketoconazole section removed because prior authorization is not required for this drug</p> <p>Added new criteria for Noxafil Tablet and Cresemba.</p> |
| October 2016 | Annual review, updated policy template |
| July 2017 | Updated background and references. Minor updates throughout the policy to align with most recent IDSA updates. |