**Clinical Pharmacy Program Guidelines for Azole Antifungals**

<table>
<thead>
<tr>
<th>Program</th>
<th>Prior Authorization</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medication</td>
<td>Sporanox (itraconazole) capsules, Sporanox (itraconazole) oral solution, Onmel (itraconazole) tablets, Vfend (voriconazole) tablets, Vfend (voriconazole) powder for oral suspension, Noxafil (posaconazole) tablets, Noxafil (posaconazole) oral suspension, Cresemba (isavuconazonium) capsules, Tolsura (itraconazole) capsule</td>
</tr>
<tr>
<td>Markets in Scope</td>
<td>Arizona, California, Florida- CHIP, Hawaii, Maryland, Nevada, New Jersey, New York, New York EPP, Ohio, Pennsylvania, Rhode Island</td>
</tr>
<tr>
<td>Issue Date</td>
<td>6/2009</td>
</tr>
<tr>
<td>Pharmacy and Therapeutics Approval Date</td>
<td>6/2019</td>
</tr>
<tr>
<td>Effective Date</td>
<td>8/2019</td>
</tr>
</tbody>
</table>

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.

**Drug Name:** Vfend (voriconazole) tablet and powder for oral suspension

**Indications**

**Invasive aspergillosis**
Indicated for use in patients 2 years of age and older in the treatment of invasive aspergillosis. In clinical trials, the majority of isolates recovered were Aspergillus fumigatus. There were a small number of cases of culture-proven disease due to species of Aspergillus other than A. fumigatus.

**Candidemia and other Candida infections**
Indicated for use in patients 2 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.

**Esophageal candidiasis**
Indicated for use in patients 2 years of age and older in the treatment of esophageal candidiasis.

**Serious fungal infections**
Indicated for use in patients 2 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.

**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 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 mycormycosis and invasive aspergillosis.

**Drug Name:** Tolsura (itraconazole)

**Indications**

**Aspergillosis**
Indicated for the treatment of aspergillosis, pulmonary and extrapulmonary in immunocompromised and non-immunocompromised adult patients who are intolerant of or who are refractory to amphotericin B therapy.

**Blastomycosis**
Indicated for the treatment of blastomycosis, pulmonary and extrapulmonary in immunocompromised and non-immunocompromised adult patients.

**Histoplasmosis**
Indicated for the treatment of histoplasmosis, including chronic cavitary pulmonary disease and dissemination, non-meningeval histoplasmosis in immunocompromised and non-
immunocompromised adult patients.

2. **Coverage Criteria:**

A. **Itraconazole Capsules – Systemic Fungal Infections**
   
   **NOTE:** This section does not apply to Tolsura.

   1. Diagnosis of one of the following fungal infections:
      
      a. Blastomycosis
      b. Histoplasmosis
      c. Aspergillosis

   **-OR-**

   2. **Both** of the following:
      
      a. Diagnosis of coccidioidomycosis
      b. History of failure, contraindication, intolerance, or resistance to fluconazole (generic Diflucan)

   **Authorization will be issued for 12 months.**

B. **Itraconazole Capsules – Onychomycosis Fingernails**
   
   **NOTE:** This section does not apply to Tolsura.

   1. **Initial Authorization**
      
      a. Diagnosis of fingernail onychomycosis confirmed by one of the following:
         
         i. KOH test
         ii. Fungal culture
         iii. 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
C. **Itraconazole Capsules – Onychomycosis Toenails**

*NOTE: This section does not apply to Tolsura.*

1. **Initial Authorization**
   
   a. Diagnosis of toenail onychomycosis confirmed by one of the following:
      
      i. KOH test
      ii. Fungal culture
      iii. 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:
   
   a. Oropharyngeal candidiasis
   b. 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:
      
      i. KOH test
      ii. Fungal culture
iii. Nail biopsy

-AND-

b. History of failure to generic itraconazole (generic Sporanox)

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:

      i. Candidemia
      ii. Patient is non-neutropenic
      iii. History of failure, contraindication, intolerance, or resistance to fluconazole (generic Diflucan)

   -OR-

   c. Both of the following:

      i. One of the following:

         a) *Candida* infection in the abdomen
         b) *Candida* infection in the kidney
         c) *Candida* infection in the bladder wall
         d) *Candida* infection in wounds
         e) Disseminated *Candida* infections in skin
f) Esophageal candidiasis

-AND-

ii. History of failure, contraindication, intolerance, or resistance to fluconazole (generic Diflucan)

-OR-

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

-OR-

e. *Fusarium spp.* infection including *Fusarium solani*

-OR-

e. *Exserohilum* species infection

**Authorization will be issued for 12 months.**

G. **Voriconazole Powder for Oral Suspension**

1. Both of the following:
   a. One of the following diagnoses:
      i. Invasive aspergillosis including *Aspergillus fumigatus*

-OR-

ii. All of the following:
   a) Candidemia
   b) Patient is non-neutropenic
   c) History of failure, contraindication, intolerance, or resistance to fluconazole (generic Diflucan)

-OR-

iii. Both of the following:

   a) 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-

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

-OR-

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

-OR-

v. *Fusarium spp.* infection including *Fusarium solani*

-OR-

vi. *Exserohilum* species infection

-AND-

b. Physician has provided rationale for the patient needing to use voriconazole oral suspension instead of voriconazole tablets.

**Authorization will be issued for 12 months.**

**H. Noxafil Tablets**

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

   a. *Aspergillus*
   b. *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:

   i. Hematopoietic stem cell transplant (HSCT) with graft-versus-host
disease (GVHD)

ii. 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 –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:

   i. Hematopoietic stem cell transplant (HSCT) with graft-versus-host disease (GVHD)
   
   ii. 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.

J. Noxafil Suspension –Oropharyngeal Candidiasis (OPC)

1. Diagnosis of oropharyngeal candidiasis (OPC)

-AND-

2. History of failure, contraindication, or intolerance to one of the following:
a. Fluconazole (generic Diflucan)
b. Itraconazole (generic Sporanox)

**Authorization will be issued for 12 months**

K. Cresemba

1. **One** of the following:
   
a. **Both** of the following:
      
i. Diagnosis of invasive aspergillosis
      
      -AND-

      ii. History of failure, contraindication, or intolerance to voriconazole (generic Vfend)
      
      -OR-

   b. Diagnosis of invasive mucormycosis

   **Authorization will be issued for 3 months.**

L. Tolsura

1. **Both** of the following:

   a. Diagnosis of one of the following fungal infections:
      
i. Blastomycosis
      ii. Histoplasmosis
      iii. Aspergillosis
      
      -AND-

   b. History of failure, contraindication, or intolerance to itraconazole capsules (generic Sporanox)

   **Authorization will be issued for 3 months.**

M. **Infectious Diseases Society of America (IDSA) Recommended Regimens**

1. The requested medication will be approved for uses not outlined above if recognized for treatment of the indication by the Infectious Diseases Society of America (IDSA).
Authorization duration based on provider and IDSA recommended treatment durations, up to 12 months.

3. References:

<table>
<thead>
<tr>
<th>Date</th>
<th>Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>June 2009</td>
<td>Itraconazole:</td>
</tr>
<tr>
<td></td>
<td>Criteria taken from previously approved AmeriChoice policy.</td>
</tr>
<tr>
<td></td>
<td>Added coverage for pulmonary coccidiodomycosis (Valley Fever). Policy reformatted.</td>
</tr>
<tr>
<td>Sept 2010</td>
<td>New Policy - Voriconazole</td>
</tr>
<tr>
<td>Dec 2010</td>
<td>Annual Review - Itraconazole</td>
</tr>
<tr>
<td>June 2011</td>
<td>Annual Review - Voriconazole</td>
</tr>
<tr>
<td>Dec 2011</td>
<td>Annual Review - Itraconazole</td>
</tr>
<tr>
<td></td>
<td>No clinical changes. Updated references.</td>
</tr>
<tr>
<td>June 2012</td>
<td>VORICONAZOLE:</td>
</tr>
<tr>
<td></td>
<td>Expanded diagnoses in section III.A.1, diagnoses that do not require a preferred alternative trial.</td>
</tr>
<tr>
<td></td>
<td>Created new section III.A.3 for separate diagnoses where voriconazole is recommended as second line therapy, only one preferred alternative trial is required</td>
</tr>
<tr>
<td>June 2012</td>
<td>ITRACONAZOLE</td>
</tr>
<tr>
<td></td>
<td>Annual Review. Removed requirement for trial and failure of amphoterecin B for the following diagnoses: aspergillosis, blastomycosis, and empiric therapy of febrile neutropenia.</td>
</tr>
<tr>
<td>March 2013</td>
<td>Itraconazole and Voriconazole criteria combined into a single policy, Azole antifungals. Added criteria for posaconazole, ketoconazole and other non-preferred itraconazole products (pulse pack).</td>
</tr>
<tr>
<td></td>
<td>Thorough update of all criteria.</td>
</tr>
<tr>
<td>June 2015</td>
<td>Removed Sporanox pulse pack from Itraconazole Onychomycosis criteria because Sporanox pulse pack is non-preferred and itraconazole is the preferred drug list option.</td>
</tr>
<tr>
<td></td>
<td>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).</td>
</tr>
</tbody>
</table>
Removed the off-label criteria for febrile neutropenia, histoplasmosis, and aspergillosis for Sporanox oral solution.

Voriconazole tablet section:
- 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

Ketoconazole section removed because prior authorization is not required for this drug

Added new criteria for Noxafil Tablet and Cresemba.

<table>
<thead>
<tr>
<th>Date</th>
<th>Details</th>
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<tbody>
<tr>
<td>October 2016</td>
<td>Annual review, updated policy template</td>
</tr>
<tr>
<td>July 2017</td>
<td>Updated background and references. Minor updates throughout the policy to align with most recent IDSA updates.</td>
</tr>
<tr>
<td>April 2018</td>
<td>Minor updates throughout the policy to align with most recent IDSA updates. Added IDSA off-label uses section.</td>
</tr>
<tr>
<td>April 2019</td>
<td>Annual review, updated background and references.</td>
</tr>
<tr>
<td>June 2019</td>
<td>Added Vfend powder for oral suspension and Tolsura. Updated references.</td>
</tr>
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</table>