UnitedHealthcare Community Plan

Clinical Pharmacy Program Guidelines for Azole Antifungals

Program	Prior Authorization
Medication	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
Markets in Scope	Colorado, California, Hawaii, Maryland, Nevada, New Jersey, New York, New York EPP, Pennsylvania- CHIP, Rhode Island, South Carolina
Issue Date	6/2009
Pharmacy and Therapeutics Approval Date	12/2020
Effective Date	2/2021

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 candidasis
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 disseminated, non-meningeal histoplasmosis in immunocompromised and non-immunocompromised adult patients.

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2. Coverage Criteria:

A. <u>Itraconazole Capsules –Systemic Fungal Infections</u>
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. <u>Itraconazole Capsules –Onychomycosis Fingernails</u>
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

Authorization will be issued for 2 months.

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. <u>Voriconazole Tablets</u>

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. <u>Voriconazole Powder for Oral Suspension</u>

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. <u>Noxafil Tablets</u>

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. Additional Clinical Rules:

- Notwithstanding Coverage Criteria, UnitedHealthcare may approve initial and re-authorization based solely on previous claim/medication history, diagnosis codes (ICD-10) and/or claim logic. Use of automated approval and re-approval processes varies by program and/or therapeutic class.
- Supply limits may be in place.

4. References:

1. Sporanox Capsules[package insert]. Titusville, NJ: Janssen Pharmaceuticals, Inc.;December 2019.
2. Sporanox Oral Solution[package insert]. Titusville, NJ: Janssen Pharmaceuticals, Inc.; September 2020.
3. Vfend[package insert]. New York, NY: Pfizer Inc.; September 2020.
4. Diflucan [package insert]. New York, NY: Roerig Inc.; September 2020.
5. Pappas PG, Kauffman CA, Andes D, , et al. Clinical Practice Guideline for the Management of Candidiasis: 2016 Update by the Infectious Diseases Society of America: Clin Infect Dis.2016; 62 (4):1-50.
6. Patterson TF, Thompson GR, Denning DW, et al. Practice Guidelines for the Diagnosis and Management of Aspergillosis: 2016 Update by the Infectious Diseases Society of America. Clin Infect Dis. 2016;63(4):1-60.
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8. Wheat LJ, Freifeld AG, Kleiman MB, Baddley JW, McKinsey DS, Loyd JE, et al. Clinical practice guidelines for the management of patients with histoplasmosis: 2007 update by the Infectious Diseases Society of America. Clin Infect Dis. 2007;45:807-825.
9. Perfect JR, Dismukes WE, Dromer F et al. Clinical Practice Guidelines for the Management of Cryptococcal Disease: 2010 Update by the Infectious Diseases Society of America. Clin Infect Dis. 2010;50(3): 291-322.
10. Onmel [package insert]. Research Triangle Park, NC: Stiefel Laboratories, Inc.; January 2019.
11. Per Clinical Consultation with an Infectious Disease Specialist. January 24, 2014.
12. Cresemba [package insert]. Northbrook, IL: Astellas Pharma US, Inc.; December 2019.
13. Galgiani JN, Ampel NM, Blair JE, et al; 2016 Infectious Diseases Society of America (IDSA) Clinical Practice Guideline for the Treatment of Coccidioidomycosis, *Clinical*

Infectious Diseases, Volume 63, Issue 6, 15 September 2016, Pages e112–e146, https://doi.org/10.1093/cid/ciw360.
14. Noxafil [package insert]. Whitehouse Station, NJ: Merck & Co. Inc.; September 2020. 15. Tolsura [package insert]. Greenville, NC: Mayne Pharma; July 2020.

Program	Prior Authorization –Azole Antifungals
Change Control	
Date	Change
June 2009	Itraconazole: Criteria taken from previously approved AmeriChoice policy. Added coverage for pulmonary coccidiodomycosis (Valley Fever). Policy 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: • 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.
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.
April 2018	Minor updates throughout the policy to align with most recent IDSA updates. Added IDSA off-label uses section.
April 2019	Annual review, updated background and references.
June 2019	Added Vfend powder for oral suspension and Tolsura. Updated references.
12/2020	Annual review. Added additional clinical rules section, updated references