Clinical Policy Title:	itraconazole
Policy Number:	RxA.284
Drug(s) Applied:	Sporanox®, itraconazole
Original Policy Date:	02/07/2020
Last Review Date:	11/30/2023
Line of Business Policy Applies to:	All lines of business (except Medicare)

Criteria

The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

I. Initial Approval Criteria

A. Onychomycosis (must meet all)**:**

1. Diagnosis of onychomycosis;
2. Request is for Sporanox® or itraconazole capsules;
3. Member meets one of the following (a or b):
   a. For fingernail disease: Trial and failure of a 6-week trial of oral terbinafine at 250 mg/day, unless contraindicated or clinically significant adverse effects are experienced;
   b. For toenail disease: Trial and failure of a 12-week trial of oral terbinafine at 250 mg/day, unless contraindicated or clinically significant adverse effects are experienced;

Approval Duration

All Lines of Business (except Medicare): Fingernail disease: 5 months; toenail disease: 10 months

B. Oropharyngeal Candidiasis (must meet all):

1. Diagnosis of oropharyngeal candidiasis;
2. Request is for Sporanox® or itraconazole oral solution;
3. Trial and failure of 14-days trial at least one of the following oropharyngeal candidiasis therapies unless contraindicated of clinically significant adverse effects are experienced (a or b):
   a. nystatin suspension;
   b. clotrimazole troches/lozenges.
4. Trial and failure of a 14-day trial of fluconazole, unless contraindicated or clinically significant adverse effects are experienced;

Approval Duration

All Lines of Business (except Medicare): 28 days

C. Esophageal Candidiasis (must meet all):

1. Diagnosis of esophageal candidiasis;
2. Request is for Sporanox® or itraconazole oral solution;
3. Trial and failure of a 21-day trial of fluconazole at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;

Approval Duration

All Lines of Business (except Medicare): 56 days

D. Aspergillosis (must meet all):
1. Diagnosis of aspergillosis;
2. Request is for Sporanox® or itraconazole capsules;
3. ;
4. Trial and failure of a 3-month trial of voriconazole at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;

Approval Duration
All Lines of Business (except Medicare): 6 months

E. Blastomycosis or Histoplasmosis (must meet all)**:**
1. Diagnosis of blastomycosis or histoplasmosis;
2. Request is for Sporanox® or itraconazole capsules;
3. Trial and failure of generic itraconazole capsules, unless contraindicated or clinically significant adverse effects are experienced;

Approval Duration
All Lines of Business (except Medicare): Blastomycosis: 6 months; Histoplasmosis: 12 months

F. Febrile neutropenia with other fungal infection (must meet all)**:**
1. Diagnosis of febrile neutropenia with suspected fungal infection;
2. Request is for Sporanox® or itraconazole solution;
3.

Approval Duration
All Lines of Business (except Medicare): 28 days

II. Continued Therapy Approval

A. Onychomycosis (must meet all):
1. Member is currently receiving or has been treated with this medication within the past 90 days, excluding manufacturer samples;
2. Member has not received more than 90 days of treatment;

Approval Duration
All Lines of Business (except Medicare): Fingernail disease: 2 months; toenail disease: 3 months

B. Oropharyngeal/Esophageal Candidiasis (must meet all):
1. Member is currently receiving or has been treated with this medication within the past 90 days, excluding manufacturer samples;

Approval Duration
All Lines of Business (except Medicare): 14 days

C. Blastomycosis, Histoplasmosis, or Aspergillosis (must meet all):
1. Member is currently receiving or has been treated with this medication within the past 90 days, excluding manufacturer samples;

Approval Duration
All Lines of Business (except Medicare): Blastomycosis: 6 months; Histoplasmosis: 42 days; Aspergillosis: 3 months

References

1. Chapman SW, Dismukes WE, Proia LA, et al. Clinical practice guidelines for the management of blastomycosis: 2008

update by the Infectious Diseases Society of America. Clin Infect Dis. 2008;46(12):1801. Available at: https://academic.oup.com/cid/article/46/12/1801/296953. Accessed September 05, 2023.
2. Pappas PG, Kauffman CA, Andes DR et al. Clinical practice guidelines for the management of candidiasis: 2016 update by the Infectious Disease Society of America. Clin Infect Dis. 2016 Feb 15;62(4):e1-50. doi: 10.1093/cid/civ933. Available at: https://pubmed.ncbi.nlm.nih.gov/26679628/. Accessed September 05, 2023.
3. Wheat LJ, Freifeld AG, Kleiman MB, 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(7):807. Available at: https://academic.oup.com/cid/article/45/7/807/541502. Accessed September 05, 2023.
4. 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 Aug 15;63(4):e1-e60. doi: 10.1093/cid/ciw326. Available at: https://pubmed.ncbi.nlm.nih.gov/27365388/. Accessed September 05, 2023.
5. Ameen M, Lear JT, Madan V, Mustapa MFM, Richardson M. British Association of Dermatologists' guidelines for the management of onychomycosis 2014. British Journal of Dermatology. 2014;171(5):937-958. Available at: https://onlinelibrary.wiley.com/doi/10.1111/bjd.13358. Accessed September 05, 2023.
6. Freifeld AG, Bow EJ, Sepkowitz KA et al. Clinical practice guideline for the use of antimicrobial agents in neutropenic patients with cancer: 2010 update by the infectious diseases society of america. Clin Infect Dis. 2011 Feb 15;52(4):e56-93. doi: 10.1093/cid/cir073. Available at: https://pubmed.ncbi.nlm.nih.gov/21258094/. Accessed September 05, 2023.
7. Kaplan JE, Benson C, Holmes KK, et al. Guidelines for prevention and treatment of opportunistic infections in hiv-infected adults and adolescents: recommendations from cdc, the national institutes of health, and the hiv medicine association of the infectious diseases society of america. MMWR Recomm Rep. 2009;58(RR-4):1-207; quiz CE1-4. Available at: https://pubmed.ncbi.nlm.nih.gov/19357635/. Accessed September 05, 2023.
8. What's new in the guidelines | nih. Available at: https://clinicalinfo.hiv.gov/en/guidelines/hiv-clinical-guidelines-pediatric-opportunistic-infections/whats-new-guidelines. Accessed August 29, 2023.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established	01/2020	02/07/2020
Policy was reviewed: 1. Clinical Policy Title was updated. 2. Line of Business Policy Applies to was updated to "All lines of business". 3. Initial and Continued approval duration was updated to include Medicaid, Commercial & HIM approval duration. 4. Continued therapy criteria II.A.1, II.B.1, II.C.1 & II.D.1 was rephrased to "Currently receiving medication that has been authorized by RxAdvance…". 5. Updated Appendix A: added CHF. 6. References were reviewed and updated.	07/22/2020	09/14/2020
Policy was reviewed: 1. Approval durations for HIM were removed. 2. Appendix B (Therapeutic Alternatives): Fixed header verbiage was updated as 'Below are suggested therapeutic alternatives.' Discontinued brands Lamisil®, and Mycelex® were removed. 3. Appendix C: Contraindication(s) was updated.	04/15/2021	06/10/2021

4. Appendix D: General Information was added. 5. References were updated.		
Policy was reviewed: 1. RxA.284, Drug(s) Applied: Updated to remove discontinued drug Onmel; Onmel removed from rest of the policy. 2. Background: Updated to include limitation(s) of use: 3. Tolsura® is not indicated for the treatment of onychomycosis 4. Tolsura® is not interchangeable or substitutable with other itraconazole products 5. Dosing Information, Dosing Regimen, Tolsura®: Updated dosing information from 130 mg orally once daily or Twice daily to 130 mg orally once daily or 260 mg/day Twice daily for indication Aspergillosis. 6. Dosing Information, Indication: Updated to include new indication in life-threatening situations. 7. Dosing Information, Dosing Regimen, Tolsura: Updated to include dosing information for indication In life-threatening situations. 8. Dosing Information, Maximum Dose, Tolsura: Updated to include maximum dosing information for indication In life-threatening situations. 9. Initial Approval Criteria, 1.B.3: Updated trial and failure criteria from Failure of a 14-day trial of nystatin suspension or clotrimazole troches/lozenges, unless contraindicated or clinically significant adverse effects are experienced to Failure of 14-days trial at least one of the following oropharyngeal Candidiasis therapies unless contraindicated of clinically significant adverse effects are experienced (a or b): a. nystatin suspension b. clotrimazole troches/lozenges 10. Initial Approval Critiera, I.F: Updated to remove Tolsura. 11. Continued Therapy Approval Criteria II.A.1, II.B.1, II.C.1 & II.D .1 were rephrased to "Member is currently receiving medication that has been authorized by RxAdvance...". 12. Continued Approval Criteria, II.D: Updated to remove Tolsura. 13. Statement about drug listing format in Appendix B is rephrased to "Therapeutic alternatives are	01/10/2022	04/18/2022

listed as generic (Brand name®) when the drug is available by both generic and brand; Brand name® when the drug is available by brand only and generic name when the drug is available by generic only" 14. Disclaimer about contraindications "Contraindications listed reflect statements made in the manufacturer's package insert..." was added to Appendix C. 15. References were reviewed and updated.		
Policy was reviewed: 1. Dosage Forms: Updated dosage form from Itraconazole (Sporanox®): Capsules 100 mg, Oral solution 10 mg/ml to Itraconazole (Sporanox®): Capsules 100 mg, Oral solution 10 mg/ml (150 ml). 2. Initial Approval Criteria I.E.3: Updated from for Tolsura® requests, failure of generic itraconazole capsules unless contraindicated or clinically significant adverse effects are experienced (e.g., contraindications to the excipients) to Trial and failure of generic itraconazole capsules, unless contraindicated or clinically significant adverse effects are experienced. 3. Appendix A: Updated to remove abbreviations FDA: Food and Drug Administration 4. Appendix B, Maximum Dose, voriconazole (Vfend®): Updated maximum dose information from Weight ≥ 40 kg: 800 mg per day, Weight < 40 kg: 400 mg per day to Weight ≥ 40 kg: 600 mg per day Weight < 40 kg: 300 mg per day for indication aspergillosis. 5. Appendix C, Contraindications: Updated to include new contraindication Coadministration with venetoclax is contraindicated in patients with chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL) during the dose initiation and ramp-up phase of venetoclax. 6. Appendix C, Contraindications: Updated to remove contraindication Onmel™: levacetylmethadol (levomethadyl) 7. References were reviewed and updated.	01/04/2023	04/13/2023
Policy was reviewed: 1. Updated Lines of Business Policy Applies to All lines of business (except Medicare). 2. Dosage form updated. 3. Statement about provider sample was updated.	09/05/2023	10/19/2023

4. Initial Approval Criteria I.F: Updated to remove prior off-label indication (Hematologic Malignancy). 5. Continued Therapy Approval Criteria, II.A.1, II.B.1, II.C.1: updated to "Member is currently receiving…" 6. Initial Approval duration and Continued Therapy Approval, I.A, II.A: Initial Approval duration and Continued Therapy Approval duration was updated to All Lines of Business (except Medicare): Fingernail disease: 2 months; toenail disease: 3 months. 7. Initial Approval duration, I.B, I.C: Initial Approval duration was updated to All Lines of Business (except Medicare): 28 days. 8. Initial Approval duration, I.D: Initial Approval duration was updated to All Lines of Business (except Medicare): 3 months. 9. Initial Approval duration, I.E: Initial Approval duration was updated to All Lines of Business (except Medicare): Blastomycosis: 6 months; Histoplasmosis: 42 days. 10. Continued Therapy Approval, II.B: Continued Therapy Approval duration was updated to All Lines of Business (except Medicare):14 days. 11. Continued Therapy Approval, II.C: Continued Therapy Approval duration was updated to All Lines of Business (except Medicare): Blastomycosis: 6 months; Histoplasmosis: 42 days; Aspergillosis: 3 months. 12. Continued Approval Criteria, I.D: Updated to remove prior off-label indication (Hematologic Malignancy). 13. Appendix A: Updated to add abbreviations CLL, SLL. 14. Appendix B: Therapeutic alternatives was removed. 15. Appendix C: Contraindications/Boxed Warnings was removed. 16. Renamed Appendix D as Appendix B: General information. 17. References were reviewed and updated.		