Clinical Policy: Itraconazole (Sporanox, Tolsura)

Reference Number: NH.PMN.124
Effective Date: 06.24
Last Review Date: 06.24
Line of Business: Medicaid

Revision Log

See Important Reminder **at the end of this policy for important regulatory and legal information.**

Description

Itraconazole (Sporanox®, Tolsura®) is an azole antifungal agent.

FDA Approved Indication(s)

Sporanox and Tolsura capsules are indicated in:

- Immunocompromised and non-immunocompromised patients for the treatment of:
  - Blastomycosis, pulmonary and extrapulmonary
  - Histoplasmosis, including chronic cavitary pulmonary disease and disseminated, nonmeningeal histoplasmosis
  - Aspergillosis, pulmonary and extrapulmonary, in patients who are intolerant of or who are refractory to amphotericin B therapy

Sporanox capsules are additionally indicated in:

- Non-immunocompromised patients for the treatment of:
  - Onychomycosis of the toenail, with or without fingernail involvement, due to dermatophytes (tinea unguium)
  - Onychomycosis of the fingernail due to dermatophytes (tinea unguium)

Sporanox oral solution is indicated for the treatment of oropharyngeal and esophageal candidiasis.

Limitation(s) of use: Tolsura is not indicated for the treatment of onychomycosis. Tolsura is not interchangeable or substitutable with other itraconazole products.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Sporanox and Tolsura are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

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

1. Diagnosis of onychomycosis;
2. Trial and failure of two (2) preferred products unless clinically significant adverse effects or contraindications exist;
3. Dose does not exceed 400 mg (4 capsules) per day.

Approval duration: Fingernail disease: 2 months; toenail disease: 3 months

B. Oropharyngeal Candidiasis (must meet all)**:**
1. Diagnosis of oropharyngeal candidiasis;
2. Trial and failure of two (2) preferred products unless clinically significant adverse effects or contraindications exist;
3. Failure of a 7-day trial of nystatin suspension or clotrimazole troches/lozenges, unless clinically significant adverse effects are experienced or both are contraindicated;
4. Dose does not exceed 200 mg (20 mL) per day.

Approval duration: 4 weeks

C. Esophageal Candidiasis (must meet all)**:**
1. Diagnosis of esophageal candidiasis;
2. Trial and failure of two (2) preferred products unless clinically significant adverse effects or contraindications exist;
3. Dose does not exceed 200 mg (20 mL) per day.

Approval duration: 4 weeks

D. Aspergillosis (must meet all)**:**
1. Diagnosis of aspergillosis;
2. Trial and failure of two (2) preferred products unless clinically significant adverse effects or contraindications exist;
3. Dose does not exceed one of the following (a or b):
   a. Itraconazole or Sporanox capsules: 400 mg (4 capsules) per day;
   b. Tolsura capsules: 260 mg (4 capsules) per day.

Approval duration: 3 months

E. Blastomycosis or Histoplasmosis (must meet all)**:**
1. Diagnosis of blastomycosis or histoplasmosis;
2. Trial and failure of two (2) preferred products unless clinically significant adverse effects or contraindications exist;
3. Dose does not exceed one of the following (a or b):
   a. Itraconazole or Sporanox capsules: 400 mg (4 capsules) per day;
   b. Tolsura capsules: 260 mg (4 capsules) per day.

Approval duration: Blastomycosis: 6 months; Histoplasmosis: 6 weeks

F. Hematologic Malignancy (off-label) (must meet all)**:**
1. Diagnosis of hematologic malignancy;
2. Trial and failure of two (2) preferred products unless clinically significant adverse effects or contraindications exist;
3. Member meets one of the following (a or b):
   a. Request is for prophylaxis of aspergillosis;
   b. Request is for prophylaxis of candidiasis;
4. Dose does not exceed one of the following (a, b, or c):
   a. Itraconazole or Sporanox capsules: 400 mg (4 capsules) per day;
   b. Itraconazole or Sporanox oral solution: 200 mg (20 mL) per day;

c. Tolsura capsules: 260 mg (4 capsules) per day.

Approval duration: 3 months

G. Coccidioidomycosis (off-label) (must meet all)**:**

1. Diagnosis of coccidioidomycosis infection, and member is infected with one of the following (a, b, or c):
   a. HIV-1, and member has peripheral blood CD4 < 250 cells/mm^3;
   b. Focal pulmonary disease;
   c. Disseminated extrathoracic nonmeningeal or meningeal coccidioidomycosis;
2. Trial and failure of two (2) preferred products unless clinically significant adverse effects or contraindications exist;
3. Prescribed by or in consultation with an infectious disease specialist, pulmonologist, or HIV specialist;
4. Dose does not exceed one of the following (a, b, or c):
   a. For disseminated extrathoracic nonmeningeal or meningeal coccidioidomycosis (i or ii):
      i. Capsules: 600 mg (6 capsules) per day;
      ii. Oral solution: 600 mg (60 mL) per day;
   b. For coccidioidomycosis with HIV-1 co-infection (i or ii):
      i. Capsules: 600 mg (6 capsules) per day for the first three days, then 400 mg (4 capsules) per day thereafter;
      ii. Oral solution: 600 mg (60 mL) per day for the first three days, then 400 mg (40 mL) per day thereafter;
   c. For all other coccidioidomycosis infections (i or ii):
      i. Capsules: 400 mg (4 capsules) per day;
      ii. Oral solution: 400 mg (40 mL) per day.

Approval duration: 6 months

H. Sporotrichosis (off-label) (must meet all)**:**

1. Diagnosis of sporotrichosis infection, and member is infected with one of the following (a or b):
   a. Lymphocutaneous, cutaneous, non-severe pulmonary or osteoarticular sporotrichosis;
   b. Severe pulmonary, meningeal, or disseminated systemic sporotrichosis;
2. Prescribed by or in consultation with an infectious disease specialist or pulmonologist;
3. Trial and failure of two (2) preferred products unless clinically significant adverse effects or contraindications exist;
4. For severe pulmonary, meningeal, or disseminated systemic sporotrichosis: Previous use of amphotericin B, unless contraindicated or clinically significant adverse effects are experienced;
5. Dose does not exceed one of the following (a or b):
   a. Capsules: 400 mg (4 capsules) per day;
   b. Oral solution: 400 mg (40 mL) per day.

Approval duration: 12 months

I. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the PDL, the no coverage criteria policy: CP.PMN.255; or
   b. For drugs NOT on the PDL, the non-formulary policy: CP.PMN.16; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy: CP.PMN.53.

II. Continued Therapy

A. Onychomycosis (must meet all)**:**
1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
2. Member is responding positively to therapy;
3. Member has not received more than 90 days of treatment;
4. If request is for a dose increase, new dose does not exceed 400 mg (4 capsules) per day.

Approval duration: Fingernail disease: up to 2 months total; toenail disease: up to 3 months total

B. Oropharyngeal/Esophageal Candidiasis (must meet all)**:**
1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed 200 mg (20 mL) per day.

Approval duration: 2 weeks

C. Blastomycosis, Histoplasmosis, or Aspergillosis (must meet all)**:**
1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed one of the following (a or b):

a. Itraconazole or Sporanox capsules: 400 mg (4 capsules) per day;
b. Tolsura capsules: 260 mg (4 capsules) per day.

Approval duration: Blastomycosis: 6 months; Histoplasmosis: 6 weeks; Aspergillosis: 3 months

D. Hematologic Malignancy (off-label) (must meet all)**:**
1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed one of the following (a, b, or c):
   a. Itraconazole or Sporanox capsules: 400 mg (4 capsules) per day;
   b. Itraconazole or Sporanox oral solution: 200 mg (20 mL) per day;
   c. Tolsura capsules: 260 mg (4 capsules) per day.

Approval duration: 6 months

E. Coccidioidomycosis (off-label) (must meet all)**:**
1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
2. If HIV-1 positive, member has peripheral blood CD4 < 250 cells/mm^3;
3. If request is for a dose increase, new dose does not exceed one of the following (a or b):
   a. For disseminated extrathoracic nonmeningeal or meningeal coccidioidomycosis (i or ii):
      i. Capsules: 600 mg (6 capsules) per day;
      ii. Oral solution: 600 mg (60 mL) per day;
   b. For all other coccidioidomycosis infections (i or ii):
      i. Capsules: 400 mg (4 capsules) per day;
      ii. Oral solution: 400 mg (40 mL) per day.

Approval duration: 12 months

F. Sporotrichosis (off-label) (must meet all)**:**
1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*

2. If request is for a dose increase, new dose does not exceed one of the following (a or b):
   a. Capsules: 400 mg (4 capsules) per day;
   b. Oral solution: 400 mg (40 mL) per day.

Approval duration: 12 months

G. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the PDL, the no coverage criteria policy: CP.PMN.255; or
   b. For drugs NOT on the PDL, the non-formulary policy: CP.PMN.16; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy: CP.PMN.53.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.PMN.53 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
CHF: congestive heart failure
FDA: Food and Drug Administration

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
terbinafine (Lamisil®)	250 mg PO QD	500 mg per day
nystatin suspension	400,000 to 600,000 units (4 to 6 mL) per dose swished in the mouth QID	2.4 million units per day
clotrimazole troches/ lozenges (Mycelex®)	10 mg troche PO 5 times daily for 14 days	Varies
fluconazole (Diflucan®)	400 mg PO per day	800 mg per day
voriconazole (Vfend®)	Weight ≥ 40 kg: 200 mg PO every 12 hours Weight < 40 kg: 100 mg PO every 12 hours	Weight ≥ 40 kg: 800 mg per day Weight < 40 kg: 400 mg per day
amphotericin B	Adults: 0.7 to 1 mg/kg/dose IV every 24 hours until favorable response. Continue step-down therapy with	1 – 1.5 mg/kg/day IV

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	itraconazole to complete a total of at least 12 months of therapy	

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s):
  - Itraconazole should not be administered for the treatment of onychomycosis in patients with evidence of ventricular dysfunction such as congestive heart failure (CHF) or a history of CHF.
  - Concomitant coadministration of itraconazole with the following drugs: methadone, dofetilide, quinidine, ergot alkaloids (such as dihydroergotamine, ergometrine (ergonovine), ergotamine, methylergometrine (methylergonovine)), felodipine, pimozide, oral midazolam, triazolam, nisoldipine, cisapride, lovastatin, simvastatin.
  - Additional product-specific drug-drug interactions include:
    - Sporanox (capsules and oral solution), Tolsura: disopyramide, dronedarone, irinotecan, lurasidone, ivabradine, ranolazine, eplerenone, ticagrelor and, in subjects with varying degrees of renal or hepatic impairment, colchicine, fesoterodine, and solifenacin.
    - Sporanox capsules: telithromycin
    - Sporanox oral solution, Tolsura: isavuconazole, naloxegol, lomitapide, avanafil
  - Treatment of onychomycosis in women who are pregnant or contemplating pregnancy
  - Hypersensitivity and anaphylaxis to itraconazole
- Boxed warning(s):
  - CHF or history of CHF (see contraindications)
  - Drug-drug interactions (see contraindications)

V. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
Itraconazole (Sporanox) capsule	Blastomycosis	200 mg PO QD	400 mg/day
	Histoplasmosis	200 mg PO QD	400 mg/day
	Aspergillosis	200 to 400 mg PO QD	400 mg/day
	Onychomycosis	200 mg PO QD for 12 weeks (toenails with or without fingernail involvement) 200 mg PO BID for 1 week, followed by no drug for 3 weeks, then another week of 200 mg PO BID or 200 mg PO QD for 6 weeks (fingernails only)	400 mg/day

Drug Name	Indication	Dosing Regimen	Maximum Dose
	Coccidioidomycosis	200 mg PO BID or 200 mg BID-TID for nonmeningeal or meningeal coccidioidomycosis In patients co-infected with HIV: Adults: 200 mg PO TID for the first 3 days, then 200 mg PO BID Pediatrics: 5-10 mg/kg PO BID for the first 3 days, then 2-5 mg/kg PO BID	600 mg/day
	Lymphocutaneous or cutaneous sporotrichosis	200 mg PO QD for 3-6 months. If no response then increase to 200 mg PO BID.	400 mg/day
	Osteoarticular, pulmonary, meningeal, or disseminated systemic sporotrichosis	200 mg PO BID for at least 12 months	400 mg/day
	In life-threatening situations	Loading dose of 200 mg PO TID given for the first 3 days of treatment	600 mg/day
Itraconazole (Sporanox) oral solution	Oropharyngeal candidiasis	200 mg (20 mL) PO daily for 1 to 2 weeks; swish in the mouth (10 mL at a time) for several seconds and swallow	200 mg (20 mL)/day
	Coccidioidomycosis	200 mg (20 mL) PO BID or 200 mg (20 mL) BID-TID for nonmeningeal or meningeal coccidioidomycosis In patients co-infected with HIV: Adults: 200 mg PO TID for the first 3 days, then 200 mg PO BID Pediatrics: 5-10 mg/kg PO BID for the first 3 days, then 2-5 mg/kg PO BID	600 mg (60 mL)/day
	Lymphocutaneous or cutaneous sporotrichosis	200 mg (20 mL) PO QD for 3-6 months. If no response then increase to 200 mg PO BID.	400 mg (40 mL)/day
	Osteoarticular, pulmonary, meningeal, or disseminated systemic sporotrichosis	200 mg (20 mL) PO BID for at least 12 months	400 mg (40 mL)/day

Drug Name	Indication	Dosing Regimen	Maximum Dose
	Esophageal candidiasis	100 mg (10 mL) PO daily for a minimum treatment of three weeks	200 mg (20 mL)/day
Itraconazole (Tolsura)	Blastomycosis, histoplasmosis	130 mg PO QD. Increase dose if no obvious improvement or evidence of progressive fungal disease in 65 mg increments. Doses above 130 mg/day should be given in divided doses.	260 mg/day
	Aspergillosis	130 mg PO QD or BID	260 mg/day

VI. Product Availability

Drug Name	Availability
Itraconazole (Sporanox)	Capsule: 100 mg Oral solution: 10 mg/mL
Itraconazole (Tolsura)	Capsule: 65 mg

VII. References

1. Sporanox Oral Solution Prescribing Information. Titusville, NJ: Janssen Pharmaceuticals, Inc.; December 2022. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/020657s037lbl.pdf. Accessed January 31, 2023.
2. Sporanox Capsules Prescribing Information. Titusville, NJ: Janssen Pharmaceuticals, Inc., December 2022. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/020083s063lbl.pdf. Accessed January 31, 2023.
3. Tolsura Prescribing Information. Greenville, NC: Mayne Pharma. April 2022. Available at: www.tolsura.com. Accessed January 31, 2023.
4. Clinical Pharmacology [database online]. Elsevier, Inc.; 2023. Available at: https://www.clinicalkey.com/pharmacology/.
5. 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.
6. 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.
7. 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.
8. 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.
9. Ameen M, Lear JT, Madan V, et al. British Association of Dermatologists' guidelines for the management of onychomycosis 2014. Br J Dermatology. 2014;171:937-58.

10. 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.
11. Panel on Opportunistic Infections in HIV-Infected Adults and Adolescents. Guidelines for the prevention and treatment of opportunistic infections in adults and adolescents with HIV: recommendations from the Centers for Disease Control and Prevention, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. Available at: https://clinicalinfo.hiv.gov/en/guidelines/adult-and-adolescent-opportunistic-infection/whats-new-guidelines. Updated January 18, 2023. Accessed January 31, 2023.
12. Panel on Opportunistic Infections in HIV-Exposed and HIV-Infected Children. Guidelines for the prevention and treatment of opportunistic infections in children with and exposed to HIV. Department of Health and Human Services. Available at: https://clinicalinfo.hiv.gov/en/guidelines/pediatric-opportunistic-infection/whats-new. Updated September 2, 2022. Accessed January 31, 2023.
13. Kauffman C, Bustamante B, Chapman S, et al. Clinical practice guidelines for the management of sporotrichosis: 2007 update by the Infectious Diseases Society of America. 2007; 45:1255-65.
14. Fungal diseases: Sporotrichosis. Centers for Disease Control and Prevention. Available at: https://www.cdc.gov/fungal/diseases/sporotrichosis/index.html. Last updated: February 9, 2022. Accessed January 31, 2023.
15. 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. 2016; 63(6): e112–e146.
16. Taplitz RA, Kennedy EB, Bow EJ, et al. Antimicrobial prophylaxis for adult patients with cancer-related immunosuppression: ASCO and IDSA clinical practice guideline update. J Clin Oncol. 2018; 36(30): 3043-3054.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	06.24	06.24

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.