Clinical Policy: Nifurtimox (Lampit)

Reference Number: CP.PMN.256
Effective Date: 12.01.20
Last Review Date: 11.22
Line of Business: Commercial, HIM, Medicaid

Revision Log

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

Description

Nifurtimox (Lampit®) is a nitrofuran antiprotozoal.

FDA Approved Indication(s)

Lampit indicated in pediatric patients (birth to less than 18 years of age and weighing at least 2.5 kg) for the treatment of Chagas disease (American trypanosomiasis), caused by *Trypanosoma cruzi (T. cruzi)*.

This indication is approved under accelerated approval based on the number of treated patients who became immunoglobulin G (IgG) antibody negative or who showed an at least 20% decrease in optical density on two different IgG antibody tests against antigens of *T. cruzi*. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

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 Lampit is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Chagas Disease (must meet all)**:**

1. Diagnosis of Chagas disease confirmed by one of the following (a, b, or c) (*see Appendix D*):
   a. Detection of circulating *T. cruzi* trypomastigotes on microscopy;
   b. Detection of *T. cruzi* DNA by polymerase chain reaction assay;
   c. Two positive diagnostic serologic tests showing IgG antibodies to *T. cruzi* and meeting both of the following (i and ii):
      i. The two tests use different techniques (e.g., enzyme-linked immunosorbent assay [ELISA], immunofluorescent antibody test [IFA]);
      ii. The two tests use different antigens (e.g., whole-parasite lysate, recombinant antigens);
2. Prescribed by or in consultation with an infectious disease specialist;
3. Member has not yet received 60 days of Lampit therapy for the current infection;
4. Dose (weight-based) does not exceed 300 mg per day (*see Appendix D for off-label dosing requests*).

Approval duration: 60 days total

B. 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 formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; 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 for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Chagas Disease (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 has not yet received 60 days of Lampit therapy for the current infection;
3. If request is for a dose increase, new dose (weight-based) does not exceed 300 mg per day (*see Appendix D for off-label dosing requests*).

Approval duration: 60 days total

B. 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 formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; 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 for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

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.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid, or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

CDC: Centers for Disease Control and Prevention
FDA: Food and Drug Administration
IgG: immunoglobulin G
T cruzi: Trypanosoma cruzi
WHO: World Health Organization

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s):
  - Known hypersensitivity to nifurtimox or to any of the excipients in Lampit
  - Alcohol consumption during treatment
- Boxed warning(s): none reported

Appendix D: General Information

- Diagnostic tests:
  - Laboratories offering testing for Chagas disease include ARUP Laboratories, Mayo Clinic Laboratories, and Quest Diagnostics. IgG serology is performed in the majority of cases. After obtaining initial serologic IgG test results, providers should consult their state health department and the CDC for guidance on serologic confirmation. If two results are discordant, a third assay may be needed. Donor screening tests and Immunoglobulin M (IgM) serology tests are not considered diagnostic tests.
- Off-label dosing requests for Chagas disease:
  - Dosing for populations outside FDA-approved age ranges or for longer than 60 days may be appropriate and should be reviewed on a case-by-case basis. See CDC consultation resources below for questions.
- State reporting requirements:
  - According to the CDC (https://www.cdc.gov/mmwr/volumes/67/wr/mm6726a2.htm), in 2017 Chagas disease was reportable in six states: Arizona, Arkansas, Louisiana, Mississippi, Tennessee, and Texas.
- Consultation resources:
  - Centers for Disease Control and Prevention (CDC)

- Parasitic Diseases: https://www.cdc.gov/parasites/chagas/ - 404-718-4745, chagas@cdc.gov
  - CDC recommended guidance document: Bern C, Montgomery SP, Herwaldt BL, et al. Evaluation and treatment of Chagas disease in the United States: a systematic review. JAMA 2007; 298:2171.
- CDC Drug Service: 404-639-3670
- CDC Emergency Operations Center: 770-488-7100

- World Health Organization (WHO)
  - Outside the US: www.who.int/chagas/home_treatment/en/
- American Society of Tropical Medicine and Hygiene
  - Directory of consultants: http://www.astmh.org/education-resources/clinical-consultants-directory

V. Dosage and Administration

Indication	Dosing Regimen					Maximum Dose
Chagas disease	Body Weight Range (kg)	Dose (mg)	Tablet # -- 30 mg	Tablet # -- 120 mg	Duration / Frequency	300 mg/day
	2.5 to 4.5 kg	15 mg	½ T	—	PO TID for 60 days	
	4.6 to < 9 kg	30 mg	1 T	—		
	9 to < 13 kg	45 mg	1 ½ T	—		
	13 to < 18 kg	60 mg	2 T	½ T		
	18 to < 22 kg	75 mg	2 ½ T	—		
	22 to < 27 kg	90 mg	3 T	—		
	27 to < 35 kg	120 mg	4 T	1 T		
	35 to < 41 kg	180 mg	—	1 ½ T		
	41 to < 51 kg	120 mg	—	1 T		
	51 to < 71 kg	180 mg	—	1 ½ T		
	71 to < 91 kg	240 mg	—	2 T		
	≥ 91 kg	300 mg	—	2 ½ T		

VI. Product Availability

Tablets: 30 mg, 120 mg

VII. References

1. Lampit Prescribing Information. Whippany, NJ: Bayer HealthCare Pharmaceuticals, Inc.; January 2022. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/213464s001lbl.pdf. Accessed August 21, 2020.

Pivotal Trial

2. Prospective Study of a Pediatric Nifurtimox Formulation for Chagas' Disease (CHICO) - NCT02625974. Available at: https://clinicaltrials.gov/ct2/show/NCT02625974?term=nifurtimox&draw=3&rank=2. Accessed August 21, 2020

Centers for Disease Control (CDC)
3. American Trypanosomiasis. DPDx - Laboratory identification of parasitic diseases of public health concern. Centers for Disease Control and Prevention. Available at: https://www.cdc.gov/dpdx/trypanosomiasisamerican/index.html. Last updated July 16 2021. Accessed June 17, 2022.
4. Formulary (nifurtimox): Infectious Diseases Laboratory. Centers for Disease Control and Prevention. Available at: https://www.cdc.gov/laboratory/drugservice/formulary.html#tnifurtimox. Last updated May 18, 2018. Accessed August 27, 2020.

Compendia, Guidelines, Review Articles
5. Nifurtimox Drug Monograph. Clinical Pharmacology [database online]. Elsevier.; 2022. Available at: www.clinicalkey.com/pharmacology . Accessed June 17, 2022.
6. Bern C, Messenger LA, Whitman JD, Maguire JH. Chagas Disease in the United States: a Public Health Approach. American Society for Microbiology. Clinical Microbiology Reviews. January 2020; 33(1): 1-42.
7. Guidelines for the diagnosis and treatment of Chagas disease. Joint publication of Pan-American Health Organization (PAHO) and World Health Organization (WHO), 2019, Washington D.C. Available at: https://iris.paho.org/bitstream/handle/10665.2/49653/9789275120439_eng.pdf. Accessed August 28, 2020.
8. Chagas Cardiomyopathy: An Update of Current Clinical Knowledge and Management: A Scientific Statement From the American Heart Association. Circulation. Volume 138, Issue 12, 18 September 2018; Pages e169-e209. https://doi.org/10.1161/CIR.0000000000000599.
9. Crespillo-Andujar C, Chamorro-Tojeiro S, Norman F, et al. Toxicity of nifurtimox as second-line treatment after benznidazole intolerance in patients with chronic Chagas disease: when available options fail. Clinical Microbiology and Infection 24 (2018) 1344.e1e1344.e4. https://doi.org/10.1016/j.cmi.2018.06.006
10. Perez-Molina JA, Molina I. Chagas disease: Seminar. Lancet. June 30, 2017. http://dx.doi.org/10.1016/S0140-6736(17)31612-4.
11. Bern C. Chagas disease. N Engl J Med 2015; 373: 456-66. DOI: 10.1056/NEJMra1410150.
12. Perez-Molina JA, Sojo-Dorado J, Norman F, et al. Nifurtimox therapy for Chagas disease does not cause hypersensitivity reactions in patients with such previous adverse reactions during benznidazole treatment. Acta Tropica 127 (2013) 101–104.
13. Bern C, Montgomery SP, Herwaldt BL, et al. Evaluation and treatment of Chagas disease in the United States: A systematic review. JAMA 2007; 298:2171.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	09.01.20	11.20
4Q 2021 annual review: no significant changes; updated reference for HIM off-label use to HIM.PA.154 (replaces HIM.PHAR.21); references reviewed and updated.	08.11.21	11.21
4Q 2022 annual review: no significant changes; references reviewed and updated. Template changes applied to other diagnoses/indications and continued therapy section.	06.17.22	11.22

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.