Clinical Policy: Nifurtimox (Lampit)

Reference Number: ERX.SPA.413
Effective Date: 12.01.20
Last Review Date: 11.21
Line of Business: Commercial, 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.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ 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

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

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

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
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. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 60 days (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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 policy – ERX.PA.01 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 tablet	—	PO TID for 60 days	
	4.6 to < 9 kg	30 mg	1 tablet	—		
	9 to < 13 kg	45 mg	1 ½ tablet	—		
	13 to < 18 kg	60 mg	2 tablet	½ tablet		
	18 to < 22 kg	75 mg	2 ½ tablet	—		
	22 to < 27 kg	90 mg	3 tablet	—		
	27 to < 35 kg	120 mg	4 tablet	1 tablet		
	35 to < 41 kg	180 mg	—	1 ½ tablet		
	41 to < 51 kg	120 mg	—	1 tablet		
	51 to < 71 kg	180 mg	—	1 ½ tablet		
	71 to < 91 kg	240 mg	—	2 tablet		
	≥ 91 kg	300 mg	—	2 ½ tablet		

VI. Product Availability

Tablets: 30 mg, 120 mg

VII. References

1. Lampit Prescribing Information. Whippany, NJ: Bayer HealthCare Pharmaceuticals, Inc.; October 2020. Available at https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/213464s001lbl.pdf. Accessed August 11, 2021.

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 April 30, 2019. Accessed August 27, 2020.
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]. Tampa, FL: Gold Standard, Inc.; 2020. Available at: http://www.clinicalpharmacology-ip.com/. Accessed August 21, 2020.

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; references reviewed and updated.	08.11.21	11.21

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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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.