RXADVANCE
2 Park Central Drive
Southborough, MA 01772

NEW DRUG APPROVAL

Brand Name	Lampit®
Generic Name	nifurtimox
Drug Manufacturer	Bayer Healthcare Pharmaceuticals Inc.

New Drug Approval

FDA Approval Date: August 6, 2020
Review Designation: Priority Orphan
Type of Review: Type 1 - New Molecular Entity
Dispensing Restrictions: None

Place in Therapy

DISEASE DESCRIPTION & EPIDEMIOLOGY

Chagas disease (CD) is caused by Trypanosoma cruzi, a protozoan parasite that can cause acute myopericarditis as well as chronic fibrosing myocarditis. CD is the most common cause of non-ischemic cardiomyopathy in Latin America.

About 6 million to 7 million people worldwide, mostly in Latin America, are estimated to be infected with Trypanosoma cruzi, the parasite that causes Chagas disease. Chagas disease was once entirely confined to continental rural areas of the Region of the Americas – principally Latin America (not in the Caribbean islands). Mainly because of the increased population mobility in the last decades, most infected people live in urban settings (urbanization) and the disease has been increasingly detected in the United States of America, Canada, and many European and some African, Eastern Mediterranean, and Western Pacific countries.

Efficacy

The safety and efficacy of Lampit® for the treatment of Chagas disease in pediatric patients birth to <18 years of age and weighing at least 2.5 kg were demonstrated in one prospective, randomized, double-blind trial conducted in Argentina, Bolivia, and Colombia (Trial 1, NCT02625974). Pediatric patients (n=330) with serologic evidence of T. cruzi infection and without Chagas disease-related cardiac or gastrointestinal symptoms were randomly assigned in a 2:1 fashion to a 60 day (n=219) or a 30-day (n=111) nifurtimox treatment regimen. Patients were followed up for one year. Lampit® was administered three times a day with food using the following body weight-based dosing regimens: pediatric patients weighing 40 kg received a total daily dose of 8 10 mg/kg. Chagas disease diagnosis was confirmed by direct observation of T. cruzi by concentration test in patients < 8 months of age at randomization and by demonstrating positive results for both the lysate enzyme-linked immunosorbent assay (ELISA) and the recombinant ELISA in patients ≥8 months to <18 years of age at randomization.

Serological response to treatment was defined as ≥20% decrease in optical density measured by lysate and recombinant ELISA in subjects >8 months to < 18 years or seroconversion to negative (defined as negative immunoglobulin G concentration in all patients) at 1-year post-treatment follow-up.

The results for both the lysate ELISA and the recombinant ELISA showed superiority in favor of the nifurtimox 60-day arm compared to the nifurtimox 30-day arm (not an approved dosing regimen).

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Safety

ADVERSE EVENTS

The most frequently reported adverse reactions (≥5%) are vomiting, abdominal pain, headache, decreased appetite, nausea, pyrexia, and rash.

WARNINGS & PRECAUTIONS

- Potential for Genotoxicity and Carcinogenicity.
- Embryo-Fetal Toxicity: May cause fetal harm. Pregnancy testing is recommended for females of reproductive potential. Advise females of reproductive potential of the potential risk to a fetus and to use effective contraception. Advise males to use condoms with female partners of reproductive potential.
- Worsening Neurological and Psychiatric Conditions: Patients with a history of brain injury, seizures, psychiatric disease, serious behavioral alterations may experience worsening of their conditions when receiving Lampit®. Administer Lampit® under close medical supervision in these patients or if neurological disturbances or psychiatric drug reactions occur.
- Hypersensitivity: Hypersensitivity reactions including hypotension, angioedema, dyspnea, pruritus, rash, or other severe skin reactions have been reported with the use of nifurtimox, discontinuation of treatment is recommended.
- Decreased Appetite and Weight Loss: Check body weight every 14 days as dosage may need to be adjusted.
- Porphyria: Treatment with nitrofuran derivatives, such as Lampit®, may precipitate acute attacks of porphyria. Administer Lampit® under close medical supervision in patients with porphyria.

CONTRAINDICATIONS

- Known hypersensitivity to nifurtimox or to any of the excipients in Lampit®.
- Alcohol consumption during treatment.

Clinical Pharmacology

MECHANISMS OF ACTION

Nifurtimox is an antiprotozoal drug. The mechanism of action of nifurtimox is not fully understood. Studies suggest that nifurtimox is metabolized/activated, by Type I (oxygen insensitive) and Type II (oxygen sensitive) nitoreductases (NTR) leading to production of toxic intermediate metabolites and/or reactive oxygen species that induce DNA damage and cell death of both intracellular and extracellular forms of T. cruzi.

Dose & Administration

ADULTS

N/A

PEDIATRICS

Dosage of Lampit® in Pediatric Patients (birth to less than 18 years of age) is as follows:

Body Weight Group: Total Daily Dose of nifurtimox (mg/kg)
40 kg or greater: 8 to 10 mg/kg
Less than 40 kg: 10 to 20 mg/kg

Lampit® tablets must be taken with food three times daily for 60 days. Obtain a pregnancy test in females of reproductive potential prior to initiating treatment.

GERIATRICS

N/A

RENAL IMPAIRMENT

The effect of renal impairment on the pharmacokinetics of nifurtimox is unknown. Published literature suggests that blood concentrations of nifurtimox were increased in patients with End Stage Renal Disease (ESRD) requiring hemodialysis. Administer Lampit® under close medical supervision.

HEPATIC IMPAIRMENT

The effect of hepatic impairment on the pharmacokinetics of nifurtimox is unknown. Administer Lampit® under close medical supervision.

Product Availability

DOSAGE FORM(S) & STRENGTH(S)

Tablets: 30 mg, 120 mg (functionally scored)