PDL DRUG REVIEW

Proprietary Name: Lampit®
Common Name: nifurtimox
PDL Category: Antiprotozoals

Comparable Products	Preferred Drug List Status
Benznidazole	Preferred

Summary

Pharmacology/Usage: Nifurtimox, the active ingredient of Lampit®, is an antiprotozoal. While the mechanism of action is not fully understood, studies suggest that nifurtimox is metabolized/activated by Type I (oxygen insensitive) and Type II (oxygen sensitive) nitro reductases (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.*

Indication: In pediatric patients (birth to less than 18 years of age and weighing at least 2.5kg) for the treatment of Chagas disease (American Trypanosomiasis) caused by *Trypanosoma 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).

There is no pregnancy category for this product; however, the risk summary indicates that based on animal studies, Lampit® may cause fetal harm when administered to a pregnant woman. Published post-marketing reports on use during pregnancy are not sufficient to inform a drug-associated risk of birth defects and miscarriage. There are risks to the fetus associated with Chagas disease. Advise pregnant women of the potential risk to a fetus. Pregnancy testing is recommended for females of reproductive potential prior to starting treatment. Advise females of reproductive potential to use effective contraception during treatment and for 6 months after the final dose. In addition, advise male patients with female partners of reproductive potential to use condoms during treatment and for 3 months after the final dose. The safety and efficacy of use in the pediatric population have been established but have not been established in pediatric patients weighing less than 2.5kg.

Dosage Form: Functionally Scored Tablets: 30mg, 120mg.

Tablets can be split at the scored lines by hand. Do not break tablets mechanically with a table splitting device.

Recommended Dosage: In females of reproductive potential, obtain a pregnancy test prior to starting treatment.

Must be taken with food. Tablets can also be made into a slurry as an alternative method of administration for patients who cannot swallow tablets. Complete the full course of treatment to prevent recurrence of the infection. If a dose is missed, take the missed dose as soon as possible with food. However, if it is within 3 hours of the next scheduled dose, skip the missed dose and continue treatment as prescribed. Do not take a double dose to make up for a missed dose.

Administer PO TID with food, with the total daily dosage based on the body weight of the patient. Adjust Lampit® dosage accordingly if body weight decreases during treatment. The recommended duration of treatment is 60 days. Refer to the table below for information regarding total daily recommended dosages based on body weight.

Age	Body weight group	Total daily dose of nifurtimox (mg/kg)
Birth (body weight ≥2.5kg) to <18 yrs	≥40 kg	8 to 10mg
	< 40kg	10 to 20mg

Refer to the prescribing information for additional information regarding individual dosages based on body weight in the pediatric population.

The effect of renal impairment and the effect of hepatic on the pharmacokinetics of nifurtimox are not known. Published literature suggests that blood concentrations of nifurtimox were increased in patients with end stage renal disease requiring hemodialysis. Administer Lampit® under close medical condition with renal or hepatic impairment.

Drug Interactions: Concomitant use of Lampit® with alcohol may increase the incidence and severity of undesirable effects similar to other nitrofurans and nitro heterocyclic compounds. Lampit® is contraindicated in patients who consume alcohol during treatment.

Box Warning: There is no box warning listed with this product.

Common Adverse Drug Reactions: *Listed % incidence for adverse drug reactions= reported % incidence for drug (Lampit®). Please note that there was no placebo data in the prescribing information to compare with.* The most frequently reported adverse events included anemia (2.7%), eosinophilia (2.3%), vomiting (14.6%), abdominal pain (13.2%), nausea (8.2%), diarrhea (4.6%), pyrexia (7.3%), weight decreased (2.7%), decreased appetite (10.5%), headache (12.8%), dizziness (2.7%), rash (5.5%), and urticaria (2.3%). Other adverse reactions occurring in 0.1% to less than 1% of patients treated with Lampit® for 60 days included asthenia, vertigo, arthralgia, myalgia, paresthesia, tremor, irritability, anxiety, pruritus, fatigue, somnolence, seizure, syncope, neutropenia, and leukopenia.

Genotoxicity of Lampit® has been demonstrated in humans, in vitro in several bacterial species and mammalian cell systems, and in vivo in rodents. Carcinogenicity has been observed in animals treated chronically with nitrofuran agents which are structurally similar to nifurtimox. Similar data have not been reported for Lampit®. It is not known whether Lampit® is associated with carcinogenicity in humans.

Patients with a history of brain injury, seizures, psychiatric disease, or serious behavioral alterations may experience worsening of their condition when receiving Lampit®. Administer Lampit® under close medical supervision in these patients and in patients who develop neurological disturbances or psychiatric drug reactions.

Decreased appetite and weight loss were reported with Lampit® in the clinical trials. During treatment, patients can lose their appetite or experience nausea/vomiting which can result in weight loss. Check body weight every 14 days, as the dosage may have to be adjusted.

Treatment with nitrofuran derivatives, such as Lampit®, may precipitate acute attacks of porphyria. Administer Lampit® tablets under close medical supervision in patients with porphyria.

Contraindications: In patients

- With known hypersensitivity to nifurtimox or any of the excipients of the product
- Who consume alcohol during treatment.

Manufacturer: Bayer Healthcare

Analysis: The safety and efficacy of Lampit® for the treatment of Chagas disease in pediatric patients' birth to less than 18 years of age and weighing at least 2.5kg were demonstrated in one prospective, randomized, double-blind study conducted in Argentina, Bolivia, and Columbia. Pediatric patients (N=330) with serologic evidence of *T. cruzi*

infection and without Chagas disease-related cardiac or gastrointestinal symptoms were randomly assigned to a 60-day or 30-day treatment regimen with nifurtimox. Patients were followed up for one year. 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.

Serologic 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 demonstrated superiority in favor of the nifurtimox 60-day arm compared to the nifurtimox 30-day arm (not an approved dosing regimen). Results can be seen in the table below, which was adapted from the prescribing information.

	Lysate ELISA		Recombinant ELISA	
	60-day (N=219)	30-day (N=111)	60-day (N=219)	30-day (N=111)
Serological Response	70 (32%)	21 (19%)	76 (35%)	24 (22%)
≥20% decrease in optical density	59 (27%)	15 (14%)	65 (30%)	17 (15%)
Seroconversion	11 (5%)	6 (5%)	11 (5%)	7 (6%)
Difference, p-value	13%, p=0.007		13%, p=0.010	

The F29 ELISA detects antibodies to recombinant antigens obtained from the flagellar protein F29 of *T. cruzi*. Of the 214 patients who were seropositive for the assay at baseline, 46 of 142 (32.4%) in the 60-day nifurtimox treatment arm and 20 of 72 (27.8%) in the 30-day nifurtimox treatment arm (not an approved dosing regimen) seroconverted to negative at the 1-year post-treatment follow-up. In addition, 20 of 59 patients (33.9%) between 6 and 12 years of age in the 60-day arm seroconverted to negative at the 1-year post-treatment follow-up. A similar seroconversion rate was observed in patients 6 and 12 years of age in the 30-day treatment arm. These rates were higher than the 2.8% conversion rate from historical data for untreated patients between 6 and 12 years old at 12 months using the F29 ELISA.

Place in Therapy: Lampit® is an antiprotozoal indicated in pediatric patients (birth to less than 18 years of age and weighing at least 2.5kg) for the treatment of Chagas disease (American Trypanosomiasis) caused by *Trypanosoma 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 benefits in a confirmatory trial. Lampit® tablets should not be split mechanically with a table splitting device, but rather should be broken by hand. In a randomized, double-blind trial, serologic response was superior in the 60-day arm compared with the 30-day arm treatment groups. Note that the 30-day regimen is not an approved dosing regimen.

Lampit® is a safe, effective, and relatively cost-effective medication. It is therefore recommended that Lampit® be added to the Preferred Drug List as preferred.

PDL Placement: ☒ **Preferred**
☐ **Non-Preferred**

References

[1] Lampit [package insert]. Whippany, NJ: Bayer HealthCare Pharmaceuticals; 2020.