Benznidazole – New orphan drug approval

- On August 29, 2017, the FDA announced the approval of Chemo Research's benznidazole, indicated in pediatric patients 2 to 12 years of age 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 against the recombinant antigens of *T. cruzi*. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

- Chagas disease is a parasitic infection that can be transmitted through different routes, including contact with the feces of a certain insect, blood transfusions, or from a mother to her child during pregnancy. The disease can cause serious heart illness, and it also can affect swallowing and digestion. There may be approximately 300,000 persons in the U.S. with Chagas disease.

- The safety and efficacy of benznidazole were demonstrated in 2 placebo-controlled studies of 235 patients (ages 6 – 12 years) with chronic Chagas disease. Both studies measured anti-*T. cruzi* IgG antibodies changing from positive to negative.

    — In the first study, 60% of patients treated with benznidazole vs. 13.5% treated with placebo were seronegative (Difference = 46.5; 95% CI: 24.5, 64.4).
    — In the second study, 54.7% of patients treated with benznidazole vs. 4.6% treated with placebo were seronegative (Difference = 50.1; 95% CI: 35.8, 63.4).
    — In addition, a study of the safety and pharmacokinetics of benznidazole in pediatric patients 2 - 12 years of age provided information for dosing recommendations down to 2 years of age.

- Benznidazole is contraindicated in patients with a history of hypersensitivity reaction to benznidazole or other nitroimidazole derivatives, disulfiram usage within the last two weeks, and alcoholic beverage consumption during and for at least three days after therapy.

- Other warnings and precautions of benznidazole include potential for genotoxicity and carcinogenicity, embryo-fetal toxicity, hypersensitivity skin reactions, central and peripheral nervous system effects, and hematological manifestations of bone marrow depression.

- The most common adverse reactions with benznidazole use were abdominal pain, rash, decreased weight, headache, nausea, vomiting, neutropenia, urticaria, pruritus, eosinophilia, and decreased appetite.

- The recommended dosage of benznidazole is 5 mg/kg to 8 mg/kg orally administered in two divided doses separated by approximately 12 hours, for a duration of 60 days as outlined in the following table:

Body weight range (kg)	Dose	Number of benznidazole tablets 12.5 mg	Number of benznidazole tablets 100 mg
< 15 kg	50 mg	4 tablets	½ tablet
15 kg to < 20 kg	62.5 mg	5 tablets	--
20 kg to < 30 kg	75 mg	6 tablets	¾ tablet
30 kg to < 40 kg	100 mg	--	1 tablet
40 kg to < 60 kg	150 mg	--	1 ½ tablets
≥ 60 kg	200 mg	--	2 tablets

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- Chemo Research/Exeltis plans to launch benznidazole in November of 2017. Benznidazole will be available as 12.5 mg and 100 mg tablets.