CLINICAL UPDATE

Brand Name	Banzel®
Generic Name	rufinamide
Drug Manufacturer	Hetero Labs LTD III

Clinical Update

TYPE OF CLINICAL UPDATE

New formulation

FDA APPROVAL DATE

May 11, 2021

LAUNCH DATE

June 1, 2021

REVIEW DESIGNATION

Standard

TYPE OF REVIEW

Abbreviated New Drug Application (ANDA): 204993

DISPENSING RESTRICTIONS

N/A

Overview

INDICATION(S) FOR USE

Rufinamide tablets are indicated for adjunctive treatment of seizures associated with Lennox-Gastaut Syndrome (LGS) in pediatric patients 1 year of age and older, and in adults.

MECHANISMS OF ACTION

The precise mechanism(s) by which rufinamide exerts its antiepileptic effect is unknown. The results of in vitro studies suggest that the principal mechanism of action of rufinamide is modulation of the activity of sodium channels and, in particular, prolongation of the inactive state of the channel. Rufinamide (≥1 µM) significantly slowed sodium channel recovery from inactivation after a prolonged prepulse in cultured cortical neurons, and limited sustained repetitive firing of sodium-dependent action potentials (EC50 of 3.8 µM).

DOSAGE FORM(S) AND STRENGTH(S)

Film-coated tablets: 200 MG (pink), 400 MG (pink)

DOSE & ADMINISTRATION

Rufinamide tablets should be given with food. Tablets can be administered whole, as half tablets, or crushed.

Pediatric patients ≥1 year:

- Starting daily dose: 10 mg/kg per day in two equally divided doses.

- Increase by 10 mg/kg increments every other day to maximum dose of 45 mg/kg per day, not to exceed 3200 mg per day, in two divided doses

Adults:

- Starting daily dose: 400-800 mg per day in two equally divided doses.
- Increase by 400-800 mg every other day until a maximum dose of 3200 mg per day, in two divided doses, is reached.

EFFICACY

Adult and Pediatric Patients Ages 4 Years and Older:
The study was established in a single multicenter, double-blind, placebo-controlled, randomized, parallel-group study (N = 138). Male and female patients (between 4 - 30 years of age) were included if they had a diagnosis of inadequately controlled seizures associated with LGS (including both atypical absence seizures and drop attacks) and were being treated with 1 to 3 concomitant stable dose AEDs. Each patient must have had at least 90 seizures in the month prior to study entry. After completing a 4-week Baseline Phase on stable therapy, patients were randomized to have rufinamide or placebo added to their ongoing therapy during the 12-week Double-blind Phase. The Double-blind Phase consisted of 2 periods: the Titration Period (1 to 2 weeks) and the Maintenance Period (10 weeks). During the Titration Period, the dose was increased to a target dosage of approximately 45 mg/kg per day (3200 mg in adults of ≥ 70 kg), given on a BID schedule.
The primary efficacy variables were:

- The percent change in total seizure frequency per 28 days;
- The percent change in tonic-atonic (drop attacks) seizure frequency per 28 days;
- Seizure severity from the Parent/Guardian Global Evaluation of the patient's condition. This was a 7-point assessment performed at the end of the Double-blind Phase. A score of +3 indicated that the patient's seizure severity was very much improved, a score of 0 that the seizure severity was unchanged, and a score of -3 that the seizure severity was very much worse.

The results of the three primary endpoints are shown in Table below.

Table: Lennox -Gastaut Syndrome Trial Seizure Frequency Primary Efficacy Variable Results

Variable	Placebo	Rufinamide
Median percent change in total seizure frequency per 28 days	-11.7	-32.7 (p = 0.0015)
Median percent change in tonic-atonic seizure frequency per 28 days	1.4	-42.5 (p < 0.0001)
Improvement in Seizure Severity Rating from Global Evaluation	30.6	53.4 (p = 0.0041)

Pediatric Patients Ages 1 to Less Than 4 Years:
The Study was established based on a single multi-center, open-label, active-controlled, randomized, pharmacokinetic bridging study. The pharmacokinetic profile of rufinamide is not significantly affected by age either as a continuous covariate (1 to 35 years) or as a categorical covariate (age categories: 1 to less than 4 years and 4 years of age and older), after body weight is taken into consideration.