**DESCRIPTION**

BANZEL (rufinamide) is a triazole derivative structurally unrelated to currently marketed antiepileptic drugs (AEDs). Rufinamide has the chemical name 1-(2,6-dihydroxyphenyl)ethyl)-1H,1,2,3-triazole-4-carboxamide. It has an empirical formula of C_{16}H_{16}N_{4}O_{2} and a molecular weight of 238.2. The drug is a white, crystalline, odorless and slightly bitter tasting neutral powder. Rufinamide is practically insoluble in water, slightly soluble in tetrahydrofuran and in methanol, and very slightly soluble in ethanol and in acetonitrile.

**CLINICAL PHARMACOLOGY**

**Mechanism 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 (EC_{50} of 3.8 µM).

**PHARMACOKINETICS**

**Overview**

BANZEL is well absorbed after oral administration. However, the rate of absorption is relatively slow and the extent of absorption is decreased as dose is increased. The pharmacokinetics does not change with multiple dosing. Most elimination of rufinamide is via metabolism, with the primary metabolite resulting from enzymatic hydrolysis of the carboxamide moiety to form the carboxylic acid. This metabolic route is not cytochrome P450 dependent. There are no known active metabolites. Plasma half-life of rufinamide is approximately 6–10 hours.

**Absorption and Distribution**

Following oral administration of BANZEL, peak plasma concentrations occur between 4 and 6 hours (Tmax) both under fed and fasted conditions. BANZEL tablets display decreasing bioavailability with increasing dose after single and multiple dose administration. Based on urinary excretion, the extent of absorption was at least 85% following oral administration of a single dose of 600 mg rufinamide under fed conditions.

Multiple dose pharmacokinetics can be predicted from single dose data for both rufinamide and its metabolite. Given the dosing frequency of every 12 hours and the half-life of 6 to 10 hours, the observed steady-state peak concentration of about two to three times the peak concentration after a single dose is expected. Food increased the extent of absorption of rufinamide in healthy volunteers by 34% and increased peak exposure by 56% after a single dose of 400 mg, although the Tmax was not elevated. Clinical trials were performed under fed conditions and dosing is recommended with food (see DOSAGE AND ADMINISTRATION).

Only a small fraction of rufinamide (34%) is bound to human serum proteins, predominantly to albumin (27%), giving little risk of displacement drug-drug interactions. Rufinamide was evenly distributed between erythrocytes and plasma. The apparent volume of distribution is dependent upon dose and varies with body surface area. The apparent volume of distribution was about 50 L at 3000 mg/day.

**Metabolism**

Rufinamide is extensively metabolized but has no active metabolites. Following a radiolabeled dose of rufinamide, less than 2% of the dose was recovered unchanged in urine. The primary biotransformation pathway is carboxylesterase(s) mediated hydrolysis of the carboxamide group to the acid derivative CDP 47292. A few minor additional metabolites were detected in urine, which appeared to be acyl-glucuronides of CDP 47292. There is no involvement of oxidizing cytochrome P450 enzymes or glutathione in the biotransformation process. Rufinamide is a weak inhibitor of CYP 2E1. It did not show significant inhibition of other CYP enzymes. Rufinamide is a weak inducer of CYP 3A4 enzymes.

**Elimination/Excretion**

Renal excretion is the predominant route of elimination for drug related material, accounting for 85% of the dose based on a radiolabeled study. Of the metabolites identified in urine, at least 66% of the rufinamide dose was excreted as the acid metabolite CDP 47292, with 2% of the dose excreted as rufinamide.

The plasma elimination half-life is approximately 6–10 hours in healthy subjects and patients with epilepsy.

**Special Populations**

**Gender**: Population pharmacokinetic analyses of females show a 6–14% lower apparent clearance of rufinamide compared to males. This effect is not clinically important.

**Race**: In a population pharmacokinetic analysis of clinical studies, no difference in clearance or volume of distribution of rufinamide was observed between the black and Caucasian subjects, after controlling for body size. Information on other races could not be obtained because of smaller numbers of these subjects.

**Pediatrics**: Based on a population analysis in 117 children (age 4–11 years) and 99 adolescents (age 12–17 years), the pharmacokinetics of rufinamide in these patients is similar to the pharmacokinetics in adults. The results of a study evaluating single-dose (400 mg) and multiple dose (800 mg/day for 6 days) pharmacokinetics of rufinamide in 8 healthy elderly subjects (65–80 years old) and 7 younger healthy subjects (18–45 years old) found no significant age-related differences in the pharmacokinetics of rufinamide.

**Renal Impairment**: Rufinamide pharmacokinetics in 9 patients with severe renal impairment (creatinine clearance <30 mL/min) was similar to that of healthy subjects. Patients undergoing dialysis 3 hours post rufinamide dosing showed a reduction in AUC and Cmax by 25% and 16% respectively. Adjusting rufinamide dose for the loss of drug on dialysis should be considered.

**Hepatic Impairment**: There have been no specific studies investigating the effect of hepatic impairment on the pharmacokinetics of rufinamide. Therefore, use in patients with severe hepatic impairment is not recommended. Caution should be exercised in treating patients with mild to moderate hepatic impairment.

**Antiepileptic Drugs**

**Effects of BANZEL on other AEDs**

Population pharmacokinetic analysis of average concentration at steady state of carbamazepine, lamotrigine, phenobarbital, phenytoin, topiramate, and valproate showed that typical rufinamide C_{AUC} levels had little effect on the pharmacokinetics of other AEDs. Any effects, when they occur, have been more marked in the pediatric population.

Table 1 summarizes the drug–drug interactions of BANZEL with other AEDs.

**Table 1: Summary of drug–drug interactions of BANZEL with other anti-epileptic drugs**

<table>
<thead>
<tr>
<th>AED</th>
<th>Co-administered</th>
<th>Influence of Rufinamide on AED concentration</th>
<th>Influence of AED on Rufinamide concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbamazepine</td>
<td>Decrease by 7 to 13%</td>
<td>Decrease by 19 to 26%</td>
<td>Dependent on dose of carbamazepine</td>
</tr>
<tr>
<td>Lamotrigine</td>
<td>Decrease by 7 to 13%</td>
<td>No Effect</td>
<td></td>
</tr>
<tr>
<td>Phenobarbital</td>
<td>Increase by 8 to 13%</td>
<td>Decrease by 25 to 46%</td>
<td>Independent of dose or concentration of phenobarbital</td>
</tr>
<tr>
<td>Phenytoin</td>
<td>Increase by 7 to 21%</td>
<td>Decrease by 25 to 46%</td>
<td>Independent of dose or concentration of phenytoin</td>
</tr>
<tr>
<td>Topiramate</td>
<td>No Effect</td>
<td>No Effect</td>
<td></td>
</tr>
<tr>
<td>Valproate</td>
<td>No Effect</td>
<td>Increase by &lt;16 to 70%</td>
<td>Dependent on concentration of valproate</td>
</tr>
<tr>
<td>Primidone</td>
<td>Not Investigated</td>
<td>Decrease by 25 to 46%</td>
<td>Independent of dose or concentration of primidone</td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td>Not Investigated</td>
<td>No Effect</td>
<td></td>
</tr>
</tbody>
</table>

a) Predictions are based on BANZEL concentrations at the maximum recommended dose of BANZEL.

b) Maximum changes predicted to be in children and in patients who achieve significantly higher levels of BANZEL, as the effect of rufinamide on these AEDs is concentration-dependent.

c) Larger effects in children at high doses/concentrations of AEDs.

d) Phenobarbital, primidone and phenytoin were treated as a single covariate (phenobarbital-type inducers) to examine the effect of these agents on BANZEL clearance.

e) All compounds of the benzodiazepine class were pooled to examine for ‘class effect’ on BANZEL clearance.

**Effects of Other AEDs on BANZEL**

Potent cytochrome P450 enzyme inducers, such as carbamazepine, phenytoin, primidone, and phenobarbital appear to increase the clearance of BANZEL (see Table 1). Given that the majority of clearance of BANZEL is via a non-CYP-dependent route, the observed decreases in blood levels seen with carbamazepine phenytoin, phenobarbital, and primidone are unlikely to be entirely attributable to induction of a P450 enzyme. Other factors explaining this interaction are not understood.

**Effects of BANZEL on other Medications**

**Hormonal contraceptives**: Co-administration of BANZEL (400 mg bid) for 14 days and Ortho-Novum 1/50® resulted in a mean decrease in the ethinyl estradiol AUC_{0-24} of 22% and C_{max} by 18% and norethindrone AUC_{0-24} by 14% and C_{max} by 18%, respectively. The clinical significance of this decrease is unknown. Female patients of childbearing age should be warned that the concurrent use of BANZEL with hormonal contraceptives may render this method of contraception less effective. Additional non-hormonal forms of contraception are recommended when using BANZEL (see Information for Patients).

**Triazolam**: Co-administration and pre-treatment with BANZEL (400 mg bid) resulted in a 37% decrease in AUC and a 23% decrease in C_{max} of triazolam, a CYP 3A4 substrate.

**Olanzapine**: Co-administration and pre-treatment with BANZEL (400mg bid) resulted in no change in AUC and C_{max} of olanzapine, a CYP 1A2 substrate.

**CLINICAL STUDIES**

The effectiveness of BANZEL as adjunctive treatment for the seizures associated with Lennox-Gastaut syndrome (LGS) was established in a single multicenter, double-blind, placebo-controlled, randomized, parallel-group study (N=138). Male and female patients (between 4 and 30 years of age) were included if they had a diagnosis...
The results of the three primary endpoints are shown in Table 2 below.

### Table 2: Lennox-Gastaut Syndrome Trial Seizure Frequency Primary Efficacy Variable Results

<table>
<thead>
<tr>
<th>Variable</th>
<th>Placebo</th>
<th>Rufinamide</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median percent change in total seizure frequency per 28 days</td>
<td>-11.7</td>
<td>-32.7</td>
</tr>
<tr>
<td>Improvement in Seizure Severity Rating from Global Evaluation</td>
<td>1.4</td>
<td>-42.5</td>
</tr>
</tbody>
</table>

### INDICATIONS AND USAGE

**BANZEL** (rufinamide) is indicated for adjunctive treatment of seizures associated with Lennox-Gastaut syndrome in children 4 years and older and adults.

**CONTRAINDICATIONS**

BANZEL is contraindicated in patients with Familial Short QT syndrome (see PRECAUTIONS, QT Shortening).

**WARNINGS**

Suicidal Behavior and Ideation

Antiepileptic drugs increase the risk of suicidal thoughts or behavior in patients taking these drugs for any indication. Patients treated with any antiepileptic drug for any indication should be monitored for the emergence or worsening of depression, suicidal thoughts or behavior, or any unusual changes in mood or behavior. With clinical trials for epilepsy and Alzheimer’s disease

- **Table 3: Absolute and Relative Risk of Suicidal Behavior and Ideation**

<table>
<thead>
<tr>
<th>Indication</th>
<th>Placebo Patients with Events Per 1000 Patients</th>
<th>Drug Patients with Events Per 1000 Patients</th>
<th>Relative Risk: Incidence of Events in Drug Patients/Incidence in Placebo Patients</th>
<th>Risk Difference: Additional Drug Patients with Events Per 1000 Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epilepsy</td>
<td>1.0</td>
<td>3.4</td>
<td>3.3</td>
<td>2.4</td>
</tr>
<tr>
<td>Psychiatric</td>
<td>5.7</td>
<td>8.5</td>
<td>1.5</td>
<td>2.9</td>
</tr>
<tr>
<td>Other</td>
<td>1.0</td>
<td>1.8</td>
<td>1.9</td>
<td>0.9</td>
</tr>
<tr>
<td>Total</td>
<td>2.4</td>
<td>4.3</td>
<td>1.8</td>
<td>1.9</td>
</tr>
</tbody>
</table>

The relative risk for suicidal thoughts or behavior was higher in clinical trials for epilepsy than in clinical trials for psychiatric or other conditions, but the absolute risk differences were similar.

Anyone considering prescribing BANZEL or any other antiepileptic drug must balance this risk with the risk of untreated illness. Epilepsy and many other diseases for which antiepileptics are prescribed are associated with morbidity and mortality and an increased risk of suicidal thoughts and behavior.

- **Central Nervous System Reactions:**
  - Use of BANZEL has been associated with central nervous system–related adverse reactions. The most significant of these can be classified into two general categories:
    - Somnolence and fatigue
    - Coordination abnormalities, dizziness, gait disturbances, and ataxia
  - This can be assessed in the following ways:
    - **Precautions:**
      - **QT Shortening:**
        - Patients with Short QT syndrome should not be treated with BANZEL. See CONTRAINDICATIONS.
      - **Withdrawal of AEDs:**
        - As with all antiepileptic drugs BANZEL should be withdrawn gradually to minimize the risk of precipitating seizures, seizure exacerbation, or status epilepticus. Abrupt discontinuation of the drug is medically necessary, the transition to another AED should be made under close medical supervision.
      - **Status Epilepticus:**
        - Estimates of the incidence of treatment emergent status epilepticus among patients treated with BANZEL are difficult because standard definitions were not employed. In a controlled Lennox Gastaut syndrome trials, 3 of 74 (4.1%) BANZEL-treated patients had episodes that could be described as status epilepticus in the BANZEL-treated patients compared with none of 635 patients in the placebo-treated patients. In controlled trials in patients with partial-onset seizures, the incidence of status epilepticus compared with none of 635 patients in the placebo-treated patients.

- **Laboratory Tests:**
  - Leucopenia (white cell count < 3×10^9/L) was more commonly observed in BANZEL-treated patients (43 of 1171, 3.7%) than placebo-treated patients (7 of 578, 1.2%) in all controlled trials.

- **Drug Interactions:**
  - In vitro and in vivo studies have shown that BANZEL is unlikely to be involved in significant pharmacokinetic interactions.

  **BANZEL** can increase plasma concentrations of phenytoin by 21% or more due to non-linear pharmacokinetics. Valsartan may increase **BANZEL** concentrations up to 70%. Patients stabilized on **BANZEL** before being prescribed valsartan should begin valsartan therapy at a low dose, and titrate to a clinically effective dose. Similarly, patients on valsartan who discontinue **BANZEL** for any reason should be rescreened for potential adverse drug interactions before resuming **BANZEL** therapy.

For patients with elevated liver transaminase (ALT, AST) levels, an increased total bilirubin level, or a decreased hemoglobin level, it may be important to consider these results in the context of other possible explanations for the observed changes.
Drug/Laboratory Test Interactions

There are no known interactions of BANZEL with commonly used laboratory tests.

Carcinogenicity, Mutagenicity, Impairment of Fertility

Carcinogenicity: Rufinamide was given in the diet to mice at 40, 120, and 400 mg/kg/day and to rats at 20, 60, and 200 mg/kg/day for two years. The doses in mice were associated with plasma AUCs 0.1 to 1 times the human plasma AUC at the maximum recommended human dose (MRHD, 3200 mg/day). Increased incidences of tumors (benign bone tumors (osteomas) and/or hepatocellular adenomas and carcinomas) were observed in mice at all doses. Increased incidences of thyroid follicular adenomas were observed in rats at all but the low dose; the low dose is <0.1 times the MRHD on a mg/m² basis.

Mutagenicity: Rufinamide was not mutagenic in the in vitro bacterial reverse mutation (Ames) assay or the in vivo mammalian cell chromosome abberation assay or the in vitro rat bone marrow micronucleus assay.

Impairment of Fertility: Oral administration of rufinamide (doses of 20, 60, 200, and 600 mg/kg/day) to male and female rats prior to mating and throughout mating, and continuing in females up to day 6 of gestation resulted in impaired parturition of fertility (decreased conception rates and mating and fertility indices; decreased numbers of corpora lutea, implantations, and live embryos; increased preimplantation loss; decreased sperm count and motility) at all doses tested. Therefore, a no-effect dose was not established. The lowest dose tested was associated with a plasma AUC = 0.2 times the human plasma AUC at the MRHD.

PREGNANCY

Pregnancy Category C

Rufinamide produced developmental toxicity when administered orally to pregnant animals at clinically relevant doses.

Rufinamide was administered orally to rats at doses of 20, 100, and 300 mg/kg/day and to rabbits at doses of 30, 200, and 1000 mg/kg/day during the period of organogenesis (implantation to closure of the hard palate); the high doses were associated with plasma AUCs <2 times the human plasma AUC at the maximum recommended human dose (MRHD, 3200 mg/day). Decreased fetal weights and increased incidences of fetal skeletal abnormalities were observed in rats at doses associated with maternal toxicity. In rabbits, embryo-fetal death, decreased fetal body weights, and increased incidences of fetal visceral and skeletal abnormalities occurred at all but the low dose. The highest dose tested in rabbits was associated with abortion. The no-effect doses for adverse effects on rat and rabbit embryo-fetal development (20 and 30 mg/kg/day, respectively) were associated with plasma AUCs = 0.2 times that in humans at the MRHD.

In a rat pre- and post-natal development study (dosing from implantation through weaning) conducted at oral doses of 5, 30, and 150 mg/kg/day (associated with plasma AUCs up to 21 times that in humans at the MRHD), decreased offspring growth and survival were observed at all doses tested. A no-effect dose for adverse effects on pre- and post-natal development was not established. The lowest dose tested was associated with plasma AUC = 0.1 times that in humans at the MRHD.

There are no adequate and well-controlled studies in pregnant women. BANZEL should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Labor and Delivery

The effect of BANZEL on labor and delivery in humans is not known.

Nursing Mothers

Rufinamide is likely to be excreted in breast milk. Because of the potential for serious adverse reactions in nursing infants from BANZEL, a decision should be made whether to discontinue nursing or discontinue the drug taking into account the importance of the drug to the mother.

Pediatric Use

The safety and effectiveness in patients with Lennox-Gastaut syndrome have not been established in children less than 4 years.

Geriatric Use

Clinical studies of BANZEL did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosage range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

A study evaluating the pharmacokinetics of rufinamide in elderly subjects showed that there were no significant differences in the plasma and urine pharmacokinetic parameters of rufinamide between the younger and elderly subjects under both single and multiple dose treatments (see Special Populations: Elderly).

Adverse Reactions

Placebo-controlled double-blind studies were performed in adults and in pediatric patients, down to age of 4, in other forms of epilepsy, in addition to the trial in Lennox-Gastaut syndrome. Data on CNS Reactions (see WARNINGS) from the Lennox-Gastaut study are presented first. Because there is no reason to suspect that adverse reactions would substantially differ between these patient populations, safety data from all of these controlled studies are then presented. Most of these adverse reactions were mild to moderate and transient in nature.

Common central nervous system reactions in the controlled trial of patients 4 years or older with Lennox-Gastaut syndrome. Data on CNS Reactions (see WARNINGS) from the Lennox-Gastaut study are presented first. Because there is no reason to suspect that adverse reactions would substantially differ between these patient populations, safety data from all of these controlled studies are then presented. Most of these adverse reactions were mild to moderate and transient in nature.

Discontinuation in Controlled Clinical Studies

In controlled double-blind adjunctive clinical studies, 9.0% of patients receiving BANZEL as adjunctive therapy and 4.4% receiving placebo discontinued as a result of an adverse reaction. The adverse reactions most commonly leading to discontinuation of BANZEL (≥1%) used as adjunctive therapy were generally similar in adults and children.

In pediatric double-blind adjunctive clinical studies, 8.0% of patients receiving BANZEL as adjunctive therapy and 2.2% receiving placebo discontinued as a result of an adverse reaction. The adverse reactions most commonly leading to discontinuation of BANZEL (≥1%) used as adjunctive therapy are presented in Table 6.
In adult double-blind adjunctive clinical studies (up to 3200 mg/day), 9.5% of patients receiving BANZEL as adjunctive therapy and 5.9% receiving placebo discontinued as a result of an adverse reaction. The adverse reactions most commonly leading to discontinuation of BANZEL (>1%) used as adjunctive therapy are presented in Table 7.

<table>
<thead>
<tr>
<th>Preferred Term</th>
<th>BANZEL (N=283)</th>
<th>Placebo (N=376)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diarrhea</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Fatigue</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Headache</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Nausea</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Ataxia</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

Other Adverse Events Observed During Clinical Trials:
BANZEL has been administered to 178 individuals during all epilepsy clinical trials (placebo-controlled and open-label). Adverse events occurring during these studies were recorded by the investigators using terminology of their own choosing. To provide a meaningful estimate of the proportion of patients having adverse events, these events were categorized by body system and listed in order of decreasing frequency as follows: terms describing events common in the population. Some events occurring fewer than 3 times are also included based on their medical significance. Because the reports include events observed in open-label, uncontrolled observations, the role of BANZEL in their causation cannot be reliably determined.

Events are classified by body system and listed in order of decreasing frequency as follows: frequent adverse events (those occurring in at least 1/100 to 1/1000 patients); infrequent adverse events (those occurring in 1/100 to 1/1000 patients); rare—those occurring in fewer than 1/1000 patients.

Blood and Lymphatic System Disorders:
- Anemia
- Infringent: lymphadenopathy, leukopenia, neutropenia, iron deficiency anemia, thrombocytopenia

Cardiac Disorders:
- Infringent: bundle branch block right, atrioventricular block first degree

Metabolic and Nutritional Disorders:
- Frequent: decreased appetite, increased appetite

Renal and Urinary Disorders:
- Pollakiuria
- Infrequent: urinary incontinence, dysuria, hematuria, nephritis, polyuria, enuresis, nocturia, incontinence

DRUG ABUSE AND DEPENDENCE
The abuse and dependence potential of BANZEL has not been evaluated in humans.

OVERDOSAGE
Because strategies for the management of overdose are continually evolving, it is advisable to contact a Certified Poison Control Center to determine the latest recommendations for the management of an overdose of any drug.

One overdose of 7200 mg/day of BANZEL was reported in an adult during the clinical trials. The overdose was associated with no major signs or symptoms, no medical intervention was required, and the patient continued in the study at the target dose.

Treatment or Management of Overdose: There is no specific antidote for overdose with BANZEL. If clinically indicated, elimination of unabsorbed drug should be attempted by induction of emesis or gastric lavage. Usual precautions should be observed to maintain the airway. General supportive care of the patient is indicated including monitoring of vital signs and observation of the clinical status of the patient.

Hemodialysis: Standard hemodialysis procedures may result in limited clearance of rufinamide. Although there is no experience to date in treating overdose with hemodialysis, the procedure may be considered when indicated by the patient’s clinical state.

DOSEAGE AND ADMINISTRATION
Children four years and older with Lennox-Gastaut syndrome: Treatment should be initiated at a daily dose of approximately 10 mg/kg/day administered in two equally divided doses. The dose should be increased by approximately 10 mg/kg increments every other day to a target dose of 45 mg/kg/day or 3200 mg/day, whichever is less, administered in two equally divided doses. It is not known whether doses lower than the target doses are effective.

Adults with Lennox-Gastaut syndrome: Treatment should be initiated at a daily dose of 400–800 mg/day administered in two equally divided doses. The dose should be increased by 400–800 mg/day every 2 days until a maximum daily dose of 3300 mg/day, administered in two equally divided doses is reached. It is not known whether doses lower than 3200 mg/day are effective.

BANZEL tablets are scored on both sides and can be cut in half for dosing flexibility. Tablets can be administered whole, as half tablets or crushed. BANZEL should be given with food.

Patients with Renal Impairment
Renally impaired patients (creatinine clearance less than 30 mL/min) do not require any special dosage change when taking BANZEL.

Patients Undergoing Hemodialysis
Hemodialysis may reduce exposure to a limited (about 30%) extent. Accordingly, adjusting the BANZEL dose during the dialysis process can be considered.

Patients with Hepatic Disease
Use of BANZEL in patients with hepatic impairment has not been studied. Therefore, use in patients with severe hepatic impairment is not recommended. Caution should be exercised in treating patients with mild to moderate hepatic impairment.
Medication Guide
BANZEL™ (ban'-zel)
[rufinamide]

BANZEL and Suicidal Thoughts or Actions

Read this Medication Guide before you start taking BANZEL and each time you get a refill. There may be new information. This information does not take the place of talking to your healthcare provider about your medical condition or treatment. This Medication Guide is only about the risk of suicidal thoughts and actions with BANZEL.

What is the most important information I should know about BANZEL?

1. BANZEL may cause suicidal thoughts or actions in a very small number of people, about 1 in 500.

2. Call a healthcare provider right away if you have any of these symptoms, especially if they are new, worse, or worry you:

   - thoughts about suicide or dying
   - attempt to commit suicide
   - new or worse depression
   - new or worse anxiety
   - feeling agitated or restless
   - panic attacks
   - trouble sleeping (insomnia)
   - new or worse irritability
   - acting aggressive, being angry, or violent
   - acting on dangerous impulses
   - an extreme increase in activity and talking (mania)
   - other unusual changes in behavior or mood

3. Do not stop BANZEL without first talking to a healthcare provider.

   - Stopping BANZEL suddenly can cause serious problems.
   - Suicidal thoughts or actions can be caused by things other than medicines. If you have suicidal thoughts or actions, your healthcare provider may check for other causes.

4. How can I watch for early symptoms of suicidal thoughts and actions?

   - Pay attention to any changes, especially sudden changes, in mood, behaviors, thoughts, or feelings.
   - Keep all follow-up visits with your healthcare provider as scheduled.
   - Call your healthcare provider between visits as needed, especially if you are worried about symptoms.

What else should I know about BANZEL?

- BANZEL has other side effects. For more information ask your healthcare provider or pharmacist. Tell your healthcare provider if you have any side effect that bothers you.

   Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

- BANZEL can interact with other medicines. Tell your healthcare provider about all the medicines you take, including prescription and non-prescription medicines, vitamins, and herbal supplements. Using BANZEL with certain other medicines can affect each other causing side effects.

   Know the medicines you take. Keep a list of them and show it to your healthcare provider and pharmacist each time you get a new medicine. Do not start a new medicine without first talking with your healthcare provider.

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use BANZEL for a condition for which it was not prescribed. Do not give BANZEL to other people, even if they have the same symptoms that you have. It may harm them.

This Medication Guide summarizes the most important information about BANZEL. If you would like more information, talk with your doctor. You can ask your pharmacist or doctor for information about BANZEL that is written for health professionals.

For more information, go to www.banzel.com or call 1-888-274-2376.

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This Medication Guide has been approved by the U.S. Food and Drug Administration.

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