Rufinamide

Inovelon®

200 mg

Film-Coated Tablets

Anti-epileptic

1. NAME OF THE MEDICINAL PRODUCT(S)

Rufinamide (Inovelon®) 200 mg film-coated tablets

2. FORMULATION

Each film-coated tablet contains 200 mg of rufinamide
For excipients, see Section 6.1.

3. PHARMACEUTICAL FORM

Oral Film-Coated Tablet
Pink, 'ovaloid', slightly convex, film-coated tablets, scored on both sides, embossed '€262' on one side and blank on the other side.

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

Rufinamide is indicated as adjunctive treatment of seizures associated with Lennox-Gastaut syndrome (LGS) in children 4 years of age and older and in adults.

4.2 Posology and Method of Administration

Posology
Rufinamide film-coated tablets are for oral use. Rufinamide should be administered twice daily. If the patient has difficulty with swallowing, tablets can be crushed and administered in half a glass of water.

Adjunctive Therapy in Patients with Seizures Associated with Lennox-Gastaut Syndrome (4 Years of Age and Older).

Use in children and adults less than 30 kg

Treatment should be initiated at a daily dose of 200 mg. According to clinical response and tolerability, the dose may be increased by 200 mg/day increments up to a maximum recommended dose of 1000 mg/day. In clinical trials, the dose was increased as frequently as every two days. Doses of up to 3600 mg/day have been studied in a limited number of patients.

Treatment in patients also taking Valproate should be initiated at a daily dose of 200 mg. According to clinical response and tolerability, after a minimum of 2 days the dose may be increased by 200 mg/day, to the maximum recommended dose of 600 mg/day.

Use in adults, adolescents and children of 30 kg or over

Treatment should be initiated at a daily dose of 400 mg. According to clinical response and tolerability, the dose may be increased by 400 mg/day increments up to a maximum recommended dose as indicated in the table below. In clinical trials, the dose was increased as frequently as every two days.

Weight range	30.0-50.0 kg	50.1 -70.0 kg	≥70.1 kg
Maximum recommended dose (mg/day)	1800	2400	3200

Doses of up to 4000 mg/day (in the 30-50 kg range) or 4800 mg/day (over 50 kg) have been studied in a limited number of patients.

Elderly Use

There is limited information on the use of rufinamide in the elderly. Since, the pharmacokinetics of rufinamide are not altered in the elderly (Section 5.2), dosage adjustment is not required in patients over 65 years of age.

Renal Impairment

A study in patients with severe renal impairment indicated that no dose adjustments are required for these patients. Hemodialysis may reduce exposure to a limited (about 30%) extent. Accordingly, adjusting the rufinamide dose during the dialysis process should be considered.

Hepatic Impairment

Use in patients with hepatic impairment has not been studied. Caution and careful dose titration is recommended when treating patients with mild to moderate hepatic impairment. Use in patients with severe hepatic impairment is not recommended.

Method of Administration

Rufinamide is for oral use. It should be taken twice daily with water in the morning and in the evening, in two equally divided doses. As a food effect was observed, rufinamide should be administered with food (see section 5.2).

If the patient has difficulty with swallowing, tablets can be crushed and administered in half a glass of water.

Discontinuation of Rufinamide

When rufinamide treatment is to be discontinued, it should be withdrawn gradually. In clinical trials rufinamide discontinuation was achieved by reducing the dose by approximately 25% every two days.

4.3 Contraindications

Rufinamide is contraindicated in patients with known hypersensitivity to rufinamide, triazole derivatives, or to any excipients used in the formulation.

4.4 Special Warnings and Special Precautions for Use

Status epilepticus

Status epilepticus cases have been observed during clinical development studies, under rufinamide whereas no such cases have been observed under placebo. These events led to rufinamide discontinuation in 20 % of the cases. If patients develop new seizure types and/or experience an increased frequency of status epilepticus that is different from the patient's baseline condition, then the benefit risk ratio of the therapy should be reassessed.

Withdrawal

Antiepileptic medicinal products, including rufinamide, should be withdrawn gradually to reduce the possibility of seizures on withdrawal. In clinical studies discontinuation was achieved by reducing the dose by approximately 25% every two days. There are insufficient data on the withdrawal of concomitant antiepileptic medications once seizure control has been achieved with the addition of rufinamide.

Central Nervous System Reactions

Rufinamide treatment has been associated with dizziness, somnolence, ataxia and gait disturbances, which could increase the occurrence of accidental falls in patients with LGS (-Section 4.8). Patients and caretakers should exercise caution until they are familiar with the potential effects of the medication.

Multiorgan Hypersensitivity Reactions

Serious antiepileptic drug hypersensitivity syndrome has occurred in association with rufinamide therapy. Signs and symptoms of this disorder were diverse; however, patients typically, although not exclusively, presented with fever and rash associated with other organ system involvement. Other associated manifestations included lymphadenopathy, liver function tests abnormalities, and hematuria. Because the disorder is variable in its expression, other organ system signs and symptoms not noted here may occur. The antiepileptic drug hypersensitivity syndrome occurred in close temporal association to the initiation of rufinamide therapy and in the pediatric population. In addition rare cases of DRESS (Drug Reaction with Eosinophilia and Systemic Symptoms) and Stevens-Johnson syndrome have been reported in association with rufinamide therapy post marketing. If an antiepileptic drug hypersensitivity syndrome is suspected, rufinamide should be discontinued and alternative treatment started. All patients who develop a rash while taking rufinamide must be closely supervised.

QT shortening

In a thorough QT study, rufinamide produced a decrease in QTc interval proportional to concentration. Although the underlying mechanism and safety relevance of this finding is not known, clinicians should use clinical judgment when assessing whether to prescribe rufinamide to patients at risk from further shortening their QTc duration (e.g. Congenital Short QT Syndrome or patients with a family history of such a syndrome).

Oral Contraceptives

Women of childbearing potential must use effective contraception during treatment with rufinamide. Physicians should try to ensure that appropriate contraception is used, and should use clinical judgment when assessing whether oral contraceptives, or the doses of the oral contraceptive components, are adequate based on the individual patients clinical situation (Section 4.5).

Lactose

Rufinamide contains lactose, therefore patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Suicidal ideation

Suicidal ideation and behaviour have been reported in patients treated with antiepileptic agents in several indications. A meta-analysis of randomized placebo-controlled trials of anti-epileptic medicinal products has also shown a small increased risk of suicidal ideation and behavior. The mechanism of this risk is not known and the available data do not exclude the possibility of an increased risk for rufinamide.

Therefore patients should be monitored for signs of suicidal ideation and behaviours and appropriate treatment should be considered. Patients (and caregivers of patients) should be advised to seek medical advice should signs of suicidal ideation or behavior emerge.

4.5 Interaction with Other Medicinal Products

Potential for other medicinal products to affect rufinamide

Other Anti-Epileptic Drugs

Rufinamide concentrations may be decreased by co-administration with carbamazepine, phenobarbital, phenytoin, vigabatrin or primidone.

Rufinamide concentrations may be increased by co-administration with valproate. The most pronounced increases were observed in patients of low body weight (<30 kg). In children with high concentrations of valproate (median of 100 microgram/mL), rufinamide levels may be elevated by up to 70%. Therefore, consideration should be given to a dose reduction of rufinamide in patients <30 kg who are initiated on valproate therapy (see section 4.2).

The addition or withdrawal of these drugs during rufinamide therapy may require an adjustment in dosage of rufinamide.

No significant changes in rufinamide concentration are observed following co-administration with lamotrigine, topiramate or benzodiazepines.

Potential for rufinamide to affect other medicinal products

Other Anti-Epileptic Drugs

The pharmacokinetic interactions between rufinamide and other anti-epileptic drugs have been evaluated in patients with epilepsy using population pharmacokinetic modeling. Rufinamide had no clinically relevant effect on carbamazepine, lamotrigine, phenobarbital, topiramate, phenytoin or valproate steady state concentrations.

Table 1 summarizes the drug-drug interactions of rufinamide with other AEDs.

Table 1: Summary of drug-drug interactions of rufinamide with other antiepileptic drugs

AED Co-administered	Influence of Rufinamide on AED concentration a)	Influence of AED on Rufinamide concentration
Carbamazepine	Decrease by 7 to 13% b)	Decrease by 19 to 26%. Dependent on dose of carbamazepine
Lamotrigine	Decrease by 7 to 13% b)	No effect
Phenobarbital	Increase by 8 to 13% b)	Decrease by 25 to 46% c), d). Independent of dose or concentration of phenobarbital
Phenytoin	Increase by 7 to 21% b)	Decrease by 25 to 46% c), d). Independent of dose or concentration of phenytoin
Topiramate	No effect	No effect
Valproate	No effect	Increase by <16 to 70% c) Dependent on concentration of valproate
Primidone	Not Investigated	Decrease by 25 to 46% c), d). Independent of dose or concentration of primidone
Benzodiazepines e)	Not Investigated	No effect

a) Predictions are based on rufinamide concentrations at the maximum recommended dose of rufinamide.
b) Maximum changes predicted to be in pediatric patients and in adult patients who achieve significantly higher levels of rufinamide, as the effect of rufinamide on these AEDs is concentration-dependent.
c) Larger effects in pediatric patients 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 rufinamide clearance.
e) All compounds of the benzodiazepine class were pooled to examine for 'class effect' on rufinamide clearance.

Phenytoin: The decrease in clearance of phenytoin estimated at typical levels of rufinamide (Cavss 15 μg/mL) is predicted to increase plasma levels of phenytoin by 7 to 21%. As phenytoin is known to have non-linear pharmacokinetics (clearance becomes saturated at higher doses), it is possible that exposure will be greater than the model prediction.

Oral Contraceptives

An interaction study was conducted to determine the effect of rufinamide on co-administered low-dose oral contraceptives (Ortho-Novum 1/35) in healthy female volunteers. Co-administration of rufinamide and Ortho-Novum 1/35 resulted in a mean decrease in the ethinyl estradiol $AUC_{(0-24h)}$ of 22% and in norethindrone $AUC_{(0-24)}$ of 14%. Studies with other oral or implant contraceptives have not been conducted. These changes in ethinyl estradiol and norethindrone are small and unlikely to result in diminished clinical efficacy. However, tests for ovulation were not used in this study.
Women of child-bearing potential using hormonal contraceptives are advised to use an additional safe and effective contraceptive method (Section 4.4).

Cytochrome P450 Enzymes

Rufinamide is hydrolyzed by carboxylesterases, and is not metabolized to any notable degree by cytochrome P450 enzymes. Furthermore, rufinamide does not inhibit the activity of cytochrome P450 enzymes (Section 5.2). Thus, clinically significant interactions mediated through inhibition of cytochrome P450 system by rufinamide are unlikely to occur. Rufinamide has been shown to induce the cytochrome P450 enzyme CYP3A4 and may therefore reduce the plasma concentrations of drugs which are metabolized by this enzyme. The effect was modest to moderate. The mean CYP3A activity, assessed as clearance of triazolam, was increased by 55% after 11 days of treatment with rufinamide 400 mg b.i.d. The exposure of triazolam was reduced by 36%. Higher doses may result in a more pronounced induction. It may not be excluded that rufinamide may also decrease the exposure of substances metabolized by other enzymes, or transported by transport proteins such as P-glycoprotein.

It is recommended that patients treated with substances that are metabolized by the CYP3A4 enzyme system are to be carefully monitored for two weeks at the start of, or after the end of treatment with rufinamide, or after any marked change in the dose. A dose adjustment of the concomitantly administered medicinal product may need to be considered. These recommendations should also be considered when rufinamide is used concomitantly with substances with a narrow therapeutic window such as warfarin and digoxin.

A specific interaction study in healthy subjects revealed no influence of rufinamide at a dose of 400 mg bid on the pharmacokinetics of olanzapine, a CYP1A2 substrate.

Food

Maximum plasma levels are reached approximately 6 hours after administration. Peak concentration (C_{max}) and plasma AUC of rufinamide increase less than proportionally with doses in both fasted and fed healthy subjects and in subjects, probably due to dose-limited absorption behavior. After a low single doses food increases the absorption of rufinamide by approximately 34%, however at high dose steady state there is no notable influence of food on rufinamide exposure.

4.6 Fertility, Pregnancy and Lactation

Fertility

No clinical data are available on the effects on fertility following treatment with rufinamide.

Pregnancy

Pregnancy Risk Related to Epilepsy and Antiepileptic Medicinal Products in General:

It has been shown that in the offspring of women with epilepsy, the prevalence of malformations is two to three times greater than the rate of approximately 3% in the general population. In the treated population, an increase in malformations has been noted with polytherapy; however, the extent to which the treatment and/or the illness are responsible has not been elucidated. Moreover, discontinuation of effective anti-epileptic therapy may result in disease worsening, which can be harmful to the mother and the fetus.

Risk Related to Rufinamide:

Studies in animals revealed no teratogenic effect but fetotoxicity occurred in the presence of maternal toxicity (Section 5.3, Preclinical safety data). The potential risk for humans is unknown.

For rufinamide, no clinical data on pregnancies during exposure to rufinamide are available.

Taking these data into consideration, rufinamide should not be used during pregnancy unless clearly necessary or in women of childbearing age not using adequate contraceptive measures.

If women treated with rufinamide plan to become pregnant, the indication of this product should be carefully weighed. Discontinuation of anti-epileptic treatments may result in disease worsening, which can be harmful to the mother and the fetus.

Lactation

Nonclinical data suggests that rufinamide or its metabolites may be excreted with the milk during lactation. Animal studies have shown an uptake of radioactivity in mammary glands in both rats and rabbits. Because of the potential for serious adverse reactions in nursing infants from rufinamide, a decision should be made whether to discontinue nursing or discontinue the drug taking into account the importance of the drug to the mother.

4.7 Effects on Ability to Drive and Use Machines

Rufinamide may cause dizziness and somnolence and therefore may influence the ability to drive or use machines. Patients are advised not to drive, operate complex machinery or engage in other potentially hazardous activities until it is known whether this medication affects their ability to perform these tasks.

4.8 Undesirable Effects

The clinical development program has included over 1,900 patients, with different types of epilepsy, exposed to rufinamide.

Most Common Adverse Reactions

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The most commonly reported adverse reactions overall were headache, dizziness, fatigue, and somnolence. The most common adverse reactions observed at a higher incidence than placebo in patients with Lennox-Gastaut syndrome were somnolence and vomiting. Adverse reactions were usually mild to moderate in severity. The discontinuation rate in LGS due to adverse reactions was 8.2% for patients receiving rufinamide and 0% for patients receiving placebo. The most common adverse reactions resulting in discontinuation from the rufinamide treatment group were rash and vomiting.

Adverse events that were reported in at least 2% of patients with LGS treated with rufinamide or placebo as adjunctive therapy in double-blind trials and were numerically more common in the patients treated with any dose of rufinamide are summarized in Table 2.

Table 2: Percentage of patients with adverse events that occurred in more than 2.0% of rufinamide-treated patients at higher incidences with rufinamide than placebo, listed by MedDRA preferred term (Double-blind, adjunctive therapy study in LGS)[1]

	Rufinamide	Placebo
Total number of patients studied	N=74 (%)	N=64 (%)
Percentage of patients with any adverse event	81.1	81.3
Somnolence	24.3	12.5
Vomiting	21.6	6.3
Fatigue	9.5	7.8
Decreased appetite	9.5	4.7
Nasopharyngitis	9.5	3.1
Headache	6.8	4.7
Rash	6.8	1.6
Rhinitis	5.4	4.7
Ataxia	5.4	0
Psychomotor activity	4.1	3.1
Convulsion	4.1	1.6
Ear infection	4.1	1.6
Epistaxis	4.1	0
Nystagmus	4.1	0
Status epilepticus	4.1	0
Contusion	2.7	1.6
Head injury	2.7	1.6
Loose stools	2.7	1.6
Sinusitis	2.7	1.6
Acne	2.7	0
Dizziness	2.7	0
Eating disorder	2.7	0
Exanthema	2.7	0
Influenza	2.7	0
Oligomenorrhea	2.7	0
Pneumonia	2.7	0

Post-Marketing Experience

The following adverse reactions have been identified during post approval use of rufinamide. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Decreased weight has been reported in patients receiving rufinamide both in the presence and absence of gastrointestinal symptoms.
Dermatologic: Stevens-Johnson syndrome and other serious skin rashes with mucosal involvement.

Reporting of Suspected Adverse Reactions "Applicable to The Philippines only"

Please contact:
HI-Eisai Pharmaceutical, Inc. (Philippines)
+63 2 8875837 /+63 2 8875160 / +63 9088672236

Or
Report to FDA Philippines: www.fda.gov.ph

4.9 Overdose

There is no specific antidote for overdose with rufinamide. If indicated, elimination of unabsorbed drug should be attempted by gastric lavage or by induction of emesis. Treatment should be supportive and may include hemodialysis. (Section 5.2)

Multiple dosing of 7,200 mg/day was associated with no major signs or symptoms.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic Properties

Pharmacotherapeutic group: anti-epileptics; ATC-code: N03AF03.

Mechanism of Action

Rufinamide modulates the activity of sodium channels, prolonging their inactive state. Rufinamide is active in a range of animal models of epilepsy.

Clinical Experience

Effectiveness in Seizures Associated with Lennox-Gastaut Syndrome (LGS)

Rufinamide was administered in a double blind, placebo-controlled study, at doses of up to 45 mg/kg/day for 84 days, to 139 patients with Lennox-Gastaut syndrome aged 4 and over, who were taking up to three concomitant anti-epileptic drugs. A highly significant reduction was seen in the primary variables: the percentage change in total seizure frequency per 28 days relative to baseline (-32.7% on rufinamide vs. –11.7% on placebo, p= 0.0015), the number of tonic-atonic seizures (-42.5% on rufinamide vs. 1.4% on placebo, p < 0.0001), and the seizure severity rating from the Global Evaluation performed by the parent/guardian at the end of the double-blind phase (much or very much improved in 32.2% on rufinamide vs. 14.5% on the placebo arm, p=0.0041). Secondary outcome measures which showed a benefit of rufinamide over placebo treatment included: a reduction in absence and atypical absence seizures (p=0.022); 42.5% on rufinamide versus 16.7% on placebo (p =0.002) experienced a 50% or greater reduction in tonic-atonic seizure frequency.

Population pharmacokinetic/pharmacodynamic modeling demonstrated that the reduction of total and tonic-atonic seizure frequencies, the improvement of the global evaluation of seizure severity and the increase in probability of reduction of seizure frequency were dependent on rufinamide concentrations.

5.2 Pharmacokinetic Properties

Absorption

Maximum plasma levels are reached approximately 6 hours after administration. Peak concentration (C_{max}) and plasma AUC of rufinamide increase less than proportionally with doses in both fasted and fed healthy subjects and in patients, probably due to dose-limited absorption behavior. After a low single doses food increases the absorption of rufinamide by approximately 34% and the peak plasma concentration by 56%, however at high dose steady state there is no notable influence of food on rufinamide exposure.

Distribution

In in vitro studies, only a small fraction of rufinamide (34%) was bound to human serum proteins with albumin accounting for approximately 80% of this binding. This indicates minimal risk of drug-drug interactions by displacement from binding sites during concomitant administration of other drugs. Rufinamide was evenly distributed between erythrocytes and plasma.

Biotransformation

Rufinamide is almost exclusively eliminated by metabolism. The main pathway of metabolism is hydrolysis of the carboxylamide group to the pharmacologically inactive acid derivative CGP 47292. Cytochrome P450-mediated metabolism is very minor. There is no indication of involvement of glutathione conjugation in the biotransformation process.

Rufinamide has demonstrated little or no significant capacity *in-vitro* to act as a competitive or mechanism-based inhibitor of the following human P450 enzymes: CYP1A2, CYP2A6, CYP2C9, CYP2C19, CYP2D6, CYP2E1, CYP3A4/5 or CYP4A9/11-2.

Elimination

The plasma elimination half-life is approximately 6-10 hours in healthy subjects and patients with epilepsy. When given twice daily at 12-hourly intervals, rufinamide accumulates to the extent predicted by its terminal half-life, indicating that the pharmacokinetics of rufinamide are time-independent (i.e., no autoinduction of metabolism).

In a radiotracer study in three healthy volunteers, the parent compound (rufinamide) was the main radioactive component in plasma, representing about 80% of the total radioactivity, with the metabolite CGP 47292 constituting only about 15%.[2] Renal excretion was the predominant route of elimination for drug related material, accounting for 84.7% of the dose.

Linearity/Non-Linearity

The bioavailability of rufinamide is dependent on dose. As dose increases the bioavailability decreases.

Special Populations

Hepatic Impairment

No studies have been performed in patients with hepatic impairment and therefore rufinamide should not be administered to patients with severe hepatic impairment. Caution should be exercised in treating patients with mild to moderate hepatic impairment. (Section 4.4)

Renal Impairment

The pharmacokinetics of a single 400 mg dose of rufinamide was not altered in subjects with chronic and severe renal failure compared to healthy volunteers. However, plasma levels were reduced by approximately 30% when hemodialysis was applied after administration of rufinamide, suggesting that this may be a useful procedure in case of overdose (Section 4.9).

Gender

Population pharmacokinetic modeling has been used to evaluate the influence of sex on the pharmacokinetics of rufinamide. Such evaluations indicate that sex does not have any clinically relevant affect the pharmacokinetics of rufinamide.[3]

Pediatric Population

Children generally have lower clearance of rufinamide than adults, and this difference is related to body size. Studies in newborn infants or infants and toddlers under 2 years of age have not been conducted.

Elderly Population

A pharmacokinetic study in elderly healthy volunteers did not show a significant difference in pharmacokinetic parameters compared with younger adults.

5.3 Preclinical Safety Data

Conventional safety pharmacology studies revealed no special hazards at clinically relevant doses.

Toxicities observed in dogs at exposures similar to human exposure at the maximum recommended dose were liver changes, including bile thrombi, cholestasis and liver enzyme elevations thought to be related to increased bile secretion in this species. No evidence of an associated risk was identified in the rat and monkey repeat dose toxicity studies.

In reproductive and developmental toxicity studies, there were reductions in fetal growth and survival, and some stillbirths secondary to maternal toxicity. However, no effects on morphology and function, including learning or memory, were observed in the offspring. Rufinamide was not teratogenic in mice, rats or rabbits.

Rufinamide was not genotoxic and had no carcinogenic potential. Adverse effects not observed in clinical studies, but seen in animals at exposure levels similar to clinical exposure levels and with possible relevance to human use, was myelofibrosis of the bone marrow in the mouse carcinogenicity study. Benign bone neoplasms (osteomas) and hyperostosis seen in mice were considered a result of the activation of a mouse specific virus by fluoride ions released during the oxidative metabolism of rufinamide.

Regarding the immunotoxic potential, small thymus and thymic involution were observed in dogs in a 13-week study with significant response at the high dose in male. In the 13-week study, female bone marrow and lymphoid changes are reported at the high dose with a weak incidence. In rats, decreased cellularity of the bone marrow and thymic atrophy were observed only in the carcinogenicity study.

Oral administration of rufinamide (doses of 20, 60, 200, and 600 mg/kg per day) to male and female rats prior to mating and throughout mating, and continuing in females up to day 6 of gestation resulted in impairment 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 dosed 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 max recommended human dose.

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

The excipients used for the rufinamide film-coated tablets are all of pharmacopoeial quality:

Core: Sodium laurylsulfate, Colloidal anhydrous silica / Colloidal silicon dioxide, Magnesium stearate, Croscarmellose sodium, Hypromellose / Hydroxypropyl Methylcellulose, Maize starch / Corn starch, Lactose monohydrate, Microcrystalline Cellulose, Purified water.

Coat: Red iron oxide / Ferric oxide (red), Titanium dioxide, Macrogol / Polyethylene glycol, Talc, Hypromellose / Hydroxypropyl Methylcellulose, Purified water.

6.2 Incompatibilities

None

6.3 Shelf Life

Rufinamide should be used before the expiration date indicated in the package.

6.4 Storage Condition

Store at temperatures not exceeding 30°C.

6.5 Availability

Aluminum /Aluminum blister pack of 10's (box of 60 film-coated tablets)

6.6 Instructions for Use and Handling

No special requirements.

CAUTION

Foods, Drugs, Devices and Cosmetics Act prohibits dispensing without prescription.

ADMINISTRATIVE DATA

MARKETING AUTHORIZATION HOLDER (PRODUCT REGISTRATION HOLDER)

Eisai (Singapore) Pte Ltd
152 Beach Road
#15-07/08 Gateway East
Singapore 189721

MARKETING AUTHORIZATION NUMBER (PRODUCT REGISTRATION NUMBER)
SIN15146P

DATE OF FIRST AUTHORIZATION/RENEWAL OF AUTHORIZATION

16 Jan 2007 in EU

DATE OF REVISION OF PACKAGE INSERT

April 2023

Imported by:

Eisai (Singapore) Pte Ltd
152 Beach Road
#15-07/08 Gateway East
Singapore 189721

Distributed by:

Zuellig Pharma Pte Ltd
15 Changi North Way
#01-01
Singapore 498770

Manufactured by:

Bushu Pharmaceuticals Ltd. Misato Factory
950, Hiroki, Ohaza, Misato-machi, Kodama-gun,
Saitama-ken, Japan
Under License of Eisai Co., Ltd.

Packed by:

Eisai

Eisai Manufacturing Ltd
European Knowledge Centre
Mosquito Way, Hatfield,
Hertfordshire
AL10 9SN, United Kingdom

2006070