- Antiepileptic drug -

**INOVELON® Tablets 100 mg**
**INOVELON® Tablets 200 mg**

< Rufinamide preparation>

**CONTRAINDICATIONS (INOVELON is contraindicated in the following patients.)**
Patients with a history of hypersensitivity to any ingredients of INOVELON or triazole derivatives.

**DESCRIPTION**

1. **Composition**
   **100 mg Tablets**: Each light-red, scored, film-coated tablets contains 100 mg of rufinamide.
   It also contains croscarmellose sodium, light anhydrous silicic acid, microcrystalline cellulose, titanium oxide, red ferric oxide, magnesium stearate, talc, corn starch, lactose monohydrate, hypromellose, macrogol 600, and sodium lauryl sulfate as inactive ingredients.

   **200 mg Tablets**: Each light-red, scored, film-coated tablets contains 200 mg of rufinamide.
   It also contains croscarmellose sodium, light anhydrous silicic acid, microcrystalline cellulose, titanium oxide, red ferric oxide, magnesium stearate, talc, corn starch, lactose monohydrate, hypromellose, macrogol 600, and sodium lauryl sulfate as inactive ingredients.

2. **Product description**

<table>
<thead>
<tr>
<th>Brand name</th>
<th>Dosage form and identification code</th>
<th>Appearance</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Film-coated tablets</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>INOVELON Tablets 100 mg</strong></td>
<td>€261</td>
<td>Diameter (mm) 10.2 Width (mm) 5.4 Weight (mg) 187 Thickness (mm) 4.0</td>
<td>Oval, light red, scored</td>
</tr>
<tr>
<td>Film-coated tablets</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>INOVELON Tablets 200 mg</strong></td>
<td>€262</td>
<td>Diameter (mm) 15.2 Width (mm) 6.2 Weight (mg) 374 Thickness (mm) 4.5</td>
<td>Oval, light red, scored</td>
</tr>
</tbody>
</table>

**INDICATIONS**
Adjunctive therapy with other antiepileptic drugs for tonic and atonic seizures associated with Lennox-Gastaut syndrome showing insufficient response to other antiepileptics.

**DOSAGE AND ADMINISTRATION**

**Children ages ≥4 years**
Patients weighing 15.0-30.0 kg: Treatment should be initiated at an oral daily dose of 200 mg in two divided doses after meals for the first 2 days. The dose should be then gradually increased by up to 200 mg/day every two days. The maintenance dose should be 1000 mg/day in two divided doses after meals. The dose can be increased or decreased within a range not exceeding 1000 mg/day depending on patient’s condition, and should be increased by up to 200 mg/day at intervals not less than 2 days.

Patients weighing ≥30.1 kg: Dosage and administration for adults should be followed.

**Adults**
Treatment should be initiated at an oral daily dose of 400 mg in two divided doses after meals for the first 2 days. The dose should be then gradually increased by up to 400 mg/day every two days. The maintenance dose should be 1800 mg/day for patients weighing 30.1-50.0 kg, 2400 mg/day for patients weighing 50.1-70.0 kg, and 3200 mg/day for patients weighing 70.1 kg or over in two divided doses after meals. The dose can be increased or decreased within a range not exceeding the above maintenance dose depending on patient’s condition, and should be increased by up to 400 mg/day at intervals not less than 2 days.

Caution : Use only as directed by a physician.
2. Important Precautions

1. Careful Administration (INOVELON should be administered with care in the following patients.)
   (1) Patients with a history of allergy or rash to other antiepileptics. [Drug-induced hypersensitivity syndrome due to administration of INOVELON has been reported. See “Clinically significant adverse drug reactions” section.]
   (2) Patients with hepatic function disorder [Since INOVELON is metabolized in the liver, the blood concentration may increase. See “Important Precautions” section.]
   (3) Patients with congenital short QT syndrome [QT interval may be excessively shortened. See “Important Precautions” and “PHARMACOKINETICS” sections].

2. Important Precautions
   (1) Since status epilepticus may occur due to administration of INOVELON, the condition of the patient should be sufficiently monitored during treatment with this drug, and appropriate treatment should be taken if status epilepticus develops. If a new type of seizure develops or status epilepticus occurs more frequently after administration of INOVELON, the need for continuing treatment with INOVELON should be carefully evaluated.
   (2) Since administration of INOVELON may induce rash, INOVELON should be administered with care. In case of any abnormality, appropriate treatment should be taken such as discontinuing INOVELON. Early signs of rash are easily misdiagnosed as infection, particularly in children. Due care should be paid when symptoms such as rash and pyrexia develop.
   (3) Rapid dose reduction or discontinuation of INOVELON during the continued use may induce status epilepticus or worsening of epileptic seizures. When INOVELON is discontinued, the dose should be gradually decreased at least every two days over 1 week or more until discontinuation, except in cases in which INOVELON must be immediately discontinued in light of safety such as onset of rash.
   (4) Safety of INOVELON in patients with severe hepatic function disorder has not been investigated. INOVELON should thus be administered with careful attention to the condition of the patient only when expected therapeutic benefits are considered to outweigh the possible risks. Appropriate treatment such as dose adjustment should be taken as necessary.
   (5) Since administration of INOVELON may lead to excessively shortened QT interval, the drug should be administered in patients with congenital short QT syndrome only when expected therapeutic benefits are considered to outweigh the possible risks. The condition of the patient should be carefully observed by periodical electrocardiography before and during the treatment, etc. (See “PHARMACOKINETICS” section).
   (6) Since INOVELON may induce drowsiness and decreases in attentiveness, mental concentration, and reflex movement, patients should be cautioned against engaging in potentially hazardous activities requiring alertness, such as driving a car.

3. Drug Interactions
INOVELON is metabolized mainly by carboxylesterase (see “PHARMACOKINETICS” section).

Precautions for coadministration (INOVELON should be administered with care when coadministered with the following drugs.)

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Signs, Symptoms, and Treatment</th>
<th>Mechanism and Risk Factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium valproate</td>
<td>Since increase the concentration of INOVELON in the blood may occur, the dose of INOVELON should be adjusted as necessary.</td>
<td>The other drug inhibits carboxylesterase, a metabolizing enzyme, leading to a reduction in the clearance of INOVELON.</td>
</tr>
<tr>
<td>Phenytoin</td>
<td>Decrease the concentration of INOVELON in the blood may occur.</td>
<td>The mechanism is unclear.</td>
</tr>
<tr>
<td>Phenobarbital, primidone, carbamazepine</td>
<td>Decrease the concentration of INOVELON in the blood may occur.</td>
<td>The mechanism is unclear.</td>
</tr>
<tr>
<td>Drugs metabolized by CYP3A4 (or CYP3A5)</td>
<td>Promotion of metabolism of the other drugs may occur, possibly leading to reduced effects.</td>
<td>It is thought to be attributable to the induction of CYP3A4 by INOVELON.</td>
</tr>
<tr>
<td>Oral contraceptives ethinylestradiol, norethisterone</td>
<td>Promotion of metabolism of the other drugs may occur, possibly leading to reduced effects.</td>
<td>The mechanism is unclear.</td>
</tr>
</tbody>
</table>

4. Adverse Reactions
Of 58 patients who had received rufinamide by approval in the Japanese phase III study and long-term study, 41 patients (70.7%) experienced adverse drug reactions. Main
adverse reactions were somnolence (20.7%), decreased appetite (17.2%), vomiting (12.1%), and constipation (10.3%).

(1) Clinically significant adverse drug reactions\(^{Note}\)

1) Drug-induced hypersensitivity syndrome (incidence unknown): Early symptoms include rash and fever, and delayed type serious hypersensitivity symptoms may also develop along with lymphadenopathy, organ dysfunctions such as hepatic function disorder, leukocytosis, eosinophilia or development of atypical lymphocytes. Sufficient observation is thus required, and INOVELON should be discontinued and appropriate treatment should be performed if such symptoms occur.

2) Oculo-Muco-Cutaneous syndrome (Stevens-Johnson syndrome) (incidence unknown): Since Oculo-Muco-Cutaneous syndrome may occur, patients should be closely monitored. In the event of abnormalities including fever, ocular hyperemia, erythema, blisters / erosion, and sore throat, INOVELON should be discontinued and appropriate measures should be taken. Note) The incidence of adverse reactions reported only in overseas clinical studies and overseas post-marketing surveillance is regarded as unknown.

(2) Other adverse drug reactions\(^{Note}\)

If the following adverse reactions are noted, appropriate treatment should be taken depending on the severity of the symptoms.

<table>
<thead>
<tr>
<th>Hyper-sensitivity Note)</th>
<th>(\geq 10%)</th>
<th>3-10%</th>
<th>&lt; 3%</th>
<th>Incidence unknown Note)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastrointestinal</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Decreased appetite, vomiting, constipation</td>
<td>Nausea</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neuropsychiatric</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Somnolence</td>
<td>Dizziness, status epilepticus, agitation, headache</td>
<td>Psychomotor hyperactivity, ataxia, convulsion</td>
<td>Aggressive-ness, lethargy</td>
<td></td>
</tr>
<tr>
<td>Others</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight decrease</td>
<td></td>
<td></td>
<td></td>
<td>Fatigue, diplopia, blurred vision</td>
</tr>
</tbody>
</table>

\(Note)\: The incidence is shown based on the incidence of adverse reactions in Japanese clinical studies.
\(Note)\: The incidence of adverse reactions reported only in overseas clinical studies is regarded as unknown.
\(Note)\: In the event of such symptoms, treatment should be discontinued.

5. Use in the Elderly

Since elderly patients often have reduced physiological function, careful supervision is recommended. No clear differences in pharmacokinetics were noted between healthy elderly subjects and healthy adults in overseas studies. [See “PHARMACOKINETICS” section]

6. Use during Pregnancy, Delivery or Lactation

1) INOVELON should be administered in pregnant women or in women who may possibly be pregnant only when expected therapeutic benefits are considered to outweigh the possible risks.

[Animal studies reported that administration of INOVELON in pregnant rats enhanced decreases in food consumption and inhibition of weight gain compared with non-pregnant rats. When INOVELON was administered orally at 150 mg/kg in pregnant rats, the mortality rate of neonatal rats reportedly increased in the early period after birth and weight gain of neonatal rats was inhibited due to maternal toxicity.]

(2) Treatment with INOVELON should be avoided for mothers in lactation period. If treatment is unavoidable, nursing mothers should be instructed to discontinue breastfeeding. [When \(^{14}\)C-rufinamide was orally administered in rats and rabbits, it was reported to be excreted into breast milk.

7. Pediatric Use

The safety of INOVELON in low-birth-weight babies, neonates, infants, children aged <4 years or children weighing <15 kg has not been established. [No clinical experience of use in such patients is available in Japanese clinical studies]

8. Effects on Laboratory Tests

No antidotes to overdosage of INOVELON are known. In the event of an overdose, the patient should be closely monitored and measures such as inducing emesis and gastric lavage should be taken if necessary. INOVELON can be partially eliminated by hemodialysis. Implementation of hemodialysis should thus be considered depending on the severity of the symptoms.

9. Precautions concerning Use

Cautions in dispensing:

For drugs that are dispensed in a press-through package (PTP), instruct the patient to remove the drug from the package prior to use. [It has been reported that, if the PTP sheet is swallowed, the sharp corners of the sheet may puncture the esophageal mucosa, causing perforation and resulting in serious complications such as mediastinitis.]

10. Other Precautions

In 199 overseas placebo-controlled studies of various antiepileptic drugs in patients with epilepsy, psychiatric diseases, etc., the risks of suicidal ideation and suicide attempt in patients receiving antiepileptics were double those in patients receiving placebo (antiepileptic group, 0.43%; placebo group, 0.24%). Patients showing such symptoms in the antiepileptic group were 1.9 per 1000 patients more than in the placebo group (95% confidence interval, 0.6-3.9). In the subgroup of patients with epilepsy, such patients were 2.4 per 1000 patients more than in the placebo group.

PHARMACOKINETICS

1. Blood concentration

(1) Repeated administration (Foreign data)

The figure below shows the changes in mean plasma concentration and pharmacokinetic parameters at a steady state at 800, 1600, 2400, and 3200 mg/day \(^{Note}\) when rufinamide was orally administered at a starting dose of
Pharmacokinetic parameters with repeated administration of rufinamide

<table>
<thead>
<tr>
<th>Daily dose (mg/day)</th>
<th>n</th>
<th>Cmax (μg/mL)</th>
<th>tmax (hr)</th>
<th>AUC0-12 (μg·hr/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>800 mg/day</td>
<td>14</td>
<td>8.93 ± 1.89</td>
<td>3.00 (2.00, 6.04)</td>
<td>84.90 ± 22.80</td>
</tr>
<tr>
<td>1600 mg/day</td>
<td>14</td>
<td>15.58 ± 4.32</td>
<td>3.00 (3.00, 6.00)</td>
<td>153.00 ± 46.20</td>
</tr>
<tr>
<td>2400 mg/day</td>
<td>14</td>
<td>20.41 ± 5.75</td>
<td>3.50 (1.99, 6.01)</td>
<td>201.00 ± 65.70</td>
</tr>
<tr>
<td>3200 mg/day</td>
<td>10</td>
<td>23.18 ± 6.06</td>
<td>4.00 (2.00, 4.07)</td>
<td>229.00 ± 57.10</td>
</tr>
</tbody>
</table>

a) One patient who received rufinamide only at 800 mg/day was included in the calculation of mean plasma concentration-time profile, but not in the calculation of mean pharmacokinetic parameters.
b) Median value (minimum, maximum values)

(2) Effect of food (Foreign data)
When rufinamide was administered as a single oral dose of 400 mg in a fasting state and after meal, Cmax and AUC of rufinamide increased by 56% and 34%, respectively, with administration after meal compared with administration in a fasting state, while tmax and t1/2 remained in variable.  

2. Serum protein binding
34% (in vitro, concentration of 0.62-4.83 μmol/L) 

3. Metabolism
The main enzyme involved in metabolism of rufinamide in humans is carboxyesterase. The main metabolite is pharmacologically inactive. Oxidative metabolism by cytochrome P450 or glutathione conjugation was not observed in humans. 

4. Excretion (Foreign data)
When 14C-rufinamide was administered as a single oral dose of 600 mg after meal in healthy adult men, 66% of the administered dose was collected from the urine and 14% from the feces by 168 hours after administration. 

5. Elderly patients (Foreign data)
Pharmacokinetics of a single oral dose of rufinamide (400 mg) and repeated oral dose of rufinamide (800 mg/day) was evaluated in healthy elderly subjects (66-77 years) and healthy adults. The results showed no significant differences related to age in Cmax and AUC of rufinamide. 

6. Patients with renal function disorders (Foreign data)
When rufinamide 400 mg was orally administered as a single dose after meal in patients with renal function disorders (creatinine clearance, <30 mL/min), the pharmacokinetics were similar to those observed in healthy adults. In patients with renal function disorders who underwent dialysis 3 hours after receiving a single oral dose of rufinamide 400 mg after meal, Cmax and AUC decreased by 16% and 29%, respectively. 

7. Drug interactions
(1) Clinical studies (Foreign data)
(1) Antiepileptics
Effects of rufinamide on other antiepileptics
Results from population pharmacokinetic analysis showed that changes in plasma concentration of carbamazepine, lamotrigine, phenobarbital, and phenytoin stayed within 21% when these drugs were coadministered with rufinamide. Although rufinamide was expected to increase plasma phenytoin concentration by 7-21%, the plasma phenytoin concentration may exceed a model-predicted value as phenytoin shows a non-linear pharmacokinetics. No effects on topiramate and valproic acid were noted. 

Effects of other antiepileptics on rufinamide
Results from population pharmacokinetic analysis showed that carbamazepine, phenytoin, primidone, and phenobarbital decrease the plasma concentration of rufinamide. Meanwhile, valproic acid increases the plasma rufinamide concentration, and may increase the concentration up to 85%, particularly in patients weighing <30 kg. No effects of lamotrigine, topiramate, and benzodiazepines were noted. 

List of interaction of concomitant antiepileptics

<table>
<thead>
<tr>
<th>Type of concomitant antiepileptic</th>
<th>Effects of concomitant antiepileptic on the plasma concentration of rufinamide</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbamazepine</td>
<td>22-30% decrease (depends on the dose of carbamazepine)</td>
</tr>
<tr>
<td>Phenobarbital, phenytoin, primidone</td>
<td>26-50% decrease (depends on the plasma concentration of valproic acid)</td>
</tr>
<tr>
<td>Valproic acid</td>
<td>14-85% increase (depends on the body surface area and sex in addition to the effects of each concomitant antiepileptic agent (smaller body surface area and women have more effects).)</td>
</tr>
</tbody>
</table>

2) Triazolam
When rufinamide was orally administered repeatedly at 800 mg/day in two divided doses after meals for 11
days in 21 healthy adults, and the last dose was administered after meal concomitantly with triazolam 0.25 mg, C<sub>max</sub> and AUC of triazolam decreased by 24% and 36%, respectively, compared with a single administration of triazolam. 10)

3) Olanzapine When rufinamide was orally administered repeatedly at 800 mg/day (Note) in two divided doses after meals for 11 days in 19 healthy adult men, and the last dose was administered after meal concomitantly with olanzapine 5 mg, C<sub>max</sub> and AUC of olanzapine were unaffected compared with a single administration of olanzapine. 10)

4) Oral contraceptive (a combined drug of ethinyl estradiol 35 μg and norethisterone 1 mg) When rufinamide was orally administered repeatedly at 1600 mg/day (Note) in two divided doses after meals concomitantly with an oral contraceptive (once daily) for 14 days in 24 healthy adult women, C<sub>max</sub> and AUC of ethinyl estradiol coadministered with rufinamide decreased by 31% and 22%, respectively, compared with when administered without rufinamide. Meanwhile, C<sub>max</sub> and AUC of norethisterone decreased by 18% and 14%, respectively. 10)

(2) In vitro study
The study showed that metabolism of rufinamide by carbamoyltransferase may be inhibited by valproic acid. 11)

8. Effects on the QT interval (Foreign data)
QT<sub>cf</sub> was measured when rufinamide 2400, 3200, 4800, or 7200 mg/day or placebo was orally administered repeatedly in two divided doses after meals with gradual dose escalation every 3 days in 117 healthy adults, and moxifloxacin 400 mg was additionally administered as a single dose after meal following a 1-day off-treatment period in the placebo group. The QT<sub>cf</sub> interval was shortened up to 16.1-20.2 msec with rufinamide 2400-7200 mg/day, compared with placebo. 12)

Maximum difference in time-matched changes from baseline in QT<sub>cf</sub> intervals between rufinamide and placebo

<table>
<thead>
<tr>
<th>Drug</th>
<th>Time after administration (hr)</th>
<th>Maximum difference between drug and placebo [90% confidence interval] (msec)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rufinamide 2400 mg/day&lt;sup&gt;Note&lt;/sup&gt;</td>
<td>4</td>
<td>-16.7 [-20.3, -13.1]</td>
</tr>
<tr>
<td>Rufinamide 3200 mg/day&lt;sup&gt;Note&lt;/sup&gt;</td>
<td>8</td>
<td>-16.1 [-19.5, -12.7]</td>
</tr>
<tr>
<td>Rufinamide 4800 mg/day&lt;sup&gt;Note&lt;/sup&gt;</td>
<td>4</td>
<td>-20.2 [-24.2, -16.2]</td>
</tr>
<tr>
<td>Rufinamide 7200 mg/day&lt;sup&gt;Note&lt;/sup&gt;</td>
<td>4</td>
<td>-20.2 [-24.3, -16.1]</td>
</tr>
<tr>
<td>Moxifloxacin 400 mg/day</td>
<td>3</td>
<td>18.7 [14.9, 22.5]</td>
</tr>
</tbody>
</table>

Note) The dosages were different from the approved dosage and administration in Japan (See “DOSEAGE AND ADMINISTRATION” section)

CLINICAL STUDIES

1. Phase III study (double-blind comparative study)
A double-blind comparative study (concomitant treatment with other antiepileptics) of INOVELON versus placebo administered orally after meals was conducted for 12 weeks in 59 patients with Lenox-Gastaut syndrome aged 4-30 years with body weight of ≥15.0 kg. The maintenance dose was selected as 1000 mg/day for patients weighing 15.0-30.0 kg, 1800 mg/day for 30.1-50.0 kg, 2400 mg/day for 50.1-70.0 kg, and 3200 mg for ≥70.1 kg. The results showed that frequencies of tonic and atomic seizures decreased significantly in the INOVELON group compared with the placebo group. 13)

<table>
<thead>
<tr>
<th>Percent changes in frequencies of tonic and atomic seizures&lt;sup&gt;5&lt;/sup&gt;</th>
<th>Rufinamide group (28 patients)&lt;sup&gt;6&lt;/sup&gt;</th>
<th>Placebo group (30 patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median</td>
<td>24.20%</td>
<td>3.25%</td>
</tr>
<tr>
<td>Minimum</td>
<td>-93.5%</td>
<td>-81.6%</td>
</tr>
<tr>
<td>Maximum</td>
<td>27.2%</td>
<td>151.9%</td>
</tr>
<tr>
<td>Group difference&lt;sup&gt;7&lt;/sup&gt;</td>
<td>-26.55%</td>
<td>-40.30%, -11.80%</td>
</tr>
<tr>
<td>[90% confidence interval]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Superiority test&lt;sup&gt;8&lt;/sup&gt;</td>
<td>0.003</td>
<td></td>
</tr>
</tbody>
</table>

a) Rates of changes in seizure frequencies were calculated by converting the number of seizures noted during the periods of observation (4 weeks) and efficacy evaluation (2-week dose-escalation and 10-week dose-maintenance periods) into frequencies per 28 days for each period.
b) One patient in whom diagnosis of the target disease was considered inappropriate was excluded.
c) Hodges-Lehmann estimator
d) P-value of the Wilcoxon rank-sum test. The significance level was set at 10% for both sides.

2. Long-term study
A long-term (up to approximately 16.3 months) study was conducted in 54 patients who had completed the phase III study. The results showed a continuing reduction in frequencies of tonic and atomic seizures during each evaluation period. The rate of changes in tonic and atomic seizure frequencies (median value) 40 weeks after administration was -47.60%. The incidence of adverse reactions was 68.5% (37/54 patients). 14)

PHARMACOLOGY

1. Anticonvulsant activity
(1) Animal models of electroconvulsion INOVELON inhibited maximal electroshock seizure in mice and rats. The inhibitory effect was potent, with a lower effective dose (ED<sub>50</sub>) than that observed in models described in (2) below. 15)
(2) Animal models of drug-induced convulsion INOVELON inhibited pentylentetrazole-induced convulsion in mice, but not in rats. A high dose of INOVELON also partially inhibited picrotoxin-induced and strych-
nine-induced convulsions in mice.\(^{16}\)

(3) Kindling models
INOVELON inhibited the onset of convulsions in cats.\(^{17}\)

2. Mechanism of action
The precise mechanism(s) of action for rufinamide is unknown. However, the results of \textit{in vitro} studies suggest involvement of voltage-dependent sodium channels. Rufinamide slowed recovery of voltage-dependent sodium channels from an inactivated state in cerebral cortical neurons in rats. Rufinamide also inhibited persisting frequent firing of sodium-dependent action potentials in spinal cord nerve cells in mice.\(^{18}\)

**PHYSICOCHEMISTRY**

Nonproprietary name: Rufinamide
Chemical name: 1-(2, 6- Difluorobenzyl)-1H-1, 2, 3-triazole-4-carboxamide
Molecular formula: C\(_{10}\)H\(_8\)F\(_2\)N\(_4\)O
Molecular weight: 238.19
Structural formula:

![Structural formula of Rufinamide](image)

Description: Rufinamide is a white crystalline powder. It is slightly soluble in methanol and tetrahydrofuran, very slightly soluble in ethanol (99.5) and acetonitrile, and practically insoluble in water.

Melting point: Approximately 238 °C
Partition coefficient: \(\log P=0.65 \) (1-octanol/water)

**CONDITIONS FOR APPROVAL**

Until data have been accumulated for a certain number of patients after the release of INOVELON onto the market, background information about patients using INOVELON and data regarding safety etc. should be collected in early stages by conducting drug use investigation in all patients, then measures necessary for securing the proper use should be taken because the number of domestic subjects is limited.

**PACKAGING**

INOVELON Tablets 100 mg:
Boxes of 100 (10 Tabs. × 10) in press-through packages

INOVELON Tablets 200 mg:
Boxes of 100 (10 Tabs. × 10) in press-through packages

**REFERENCES**

1) In-house document: Phase I, repeated-dose study in non-Japanese healthy adults (overseas study)
2) In-house document: Study to evaluate food effects in non-Japanese healthy adults (overseas study)
3) In-house document: \textit{In vitro} protein binding rate of rufinamide in human plasma
4) In-house document: \textit{In vitro} metabolism of rufinamide
5) In-house document: Pharmacokinetic study of \(^{14}\)C-rufinamide administered as a single dose in healthy non-Japanese adults (overseas study)
6) In-house document: Phase I pharmacokinetic study of single and repeated doses in non-Japanese healthy elderly
7) In-house document: Pharmacokinetic study in patients with renal impairment (overseas study)
8) In-house document: Population-based pharmacokinetic analysis of concomitant antiepileptics
9) In-house document: Population-based pharmacokinetic analysis of rufinamide
12) In-house document: A study to evaluate QT/QTc in non-Japanese adults (overseas study)
13) In-house document: Phase III, double-blind, comparative study in patients with Lennox-Gastaut syndrome (Japanese study)
14) In-house document: Phase III, long-term, extension study in patients with Lennox-Gastaut syndrome (Japanese study)
15) In-house document: Effects on maximum electroconvulsion (in rats and mice)
16) In-house document: Effects on drug-induced convulsions (in mice)
17) In-house document: Effects on kindling (in cats)
18) In-house document: Effects on ion channels

**REQUESTS FOR LITERATURE AND PRODUCT INFORMATION SHOULD BE MADE TO:**
Customer Drug Information Service
Free Dial: 0120-419-497
Eisai Co., Ltd.

**Manufactured and marketed by:**
Eisai Co., Ltd.
6-10, Koishikawa 4-chome, Bunkyo-ku, Tokyo, 112-8088

**BRAND NAMES IN OTHER COUNTRIES**

BANZEL (USA)