PRESCRIBING INFORMATION

Inovelon® (rufinamide)

Please refer to the SmPC before prescribing. ***Presentation:*** Film coated tablets containing 100 mg, 200 mg or 400 mg rufinamide. Oral suspension 40mg/ml ***Indication:*** Adjunctive therapy in the treatment of seizures associated with Lennox-Gastaut syndrome in patients 1 year of age and older. ***Dose and administration:*** For oral use***.*** Inovelon should be administered twice daily in two equally divided doses with food in the morning and in the evening. Inovelon tablets can be broken in half or crushed and administered in half a glass of water. Inovelon oral suspension should be shaken vigorously before each administration.The oral suspension can be administered via an enteral feeding tube which must be flushed at least once with 1 ml of water following administration of the oral suspension. Inovelon oral suspension and Inovelon film coated tablets may be interchanged at equal doses. Patients should be monitored during the switch over period. Children from 1 year to less than 4 years of age not receiving valproate: Initial daily dose is 10 mg/kg/day (0.25 ml/kg/day) in two equally divided doses separated by approximately 12 hours and may be increased by up to 10 mg/kg/day every third day to a target dose of 45 mg/kg/day (1.125 ml/kg/day) (maximum recommended dose). Children from 1 year to less than 4 years of age receiving valproate: Initial daily dose is 10 mg/kg/day (0.25 ml/kg/day) in two equally divided doses separated by approximately 12 hours and may be increased by up to 10 mg/kg/day every third day to a target dose of 30 mg/kg/day (0.75 ml/kg/day) (maximum recommended dose). If the recommended calculated dose of Inovelon is not achievable, the dose should be given to the nearest whole 100 mg tablet or 0.5ml oral suspension. Children 4 years of age or older weighing < 30 kg not receiving valproate: Initial daily dose is 200 mg in two divided doses (or 5 ml dosing suspension given as two 2.5 ml doses, one in the morning and one in the evening) and may be increased by 200 mg/day increments, as frequently as every third day, up to a maximum dose of 1000 mg/day (or 25 ml/day). Children 4 years of age or older weighing < 30 kg receiving valproate: Initial daily dose is 200 mg in two divided doses and may be increased by 200 mg/day after a minimum of 2 days, up to a maximum dose of 600 mg/day (or 15 ml/day). Adults, adolescents and children 4 years or older of ≥ 30kg not receiving valproate: Initial daily dose is 400 mg in two divided doses (10 ml dosing suspension given as two 5 ml doses) and may be increased by 400 mg/day increments, as frequently as every other day, up to a maximum of 3200 mg/day (or 80 ml/day) based on patient weight (see SmPC). Adults, adolescents and children 4 years or older of ≥ 30kg receiving valproate: Initial daily dose is 400 mg in two divided doses (10 ml dosing suspension given as two 5 ml doses) and may be increased by 400 mg/day increments, as frequently as every other day, up to a maximum of 2200 mg/day (or 55 ml/day) based on patient weight (see SmPC). ***Elderly and patients with renal or hepatic impairment:*** No dosage adjustment required in elderly and renal impairment. Caution advised in mild to moderate hepatic impairment. Not recommended in severe hepatic impairment. ***Contra-Indications:*** Hypersensitivity to rufinamide, triazole derivatives or any excipients. ***Pregnancy:*** Inovelon should not be used during pregnancy, or in women of childbearing age not using contraceptive measures, unless clearly necessary. ***Lactation:*** Excretion into human breast milk is unknown. Breastfeeding should be avoided during maternal treatment with Inovelon. ***Warnings and Precautions:*** Cases of status epilepticus have been observed during clinical studies, which led to rufinamide discontinuation in 20% of the cases. The benefit risk ratio of the therapy should be reassessed if patients develop new seizure types and/or experience an increased frequency of status epilepticus. Withdraw gradually to reduce possibility of seizures on withdrawal and reduce dose by approximately 25% every two days. Inovelon has been associated with dizziness, somnolence, ataxia and gait disturbances which could increase the occurrence of accidental falls in this population, therefore patients and carers should exercise caution until they are familiar with the potential effects of Inovelon. Serious antiepileptic drug hypersensitivity syndrome including DRESS (Drug Reaction with Eosinophilia and Systemic Symptoms) and Stevens-Johnson syndrome have occurred with rufinamide. Signs, symptoms and manifestations included fever and rash associated with other organ system involvement, lymphadenopathy, liver function tests abnormalities and haematuria. Other organ system signs and symptoms may occur. If this reaction is suspected, rufinamide should be

discontinued and alternative treatment started. Closely monitor all patients on rufinamide who develop a rash. Rufinamide produced a decrease in QTc interval in a thorough QT study. However, the underlying mechanism and safety relevance is not known. Clinicians should use clinical judgment when assessing whether to prescribe rufinamide to patients at risk from further shortening of their QTc duration. Women of childbearing potential must use contraceptive measures during treatment with Inovelon. Inovelon tablets contain lactose, therefore patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take Inovelon. Inovelon oral suspension contains parahydroxybenzoates which may cause allergic reactions (possibly delayed). It also contains sorbitol and, therefore, should not be administered to patients with rare hereditary problems of fructose intolerance. Monitor patients for signs of suicidal ideation and behaviour and consider appropriate treatment. Patients and carers should also be advised to seek medical advice should such signs occur. ***Drug Interactions:*** Significant increases in rufinamide plasma concentrations may occur when co-administered with valproate. Consideration should be given to a dose reduction of rufinamide in patients who are initiated on valproate therapy. No significant changes in rufinamide concentration when co-administered with lamotrigine, topiramate or benzodiazepines or known enzyme inducing anti-epileptic medicinal products. Rufinamide appears to have no clinically relevant effect on carbamazepine, lamotrigine, phenobarbital, topiramate, phenytoin or valproate steady state concentrations. Rufinamide decreased the $AUC_{0\text{-}24}$ of a combined oral contraceptive (ethinyloestradiol 35 µg and norethindrone 1 mg). Women of child-bearing potential using hormonal contraceptives should use an additional safe and effective contraceptive method. Rufinamide does not inhibit the activity of cytochrome P450 enzymes thus clinically significant interactions mediated through the inhibition of cytochrome P450 system by rufinamide are unlikely. Rufinamide induces the CYP3A4 enzyme. Carefully monitor patients on drugs metabolised by the CYP3A enzyme system for two weeks at start of, or after the end of treatment with Inovelon, or after a marked change in dose. Dose adjustments should be considered when rufinamide is co-administered with drugs with a narrow therapeutic window such as warfarin and digoxin. No effects on the pharmacokinetics of olanzapine. No interaction data available with alcohol. ***Adverse effects:*** Please refer to the SmPC for full adverse effect details. The most common adverse reactions in the clinical development program were headache, dizziness, fatigue, and somnolence. Adverse reactions associated with Inovelon in clinical studies: Very common effects (≥1/10): somnolence, headache, dizziness, nausea, vomiting, fatigue. Common effects (≥1/100 to <1/10): pneumonia, influenza, nasopharyngitis, ear infection, sinusitis, rhinitis, anorexia, eating disorder, decreased appetite, anxiety, insomnia, status epilepticus, convulsion, coordination abnormal, nystagmus, psychomotor hyperactivity, tremor, diplopia, vision blurred, vertigo, epistaxis, abdominal pain upper, constipation, dyspepsia, diarrhoea, rash, acne, back pain, oligomenorrhoea, gait disturbance, weight decrease, head injury, contusion. Uncommon (≥1/1000 to <1/100): hypersensitivity and hepatic enzyme increase. ***Legal Category:*** POM ***Presentations:*** *Film-coated tablets:* Aluminium/aluminium blisters; *Oral suspension*: Oriented-polyethylene terephthalate (o-PET) bottle with a child-resistant polypropylene (PP) closure. ***Basic UK NHS cost:*** Inovelon Film-coated tablets 100 mg: packs of 10 £5.15, Inovelon Film-coated tablets 200 mg: packs of 60 £61.77, Inovelon Film-coated tablets 400 mg: packs of 60 £102.96***.*** Oral Suspension 40mg/ml: 460ml bottle £94.71 ***Marketing authorisation numbers:*** Inovelon 100 mg: packs of 10 EU/1/06/378/001 (IRL), PLGB 33967/0018 (GB), Inovelon 200 mg: packs of 60 EU/1/06/378/009 (IRL), PLGB 33967/0019 (GB), Inovelon 400 mg: packs of 60 EU/1/06/378/014 (IRL), PLGB 33967/0021 (GB). Oral Suspension 40mg/ml: EU/1/06/378/017 (IRL), PLGB 33967/0020 (GB). ***Marketing authorisation holder:*** Eisai GmbH (IRL), Eisai Europe Limited (GB). ***Further Information from/Marketed by:*** Eisai Limited, European Knowledge Centre, Mosquito Way, Hatfield, Hertfordshire, AL10 9SN, UK. **Date of preparation**: April 2021. UK-INO-21-00002

Adverse events should be reported. Reporting forms and information can be found at https://yellowcard.mhra.gov.uk/ or search for the MHRA Yellow Card in the Google Play or Apple App Store, or Ireland: www.hpra.ie. Adverse events should also be reported to Eisai Ltd on +44 (0)845 676 1400/ +44 (0)208 600 1400 or EUmedinfo@eisai.net