PRESCRIBING INFORMATION

Zebinix® ***(eslicarbazepine acetate)***

Please refer to the SPC before prescribing. ***Presentation:*** Tablets containing 800 mg eslicarbazepine acetate. ***Indication:*** Adjunctive therapy in adults with partial-onset seizures with or without secondary generalisation ***Dose and administration:*** May be taken with or without food. Starting dose is 400 mg once daily, increased to 800 mg once daily after one or two weeks. Dose may be increased to 1200 mg once daily. Withdraw gradually to minimise the potential of increased seizure frequency. ***Elderly patients >65 years:*** No dose adjustment is needed in the elderly population provided that the renal function is not disturbed. ***Children and adolescents <18years of age:*** Not recommended. ***Patients with renal impairment*****:** Adjust dose according to creatinine clearance (CL_{CR}) and use with caution. Not recommended in severe impairment. ***Patients with hepatic impairment:*** No dose adjustment in mild to moderate impairment and use with caution in these patients. Not recommended in severe impairment. ***Contra-Indications:*** Hypersensitivity to the active substance, other carboxamide derivatives (e.g. carbamazepine, oxcarbazepine) or any excipients. Second or third degree AV block. ***Contraceptives:*** Interacts with oral contraceptives. Use an alternative method of contraception during treatment and up to the end of the current menstrual cycle after treatment has been stopped. ***Pregnancy:*** No data on the use of Zebinix in pregnant women. Carefully re-evaluate treatment if women become pregnant or plan to become pregnant. Refer to the SPC for further information. ***Lactation:*** Excretion in human breast milk is unknown. Breastfeeding should be discontinued during treatment. ***Warnings and precautions:*** May cause some CNS reactions such as dizziness and somnolence. Do not use with oxcarbazepine. Rash has been reported. Discontinue if signs or symptoms of hypersensitivity develop. Screen for allele HLA-B*1502 in individuals of Han Chinese, and Thai origin and consider screening in other Asian populations as this has been shown to be strongly associated with the risk of developing Stevens-Johnson syndrome (SJS) when treated with carbamazepine. Allele HLA-A*3101 has been shown to increase the risk of developing carbamazepine induced cutaneous adverse reactions including SJS, TEN, drug rash with eosinophilia (DRESS) or less severe acute generalised exanthematous pustulosis (AGEP) and maculopapular rash in patients of European descent and Japanese population. Hyponatraemia was reported by 1.2% of patients in trials. Examine serum sodium levels before and during treatment in patients with pre-existing renal disease or who are treated with medicinal products which may lead to hyponatraemia. Determine sodium serum levels if clinical signs of hyponatraemia occur. Discontinue if clinically relevant hyponatraemia develops. Prolongations in PR interval have been observed. Caution in patients with medical conditions or when taking concomitant medicinal products associated with PR prolongation. Monitor for signs of suicidal ideation and behaviours and advise patients (and caregivers) to seek medical advice if these occur. May affect ability to drive and use machines. ***Drug interactions:*** Has an inducing effect on the metabolism of medicinal products mainly eliminated by CYP3A4 (e.g. Simvastatin), therefore the dose of these products may need to be increased when used concomitantly with Zebinix. May have an inducing effect on the metabolism of medicinal products mainly eliminated by UDP-glucuronyl transferases. May take 2 to 3 weeks to reach the new level of enzyme activity when initiating, discontinuing or changing dose of Zebinix, therefore take time delay into account when using with other medicines that require dose adjustment. Interactions can arise when co-administering high doses with medicinal products mainly metabolised by CYP2C19 (e.g. phenytoin). Carbamazepine: Zebinix dose may need to be increased if used concomitantly with carbamazepine. Concomitant treatment with carbamazepine increased the risk of the diplopia, abnormal coordination and dizziness. An increase in other adverse reactions cannot be excluded. Phenytoin: An increase of Zebinix dose and a decrease of phenytoin dose may be required. Lamotrigine and topiramate: No dose adjustments are required. Valproate and levetiracetam: Concomitant administration appeared not to affect the exposure to eslicarbazepine but has not been verified by conventional interaction studies. Oral contraceptives: Interacts with the oral contraceptive. Simvastatin: An increase of the simvastatin dose may be required when used concomitantly with Zebinix. Rosuvastatin: concomitant administration reduced exposure to rosuvastatin. Monitor response to therapy (e.g. cholesterol levels). Warfarin: Can decrease exposure to S-warfarin. No effects on R-warfarin or coagulation. Monitoring of INR should be

performed in the first weeks after initiation or ending concomitant treatment. Digoxin: no effect. MAOIs: an interaction between eslicarbazepine acetate and MAOIs is theoretically possible. ***Adverse events:*** Adverse reactions were usually mild to moderate in intensity and occurred predominantly during the first weeks of treatment with Zebinix. Refer to SPC for all side effects. Very common effects (≥1/10): dizziness, somnolence. Common effects (≥1/100, <1/10): Hyponatraemia, decreased appetite, insomnia, headache, disturbance in attention, tremor, ataxia, balance disorder, diplopia, vision blurred, vertigo, nausea, vomiting, diarrhoea, rash, fatigue, gait disturbance, asthenia. Serious side effects: anaemia, hypersensitivity, hypothyroidism, aphasia, peripheral neuropathy, depression, psychomotor retardation, psychotic disorder, amnesia, convulsion, nystagmus, peripheral oedema, dehydration, visual impairment, ocular hyperaemia, palpitations, bradycardia, hypertension, hypotension, chest pain, alopecia, liver disorder, hypoacusis (uncommon frequency ≥1/1,000 to <1/100), pancreatitis, thrombocytopenia, leukopenia (rare frequency ≥1/10,000 to <1/1,000), Drug reaction with eosinophilia and systemic symptoms (DRESS) (not known frequency i.e. frequency cannot be estimated from available data). Some rare adverse reactions such as bone marrow depression, anaphylactic reactions, severe cutaneous reactions (e.g. SJS), systemic lupus erythematosus or serious cardiac arrhythmias did not occur during Zebinix clinical studies but have been reported with oxcarbazepine. Their occurrence during treatment with Zebinix cannot be excluded. Decrease in bone mineral density, osteopenia, osteoporosis and fractures were reported in patients on long-term therapy with structurally related oxcarbazepine and carbamazepine. ***Legal Category:*** POM. ***Basic UK NHS cost:*** Zebinix 800mg pack of 30 £136.00. ***Irish price to wholesaler:*** Zebinix 800mg pack of 30 €143.19. ***Marketing authorisation numbers:*** EU/1/09/514/012-020. ***Marketing authorisation holder:*** Bial-Portela & Cª., S.A. À Av. da Siderurgia Nacional 4745-457 S. Mamede do Coronado – Portugal. ***Further Information from:*** Eisai Limited, European Knowledge Centre, Mosquito Way, Hatfield, Herts, AL10 9SN, UK. **Date of preparation**: June 2015

Adverse events should be reported. For UK healthcare professionals: reporting forms and information can be found at www.mhra.gov.uk/yellowcard.
Adverse events should also be reported to Eisai Ltd on 0845 676 1400 or EUmedinfo@eisai.net