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# Clinical practice data demonstrates clinical effectiveness and tolerability of Zebinix® (eslicarbazepine acetate) as adjunctive therapy in epilepsy patients with psychiatric comorbidities

**Hatfield, UK | Porto, Portugal | 06 June 2019 –** Bial and Eisai today announce clinical practice data from the Euro-Esli study demonstrating clinical effectiveness of eslicarbazepine acetate, and that it is generally well tolerated as an adjunctive therapy in focal epilepsy patients with psychiatric comorbidities, including intellectual disability, compared with people with no psychiatric comorbidities.[1] The data, which add to the body of evidence on eslicarbazepine acetate as adjunctive therapy from Phase III studies,[2,3,4,5] were published in *Journal of the Neurological Sciences*.[1]

Psychiatric comorbidities, including intellectual disability and depression, are common for adults who have epilepsy.[6,7] Prevalence of psychiatric comorbidities may be twofold higher in adult patients with epilepsy compared to the general public, and up to a quarter of people diagnosed with epilepsy are estimated to have an intellectual disability.[6,7] Psychiatric comorbidities can exacerbate the effects and increase the impact of epilepsy.[8] Furthermore, antiepileptic treatments can interfere with treatments for the psychiatric comorbidities, and thus adversely affect these psychiatric conditions. [9,10] There are many considerations for treating this patient population, thereby complicating treatment choice.[10]

“The comorbidities of epilepsy represent a substantial burden for people with epilepsy. This data provides a significant insight into how eslicarbazepine acetate performs in a routine medical setting for these patients and the results are very encouraging, demonstrating eslicarbazepine acetate's efficacy and tolerability as an adjunctive therapy in this sub-set of patients,” comments Dr Colin Doherty, Consultant Neurologist, St James’s Hospital, Dublin, Ireland, and lead author of the Euro-Esli study.

This newly published data includes patient populations that are sometimes excluded from clinical trials, including those with psychiatric comorbidities, specific comorbidities of intellectual disability, or depression.[1,11] Adverse events reported during this sub-cut of the Euro-Esli study are consistent with eslicarbazepine acetate’s safety profile established in Phase III studies.[1,2,3,4,5] Adverse events with eslicarbazepine acetate treatment were reported by 43.1% of people with psychiatric comorbidities (n=122/283) and 45.8% of people with intellectual disability (n=49/107). The most common adverse events were dizziness (11.4%; n=31/272), somnolence (8.8%; n=24/272) and fatigue (8.1%; n=22/272) for people with psychiatric comorbidities; and somnolence (10.1%; n=10/99), dizziness (7.1%; n=7/99) and fatigue (6.1%; n=6/99) for people with intellectual disability.[1]

Psychiatric comorbidities

- Treatment with eslicarbazepine acetate in people with psychiatric comorbidities showed a responder rate of 83.1% (n=128/154) (defined by ≥50% seizure frequency reduction from baseline) at 12 months, compared with 82.5% (n=326/395) of people without psychiatric comorbidities (p=0.871). Seizure freedom was achieved by 51.3% of people with psychiatric comorbidities (n=79/154) (defined as no seizures since at least the prior visit) at 12 months with eslicarbazepine acetate treatment, compared with 51.4% (n=203/395) of people in the no psychiatric comorbidities group (p=0.984).[1]
- Adverse events were reported by 43.1% of people with psychiatric comorbidities (n=122/283) compared to 30.5% of people without psychiatric comorbidities (n=261/855; p<0.001). Psychiatric



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adverse events were reported by 3.7% of people with psychiatric comorbidities (n=10/272) compared to 1.8% of people without psychiatric comorbidities (n=15/822; p=0.076). Discontinuation of treatment with eslicarbazepine acetate due to adverse events occurred in 17.2% of people with psychiatric comorbidities (n=45/262) compared with 11.6% of people without psychiatric comorbidities (n=94/811; p=0.019).[1]

Intellectual disability

- Treatment with eslicarbazepine acetate in people with intellectual disability showed a responder rate of 60.3% (n=35/58) at 12 months, compared with 76.6% (n=222/290) of people without intellectual disability (p=0.010). Seizure freedom was achieved by 22.4% of people with intellectual disability (n=13/58) at 12 months with eslicarbazepine acetate treatment, compared with 43.1% (n=125/290) of people without intellectual disability (p=0.003).[1]
- Adverse events were reported by 45.8% of people with intellectual disability (n=49/107) compared to 32.6% of people without intellectual disability (n=275/844; p=0.007). Cognitive adverse events were reported by 4.0% of people with intellectual disability (n=4/99) compared to 3.8% of people without intellectual disability (n=31/809; p=0.919). Discontinuation of treatment with eslicarbazepine acetate due to adverse events occurred in 22.4% of people with intellectual disability (n=22/98) compared with 14.8% of people without intellectual disability (n=117/789; p=0.050).[1]

Depression

- Treatment with eslicarbazepine acetate in people with depression showed a responder rate of 81.0% (n=51/63) at 12 months, compared with 82.9% (n=402/485) of people without depression (p=0.703). Seizure freedom was achieved by 46.0% (n=29/63) of people with depression at 12 months with eslicarbazepine acetate treatment, compared with 52.0% (n=252/485) of people without depression (p=0.376).[1,12]
- Adverse events were reported by 42.6% of people with depression (n=60/141) compared to 32.4% of people without depression (n=322/993; p=0.017). Psychiatric adverse events were reported by 4.4% of people with depression (n=6/136) compared to 2.0% of people without depression (n=19/955; p=0.074). Discontinuation of treatment with eslicarbazepine acetate due to adverse events occurred in 18.5% of people with depression (n=24/130) compared with 12.1% of people without depression (n=114/939; p=0.044).[1]

The Euro-Esli study presents a clinical practice data set of eslicarbazepine acetate with 2,058 patients included.[13] The Euro-Esli study has a broad set of inclusion/exclusion criteria, allowing for the representation of people with conditions sometimes excluded from clinical trials.[13,14] The Euro-Esli study includes a diverse patient population with challenging comorbidities, and provides robust evidence to support clinical practice and treatment decisions.[13,14]

Eslicarbazepine acetate is approved in the European Union (EU) as adjunctive therapy in adults, adolescents and children aged above 6 years, with partial-onset seizures with or without secondary generalisation.[15] Eslicarbazepine acetate has also been approved in the EU as monotherapy in the treatment of partial-onset seizures, with or without secondary generalisation, in adults with newly diagnosed epilepsy in 2017.[15]

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**Notes to Editors**

**About the Euro-Esli study[1,13]**

The Euro-Esli study was an exploratory, retrospective, pooled analysis of data from European clinical practice studies, conducted to audit the effectiveness, safety and tolerability in clinical practice of eslicarbazepine acetate as an adjunctive treatment for focal-onset seizures.[13] Effectiveness was assessed after 3, 6 and 12 months of eslicarbazepine acetate treatment and at final follow-up, and safety and tolerability were assessed for the duration of eslicarbazepine acetate treatment.[13] The study protocol was approved by the Ethics Committee of Hospital Universitario y Politécnico La Fe, Valencia, Spain.[13]

A sub-analysis was conducted of data from patients included in the Euro-Esli study who had data available for psychiatric comorbidities, intellectual disability and depression. Patients with and without comorbidities were treated with eslicarbazepine acetate as adjunctive therapy and effectiveness was assessed after 3, 6, 12 months and at final follow up.[1] Safety and tolerability were assessed throughout treatment.

**About Zebinix® (eslicarbazepine acetate)**
Eslicarbazepine acetate is a voltage-gated sodium channel blocker, which selectively targets the slow inactivated state of the sodium ion channel.[16] The efficacy of eslicarbazepine acetate as adjunctive therapy has been demonstrated in four Phase III double-blind placebo-controlled studies in 1,703 randomised adult patients with partial epilepsy refractory to treatment with one to three concomitant antiepileptic medicinal products,[15] and as monotherapy in a double-blind, active controlled (carbamazepine controlled release) study, involving 815 randomised adult patients with newly diagnosed partial-onset seizures.[15] In addition, the efficacy and safety of eslicarbazepine acetate as adjunctive therapy for partial-onset seizures in children was evaluated in one Phase II study in 123 children aged 6 to 16 years[17] and one Phase III study in 304 randomised children aged from 2 to 18 years.[15]

Eslicarbazepine acetate is currently marketed in Europe and Russia by Bial and by Bial's licensee, Eisai Europe Limited, a European subsidiary of Eisai Co. Ltd., under the trade name Zebinix® or Exalief®. In the United States and Canada eslicarbazepine acetate (trade name Aptiom®) is marketed by Sunovion Pharmaceuticals Inc under an exclusive license from Bial.

**About BIAL**
Founded in 1924, BIAL's mission is to discover, develop, and provide therapeutic solutions within the area of health. In recent decades, BIAL has strategically focused on quality, innovation, and internationalisation.

BIAL is strongly committed to therapeutic innovation, investing 20% of its annual turnover in Research and Development (R&D) centred on the neurosciences and cardiovascular system.

BIAL expects to strengthen its international presence by continuing to deliver innovative medicines to healthcare professionals, patients and their families worldwide, always inspired by its strong motivation: "Keeping life in mind".

For more information about BIAL, please visit www.bial.com.

**About Eisai**
Eisai is a leading global research and development-based pharmaceutical company headquartered in Japan. We define our corporate mission as "giving first thought to patients and their families and to increasing the benefits health care provides," which we call our *human health care* (*hhc*) philosophy. With over 10,000 employees working across our global network of R&D facilities, manufacturing sites and marketing subsidiaries, we strive to realise our *hhc* philosophy by delivering innovative products in multiple therapeutic areas with high-unmet medical needs, including oncology and neurology.

For more information about Eisai please visit www.eisai.com.

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