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International/Pharma/Gesundheit

# Zebinix, Novel Once-Daily Anti-Epileptic Treatment, Launches in Spain

Hatfield, England (ots/PRNewswire) - Zebinix(R) (eslicarbazepine acetate), an add-on (adjunctive) therapy for adults with partial-onset seizures, with or without secondary generalisation (where the seizure spreads to both sides of the brain), has been launched today in Spain by Eisai and BIAL in a co-promotion.

In 2009, the European Commission approved Zebinix based on data showing that it reduces seizure frequency and improves health-related quality of life.[1]

Epilepsy is one of the most common neurological diseases, affecting up to 400,000 people in Spain[2] - and the successful treatment of partial-onset seizures (the most common type of epilepsy) remains a challenge. Up to 40% of patients with partial seizures do not achieve seizure control with current treatments.[3]

"There are many patients with epilepsy whose condition is difficult to treat with existing anti-epileptic drugs. Zebinix, developed by BIAL, is the outcome of its longstanding scientific commitment to CNS research and development, and its launch in Spain now offers a new therapeutic option which is shown to decrease seizure frequency and improve quality of life in those patients with poor seizure control," commented Mark Duffy, Business Development Director, BIAL

"Eisai's mission to regard patients and their families as the most important participants in the healthcare process is demonstrated by our continued commitment to epilepsy in Europe. By increasing our European footprint, we are able to bring valuable treatment options to more patients with epilepsy. The launch of Zebinix in Spain is a clear example of our dedication to this therapeutic area," commented Dr. Bettina Bauer, Head of EU Epilepsy Business Unit, Eisai Europe Ltd.

In its first year Zebinix has had over 9,000 months of patient exposure.[4] Zebinix is already available in Germany, Austria, United Kingdom, Denmark, Norway, Iceland, Sweden, Portugal* Albania*, Cyprus*, Malta* and Spain (co promotion with BIAL from launch).

*Exclusively by BIAL

Notes to Editors

Zebinix(R) is the EU trade name for eslicarbazepine acetate.

Zebinix(R) is under license from Bial.

About epilepsy, partial-onset seizures and their treatment

Epilepsy is a chronic neurological disease characterised by abnormal discharges of neuronal activity causing seizures. Clinically, these manifest as convulsions or jerking of muscles. Depending on the seizure type, seizures may be limited to one part of the body, or may be generalised to involve the whole body. Patients may also experience abnormal sensations, altered behaviour or altered consciousness. Epilepsy is a disorder with many possible causes. Often the cause of epilepsy is unknown. However, anything that disturbs the normal pattern of neuron activity - from illness to brain damage to abnormal brain development, can lead to seizures.

Epilepsy is characterised by abnormal firing of impulses from nerve cells in the brain. In partial-onset seizures, these bursts of electrical activity are initially focused in specific areas of the brain, but may become more generalised; the symptoms vary according to the affected areas. Nerve impulses are triggered via voltage-gated sodium channels in the nerve cell membrane.

Treatment of partial-onset seizures, the most common type of epilepsy, presents a constant challenge - up to 40% of patients with partial-onset seizures do not achieve seizure control with current anti-epileptic drugs.3

Furthermore, central nervous system related adverse events, such as lightheadedness (dizziness), somnolence (sleepiness), and cognitive slowing (attention and memory deficits), are highly prevalent with existing anti-epileptic agents. Hence, there is a need for new anti-epileptic agents that offer effective reduction in seizure frequency combined with a favourable safety profile.

About Zebinix (eslicarbazepine acetate)

Zebinix is indicated as adjunctive therapy in adults with

partial-onset seizures with or without secondary generalisation.1 Zebinix is a novel, once-daily, voltage-gated sodium channel blocker.[5],[6] It preferably targets the inactivated state of the ion channel, preventing its return to the active state, and thereby reduces repetitive neuronal firing.5,6 The efficacy of Zebinix has been demonstrated an initial proof-of-concept phase II study18 and three subsequent phase III randomised, placebo controlled studies in 1049 patients with refractory partial onset seizures.[5],[7],[8] Zebinix also significantly improved patient's health related quality of life (HRQoL) as measured by the QOLIE-31 score during a one year open label extension of the above three studies.[9],[10],[11],[12],[13] Zebinix is given orally once-daily.

Clinical data

The EU approval was based on data from a phase II and three phase III clinical trials. Patients in phase III had a history of at least four partial seizures per month despite treatment with up to three concomitant anti-epileptic drugs.

During the trials, patients were randomised to various dosages of Zebinix or placebo and after a 2-week titration period, were assessed over a 12-week maintenance period, with continued follow-up over a one year open-label period.

Efficacy

Over the 12-week maintenance period, Zebinix 800mg and 1200mg once-daily significantly reduced seizure frequency, and was significantly more effective than placebo.[5,7,8,14] Long-term safety and maintenance of therapeutic effect was demonstrated in one-year open-label extensions of these studies.[15],[16],[17]

Tolerability[5],[7],[8],[14],[18]

In the Phase II and III clinical trials adverse events mainly occurred during the first 6 weeks of treatment and the majority of patients experienced adverse events of mild to moderate intensity. After 6 weeks of treatment, there were no observed differences in the incidence of side effects between patients treated with Zebinix and the placebo group. Treatment-emergent adverse events affecting >10% of patients in the pivotal studies were dizziness, headache and somnolence.

Quality of life and depressive symptoms[9],[10],[11],[12],[13]

The effect of Zebinix on quality of life was assessed using the Quality of Life Epilepsy Inventory-31 (QOLIE-31) scale. There was a statistically and clinically significant improvement from baseline during long-term open-label therapy, including a mean relative improvement in overall quality of life ($p<0.001$ - $p<0.01$ across the three studies) and improvements in individual elements of the QOLIE-31 scale including seizure worry, emotional wellbeing, energy/fatigue, medication effects and social function.

Improvement in depressive symptoms was also measured using the Montgomery Asberg Depression Rating Scale (MADRS). During long-term, open-label therapy, Zebinix demonstrated a statistically significant improvement from baseline in the overall MADRS score ($p<0.0001$) and individual domains of the MADRS scale including pessimistic thoughts, concentration difficulties, apparent sadness and inner tension.

License Agreement

Eisai Europe Limited , a European subsidiary of Eisai Co., Ltd. , announced in February 2009 that it had entered into a license and co-promotion agreement with BIAL - Portela & C(a), S.A. (Headquarters: São. Mamede do Coronado, Portugal, Chairman: Luís Portela & CEO: António Portela, "BIAL"), which gave Eisai Europe Limited rights to sell BIAL's anti-epileptic drug Zebinix(R) (eslicarbazepine acetate) in Europe.

About Eisai Europe in Epilepsy

Eisai is committed to developing and delivering highly beneficial new treatments to help improve the lives of people with epilepsy. The development of anti-epileptic drugs (AEDs) is a major strategic area for Eisai in the European market.

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In Europe, Eisai currently has three marketed treatments including:

- Zonegran(R) (zonisamide) as adjunctive therapy in adult patients with partial-onset seizures, with or without secondary generalisation
- Zebinix(R) (eslicarbazepine acetate) as adjunctive therapy in adult patients with partial-onset seizures, with or without secondary generalization
- Inovelon(R) (rufinamide) for the treatment of seizures associated with

Lennox-Gastaut Syndrome

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About Eisai

Eisai is one of the world's leading R&D-based pharmaceutical companies, that has defined its corporate mission as "giving first thought to patients and their families and to increasing the benefits health care provides," which we call human health care (hhc).

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Eisai concentrates its R&D activities in three key areas:

- Integrative Neuroscience: Alzheimer's disease, multiple sclerosis, neuropathic pain, epilepsy, depression, etc
- Integrative Oncology: Anticancer therapies; tumour regression, tumour suppression, antibodies, etc and Supportive cancer therapies; pain relief, nausea, etc
- Vascular/Immunological Reaction: Acute coronary syndrome, atherothrombotic disease, sepsis, rheumatoid arthritis, psoriasis, Crohn's disease, etc

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With operations in the U.S., Asia, Europe and its domestic home market of Japan, we employ more than 10,000 people worldwide, and reported consolidated sales of over GBP3.53 billion in FY2007, an increase of 8.9% year on year. In Europe, Eisai undertakes sales and marketing operations in over 20 markets, including the United Kingdom, France, Germany, Italy, Spain, Switzerland, Sweden, Ireland, Austria, Denmark, Finland, Norway, Portugal, Iceland, Czech Republic, Hungary, and Slovakia.

For further information please visit our web site www.eisai.co.jp

About BIAL

Founded in 1924, BIAL is an international pharmaceutical group with products available in more than 40 countries throughout four continents. BIAL is a privately held Portuguese research based pharmaceutical company and the largest Portuguese pharmaceutical company, based in S. Mamede do Coronado, Portugal, responsible for the research and development of eslicarbazepine acetate (Zebinix).

It is the partner of choice for many companies, having a strong

presence in the Iberian peninsula as well as in over 10 countries in Latin America and in around 20 French or Portuguese speaking African countries.

BIAL is strongly committed to therapeutic innovation investing more than 20% of its turnover in research and development every year. Key research areas for BIAL are the central nervous system, the cardiovascular system and allergen immunotherapy. BIAL currently has several other innovative programs under development, which the company expects to bring to the market within the next years, thereby strengthening its position throughout Europe.

Further information about BIAL can be found at http://www.bial.com

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Rückfragehinweis:
CONTACT: For further information please contact: Benjamyn Tan / HelenSwift, Tonic Life Communications, +44(0)20-7798-9262,benjamyn.tan@toniclc.com / helen.swift@toniclc.com; Eisai Europe Ltd,Cressida Robson, +44(0)845-676-5318



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