News Release

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EISAI IS APPALLED BY ARBITRARY DECISION TO REMOVE LIFE-EXTENDING BREAST CANCER THERAPY HALAVEN® (ERIBULIN) FROM CANCER DRUGS FUND

Decision means that thousands of women in England with secondary breast cancer will no longer have access to this treatment

Hatfield, UK, 08 January 2015 – Eisai today announces its extreme disappointment that the National Cancer Drugs Fund (NCDF) panel has apparently made the decision to remove Halaven® (eribulin) from the Cancer Drugs Fund (CDF), following a process of arbitrary evaluation. The decision failed to recognise the overall survival benefit of eribulin, putting a flawed and inconsistent methodological process before the overall survival benefit for people living with terminal cancer. The news is particularly devastating for the thousands of women living with secondary breast cancer in the UK who could benefit from this innovative life-extending treatment.

“Access to the CDF has ensured that drugs like eribulin have become the standard of care for women with metastatic breast cancer in England. This evaluation now means that these women can no longer be treated with the drugs thousands before them have benefited from,” commented Dr Vivek Misra, Consultant in Clinical Oncology at The Christie, Manchester.

Metastatic breast cancer is a very difficult condition to treat and only 13% of women will survive beyond five years. Eribulin remains the only single agent chemotherapy to significantly improve overall survival in women with advanced breast cancer after anthracycline and taxane treatment. To date, eribulin is the sixth most prescribed treatment in the CDF and has been used by more than 2,000 women in England since 2011.

Eribulin is indicated for the treatment of women with locally advanced or metastatic breast cancer who have progressed after at least one chemotherapeutic regimen for advanced disease. Prior therapy should have included an anthracycline and a taxane in either the adjuvant or metastatic setting, unless patients were not suitable for these treatments.[1]

“Eribulin is an effective drug and thanks to the Cancer Drugs Fund, I have been able to prescribe it extensively to my patients. I have witnessed first-hand the positive impact the treatment can have on women living with metastatic breast cancer, both in quality of life and overall life extension,” commented Dr Hartmut Kristeleit, Consultant Medical Oncologist at Guy’s and St Thomas’ NHS Foundation Trust.

“The NCDF decision implies that doctors have spent years prescribing ineffective treatments to patients, at an obvious cost to the NHS. I do not believe this is the case, nor would eribulin have received Marketing Authorisation Approval here and across the world without very sound clinical data. It’s for this reason that I believe the decision is a mistake,” commented Dr Chris Twelves, Professor of Clinical Cancer Pharmacology and Oncology, and Honorary Consultant in Medical Oncology at the

University of Leeds and St James's Institute of Oncology, who presented the benefits of eribulin to the NCDF panel.

"To say that we are disappointed by this decision would be a gross understatement; we are outraged. We will engage in further dialogue with the NCDF and NHS England and firmly stand by the clinical efficacy of eribulin. We would like to ask the Prime Minister for a pause in the process and now call on the Government to stop arbitrarily de-listing these drugs and allow women with secondary breast cancer to continue to benefit from these treatments," commented Gary Hendler, President & CEO Eisai EMEA and President, Eisai Oncology Global Business Unit.

The NCDF decision is particularly regrettable given the need for direct foreign investment into the UK and may ultimately mean Eisai is forced to scale back its operations in the country. This news comes just weeks after Eisai opened a new multi-million pound manufacturing plant for a new cancer treatment in Hatfield, Hertfordshire.

Eribulin was first approved and launched in the UK in 2011 and Marketing Authorisation Approval was extended for earlier use in advanced breast cancer from the European Commission on 3 July 2014. Eribulin is currently approved in more than 55 countries around the world including all of the European Union, Canada, United States, Russia, Switzerland, South Korea, Japan and Singapore.

Eisai is dedicated to the discovery, development and production of innovative oncology therapies that can make a difference and impact the lives of patients and their families. This passion for people is part of Eisai's *human health care (hhc)* mission, which strives to better understand the needs of patients and their families to increase the benefits health care provides.

ENDS

Notes to Editors

Halaven® (eribulin)
Eribulin is the first in the halichondrin class of microtubule dynamics inhibitors with a novel mechanism of action. Structurally eribulin is a simplified and synthetically produced version of halichondrin B, a natural product isolated from the marine sponge *Halichondria okadai*. Eribulin is believed to work by inhibiting the growth phase of microtubule dynamics which prevents cell division.

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Global Phase III Study 305 (EMBRACE)[2]
EMBRACE (Eisai Metastatic Breast Cancer Study Assessing Treatment of Physician's Choice (TPC) Versus Eribulin E7389) was an open-label, randomised, global, multi-centre, parallel two-arm study designed to compare overall survival in women treated with eribulin versus a TPC arm. TPC was defined as any single-agent chemotherapy, hormonal treatment or biologic therapy approved for the treatment of cancer; or palliative treatment or radiotherapy administered according to local practice. The study included 762 participants with metastatic breast cancer (MBC) who previously had been treated with at least two and a maximum of five prior chemotherapies, including an anthracycline and a taxane. The vast majority (96%) of participants in the TPC arm received chemotherapy.

In the total Phase III EMBRACE study population, eribulin was shown to prolong median overall survival in heavily pre-treated women with MBC compared to women receiving TPC by 2.7 months (13.2 vs. 10.5 HR 0.81 (95% CI 0.67, 0.96) nominal p=0.014). A pre-planned analysis of participants from Region 1 of the study (North America/Western Europe/Australia) showed a significant median overall survival benefit of eribulin over TPC of 3.0 months (nominal p=0.031).

The most commonly reported adverse reactions among people treated with eribulin in the EMBRACE study were fatigue (asthenia), a decrease in infection-fighting white blood cells (neutropenia), hair loss (alopecia), numbness and tingling in arms and legs (peripheral neuropathy), nausea and constipation. Peripheral neuropathy was the most common adverse event leading to discontinuation from eribulin, occurring in less than 5% of the women involved in the EMBRACE trial. Neutropenia only led to eribulin discontinuation for 0.6%. Death due to serious side effects, discontinuation and dose interruptions to treatment were lower in the eribulin arm of the trial compared with the TPC arm.

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Global Phase III Study 301[3]

Study 301 was an open-labelled, randomised, two-parallel-arm, multicentre study of eribulin versus capecitabine in 1,102 women with locally advanced or metastatic breast cancer previously treated with anthracyclines and taxanes, either in the (neo) adjuvant setting or for locally advanced or metastatic disease. Women in the study received zero to two previous chemotherapies for advanced disease.

The study opened in 2006 and the last patient was randomised in 2010. Patients were randomised to treatment with either eribulin 1.23mg/m^2 (administered intravenously over two to five minutes on days 1 and 8, every 21 days) or capecitabine 1.25 g/m^2, administered orally twice daily on day 1 to 14, every 21 days.

Study 301 had a co-primary endpoint of overall survival and progression free survival. The study demonstrated a trend favouring improved overall survival with eribulin compared to capecitabine in the ITT population, although the improvement was not statistically significant. Women treated with eribulin had a median overall survival of 15.9 months (HR 0.879; 95% CI: 0.770-1.003; p=0.056) versus 14.5 months with capecitabine. The trial did not meet the pre-specified endpoint for progression-free survival, with 4.1 and 4.2 months for eribulin and capecitabine (independent review) respectively (HR 1.079; 95% CI: 0.932-1.250; p=0.305).

1-, 2- and 3- year overall survival rates for eribulin versus capecitabine showed an early improvement which was maintained throughout the study (1 year, 64.4% eribulin vs 58.0% capecitabine (p=0.0351), 2 year 32.8% eribulin vs. 29.8% capecitabine (p=0.324), 3 year, 17.8% eribulin vs. 14.5% capecitabine (p=0.175).

Unlike studies conducted today, Study 301 included all women regardless of their human epidermal growth factor receptor 2 (HER2), oestrogen receptor (ER) or progesterone receptor (PR) status. Patients are usually tested for their HER2 status as there are now effective treatments specifically for patients with the HER2 mutation. HER2 positive patients would generally be treated with anti-HER2 positive targeted therapy. For women with HER2 negative MBC (n=755), overall survival was 15.9 months for eribulin vs. 13.5 months for capecitabine (HR 0.838; 95% CI: 0.715-0.983). In the HER2 positive population, overall survival was 14.3 months for eribulin vs. 17.1 months for capecitabine (HR; 95% 0.965; CI: 0.688-1.355).

Adverse events in Study 301 were consistent with the known profile of both drugs.

Metastatic Breast Cancer and the HER2 Protein

Over 300,000 women are diagnosed with breast cancer in Europe every year, of whom about one third subsequently develop metastatic disease.[4,5] Metastatic disease is an advanced stage of the disease that occurs when cancer spreads beyond the breast to other parts of the body.

HER2 is a protein that is found on the surface of cells. In HER2-positive breast cancer there is more (over expression) of this protein found on the surface of tumour cells compared with normal breast cells. This protein can be targeted with HER2 targeted therapies such as Herceptin, in people who overexpress HER2, but not in people with normal levels of HER2 protein (HER2-negative) breast cancer. Breast cancers are routinely tested for the presence of HER2 to decide the most appropriate treatment. Triple-negative breast cancer (TNBC) refers to any breast cancer that does not express the genes for oestrogen receptor, progesterone receptor (<1%) and HER2 (<30%).

Eisai in Oncology

Our commitment to meaningful progress in oncology research, built on scientific expertise, is supported by a global capability to conduct discovery and preclinical research, and develop small molecules, therapeutic vaccines, and biologic and supportive care agents for cancer across multiple indications.

About Eisai Co., Ltd.

Eisai Co., Ltd. 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.

As a global pharmaceutical company, our mission extends to patients around the world through our investment and participation in partnership-based initiatives to improve access to medicines in developing and emerging countries.

For more information about Eisai Co., Ltd., please visit www.eisai.com.

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