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Eisai Co., Ltd.

U.K. NICE RECOMMENDS ANTICANCER AGENT HALAVEN® AS TREATMENT FOR ADVANCED BREAST CANCER

Eisai Co., Ltd. (Headquarters: Tokyo, CEO: Haruo Naito, "Eisai") announced today that its in-house developed anticancer agent Halaven® (eribulin mesylate, "eribulin") has been recommended by the U.K. National Institute for Health and Clinical Excellence (NICE) as a treatment for patients with locally advanced or metastatic breast cancer who have received at least two chemotherapeutic regimens for advanced disease (prior therapy may have included an anthracycline or a taxane, and capecitabine) in NICE's Final Appraisal Determination (FAD).[1] Eribulin is the first breast cancer treatment to be recommended by NICE since 2007.[2]
Following the issue of the FAD by NICE, eribulin will be eligible for reimbursement for this indication via the National Health Service in England (NHS England).

The Appraisal Committee considered that the models suggest Eribulin offers a mean overall survival benefit of more than 3 months. According to the FAD, "In light of the short life expectancy at this stage of breast cancer, the committee considered this overall survival benefit to be substantial. The committee concluded that eribulin met the end-of-life criteria objectively and robustly and that it can be considered a life-extending, end-of-life treatment."

Eribulin was approved in Europe in March 2011 as a treatment for patients with locally advanced or metastatic breast cancer who have received at least two chemotherapeutic regimens for advanced disease. Prior therapy should have included an anthracycline and a taxane in either the adjuvant or metastatic setting. The agent was launched in the U.K. in April 2011. Furthermore, eribulin was approved in June 2014 for an expanded indication to include patients 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).

Eisai regards oncology as a key therapeutic area and is aiming to discover revolutionary new medicines with the potential to cure cancer. Eisai remains committed to providing further clinical evidence and expanding patient access for eribulin, and by maximizing the value of the drug, seeks to contribute further to addressing the diverse needs of, and increasing the benefits provided to, patients with cancer, their families, and healthcare providers.

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[Notes to editors]

1. About Halaven (eribulin mesylate, "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. In addition, recent non-clinical studies showed that eribulin is associated with increased vascular perfusion and permeability in tumor cores.[3] Eribulin promotes the epithelial state and decreases the capacity of breast cancer cells to migrate.[4]

Eribulin was first approved in November 2010 in the United States as a treatment for patients with metastatic breast cancer who have received at least two chemotherapeutic regimens for the treatment of metastatic disease. Prior therapy should have included an anthracycline and a taxane in either the adjuvant or metastatic setting. Eribulin is currently approved for use in the treatment of breast cancer in approximately 60 countries worldwide, including Japan and countries in Europe, the Americas and Asia. In Japan, eribulin has been approved to treat inoperable or recurrent breast cancer and was launched in the country in July 2011. In addition, eribulin has been approved in countries in Europe and Asia indicated as a treatment for patients 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.

Regarding soft tissue sarcoma, eribulin was approved in the United States for the treatment of patients with unresectable or metastatic liposarcoma who have received a prior anthracycline-containing regimen in January 2016, approved in Japan for the treatment of soft tissue sarcoma in February 2016, and approved in Europe for the treatment of adult patients with unresectable liposarcomas who have received prior anthracycline containing therapy (unless unsuitable) for advanced or metastatic disease in May 2016. Applications seeking approval for use in the treatment of soft tissue sarcoma are currently under review in countries including Switzerland, Australia, Brazil and Malaysia.

2. About NICE's New Approach to the Appraisal and Funding of Cancer Drugs

The former Cancer Drugs Fund (CDF) was established in 2009 as a means to improve patients' access to new cancer drugs including those which were "Not Recommended" by NICE. These drugs would be evaluated and listed in the CDF with their costs reimbursed through the fund. However, due to a severe increase in financial burden, a new scheme for NICE appraisal and funding of cancer drugs, including a new CDF, came into operation on July 29, 2016. All novel cancer drugs that had been newly approved would undergo NICE appraisal while cancer drugs that were listed in the former CDF would be eligible for reappraisal by NICE under the new scheme depending on the judgment of each company. The NICE appraisal process consists initially of an Appraisal Consultation Document, the issue of a Final Appraisal Determination, and ultimately the setting of Final Guidance. While cancer drugs that are "Recommended" are eligible for reimbursement through the NHS England, drugs that are "Not Recommended" require an Individual Funding Request (IFR) to be deliberated on a case-by-case basis, and therefore their use is greatly limited. Cancer drugs that could possibly be recommended but are judged to lack sufficient evidence can be given a "Limited Recommendation under the CDF", with provisional access secured under the CDF for a maximum of two years. After receiving this designation, NICE conducts a reappraisal based on the new evidence, and ultimately determines whether to either "Recommend" or "Not Recommend" the drug.

[1] "Life-extending breast cancer drug approved by NICE in draft guidance", NICE, accessed: November 3, 2016 https://www.nice.org.uk/news

[2] "Cancer patients 'denied access' to latest drugs"; The Times, accessed October 31, 2016: http://www.thetimes.co.uk/article/cancer-patients-denied-access-to-latest-drugs-b2l9xxg6n

[3] Funahashi Y et al. Eribulin mesylate reduces tumor microenvironment abnormality by vascular remodeling in preclinical human breast cancer models. *Cancer Sci.,* 2014; 105, 1334-1342

[4] Yoshida T et al. Eribulin mesilate suppresses experimental metastasis of breast cancer cells by reversing phenotype from epithelial-mesenchymal transition (EMT) to mesenchymal-epithelial transition (MET) states. *Br J Cancer,* 2014; 110, 1497-1505