EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

19 September 2013
EMA/CHMP/572965/2013
Committee for Medicinal Products for Human Use (CHMP)

Summary of opinion[1] (initial authorisation)

Kadcyla

Trastuzumab emtansine

On 19 September 2013, the Committee for Medicinal Products for Human Use (CHMP) adopted a positive opinion, recommending the granting of a marketing authorisation for the medicinal product Kadcyla, 100 mg and 160 mg, powder for concentrate for solution for infusion intended for the treatment of adult patients with HER2-positive, unresectable locally advanced or metastatic breast cancer who previously received trastuzumab and a taxane, separately or in combination.

The applicant for this medicinal product is Roche Registration Ltd. They may request a re-examination of any CHMP opinion, provided they notify the European Medicines Agency in writing of their intention within 15 days of receipt of the opinion.

The active substance of Kadcyla is trastuzumab emtansine, an antineoplastic agent (L01XC14) which contains the monoclonal antibody trastuzumab linked to a cytotoxic agent DM1 and acts by the mechanism of actions of both its components; trastuzumab by binding to HER2 extracellular domain mediates antibody dependent cell -mediated cytotoxicity inhibits shedding of the HER2 ECD and signalling through the PI3-K pathway, whereas targeted delivery of DM1 confers selective cytotoxicity to malignant cells by binding to tubulin and inducing apoptosis.

The benefits with Kadcyla have been shown in a phase III randomised multicentre, international, open label clinical study. In this study, efficacy has been shown in terms of an increased overall survival in patients who received Kadcyla (median duration of survival 30.9 months) compared with patients who received control treatment of lapatinib plus capecitabine (25.1 months) and increased progression free survival (9.6 months versus 6.4 months). The most common side effects with trastuzumab emtansine are haemorrhage (including epistaxis), increased transaminases, fatigue, musculoskeletal pain, and headache.

A pharmacovigilance plan for Kadcyla will be implemented as part of the marketing authorisation.

The approved indication is: Kadcyla, as a single agent, is indicated for the treatment of adult patients with HER2-positive, unresectable locally advanced or metastatic breast cancer who previously received trastuzumab and a taxane, separately or in combination. Patients should have either:

[1] Summaries of positive opinion are published without prejudice to the Commission decision, which will normally be issued 67 days from adoption of the opinion.

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- Received prior therapy for locally advanced or metastatic disease, or
- Developed disease recurrence during or within six months of completing adjuvant therapy.

Kadcyla should be prescribed by physicians experienced in the treatment of cancer patients. Patients treated with trastuzumab emtansine should have HER2 positive tumour status, defined as a score of 3 + by immunohistochemistry (IHC) or a ratio of ≥ 2.0 by in situ hybridization (ISH) assessed by a CE-marked In Vitro Diagnostic (IVD) medical device. If a CE-marked IVD is not available, the HER2-status should be assessed by an alternate validated test.

In order to prevent medication errors it is important to check the vial labels to ensure that the medicinal product being prepared and administered is Kadcyla (trastuzumab emtansine) and not Herceptin (trastuzumab).

Detailed recommendations for the use of this product will be described in the summary of product characteristics (SmPC), which will be published in the European public assessment report (EPAR) and made available in all official European Union languages after the marketing authorisation has been granted by the European Commission.

The CHMP, on the basis of quality, safety and efficacy data submitted, considers there to be a favourable benefit-to-risk balance for Kadcyla and therefore recommends the granting of the marketing authorisation.