

PRESCRIBING INFORMATION

Kadcyla® (trastuzumab emtansine) Please refer to Summary of Product Characteristics (SmPC) prior to use of Kadcyla. 100 mg powder for concentrate for solution for infusion, 160 mg powder for concentrate for solution for infusion.

Indications: 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 received prior therapy for locally advanced or metastatic disease, or developed disease recurrence during or within six months of completing adjuvant therapy.

Dosage and Administration: Patients should have HER2-positive tumour status, scored as 3+ by immunohistochemistry or a ratio of ≥ 2.0 by *in situ* hybridization. Kadcyla should be administered by a healthcare professional at a dose of 3.6 mg/kg bodyweight as an intravenous (IV) infusion every 3 weeks (21 day cycle). Kadcyla should not be mixed with glucose. Use of in-line filter is required for the infusion when the concentrate for infusion is diluted with sodium chloride 9 mg/ml (0.9%) solution for infusion (refer to SmPC). Initial dose should be administered as 90 minute IV infusion, followed by 90 minutes of observation for infusion-related reactions (IRR). If well tolerated, subsequent doses may be administered as 30 minute infusions, followed by 30 minutes of observation. If a dose is missed, it should be administered as soon as possible; the dosing schedule adjusted to maintain a 3-week cycle. To prevent medication errors check vial labels to ensure the medicinal product being prepared and administered is Kadcyla (trastuzumab emtansine) and not Herceptin (trastuzumab).

Contraindications: Hypersensitivity to trastuzumab emtansine or any excipients.

Precautions: Management of symptomatic adverse reactions may require temporary interruption, dose reduction, or treatment discontinuation; monitor patients closely for these adverse reactions. Symptomatic adverse reactions may include IRR, increased transaminases, hyperbilirubinemia, decreased left ventricular ejection fraction (LVEF), peripheral neuropathy, interstitial lung disease (ILD), including pneumonitis, nodular regenerative hyperplasia, or hypersensitivity reactions. Refer to SmPC for management of adverse reactions. Monitor patients with thrombocytopenia and patients on anti-coagulant treatment closely, and monitor platelet counts in all patients prior to each dose. Cases of bleeding events with a fatal outcome have been observed. Perform standard cardiac function testing prior to initiation and at regular intervals. Monitor liver function prior to initiation of treatment and each dose. Patients with baseline elevation of ALT may be predisposed to liver injury with a higher risk of a Grade 3-5 hepatic event or liver function test increase. Patients with dyspnoea at rest due to complications of advanced malignancy and co-morbidities may be at increased risk of pulmonary events.

Drug Interactions: No formal interaction studies have been performed. *In vitro* studies suggest that concomitant use of strong CYP3A4 and CYP3A5 inhibitors should be avoided. If not possible, consider a delay in administration of Kadcyla until the CYP3A4 inhibitor has cleared. If Kadcyla treatment cannot be delayed, monitor patients closely.

Pregnancy and Lactation: See box titled "Enhanced Safety Reporting for Potential Kadcyla-Exposed Pregnancies".

Adverse reactions: The most common serious reactions seen in clinical trials were haemorrhage, pyrexia, dyspnoea, musculoskeletal pain, thrombocytopenia, abdominal pain and vomiting. *Very common and common reactions:* urinary tract infection, thrombocytopenia, anaemia, neutropenia, leucopenia, drug hypersensitivity, hypokalaemia, insomnia, peripheral neuropathy, headache, dizziness, dysgeusia, memory impairment, dry eye, conjunctivitis, blurred vision, lacrimation increased, left ventricular dysfunction, haemorrhage, hypertension, epistaxis, cough, dyspnea, stomatitis, diarrhoea, vomiting, nausea, constipation, dry mouth, abdominal pain, dyspepsia, gingival bleeding, rash, pruritus, alopecia, nail disorder, palmar-plantar erythrodysesthesia syndrome, urticaria, musculoskeletal pain, arthralgia, myalgia, fatigue, pyrexia, asthenia, chills, peripheral oedema, transaminases increased blood alkaline phosphatase increased, infusion related reactions. *Other serious reactions:* Pneumonitis (ILD), hepatic failure. *Laboratory abnormalities:* Both hepatic and haematological abnormalities were observed.

Legal Category: POM

Presentation, Basic NHS Cost and Marketing Authorisation Number:

Kadcyla (trastuzumab emtansine) one 100mg glass vial - £1641.01. EU/1/13/885/001.

Kadcyla (trastuzumab emtansine) one 160mg glass vial - £2625.62. EU/1/13/885/002.

Marketing Authorisation Holder: Roche Registration Limited, 6 Falcon Way, Shire Park, Welwyn Garden City, AL7 1TW, United Kingdom
Kadcyla® is a registered trade mark

RXUKMEDI00223(1)

Date of Preparation: February 2016

▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions.

Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard. Adverse events should also be reported to Roche Products Ltd. Please contact Roche Drug Safety Centre by emailing welwyn.uk_dsc@roche.com or calling +44(0)1707 367554. As Kadcyla is a biological medicine, healthcare professionals should report adverse reactions by brand and batch number.

Enhanced Safety Reporting for Potential Kadcyla-Exposed Pregnancies

If a pregnancy occurs while using Kadcyla or within 7 months following the last dose of Kadcyla, please immediately report the pregnancy to the Roche Drug Safety centre by emailing welwyn.uk_dsc@roche.com or calling +44(0) 1707 367554.

Additional information will be requested during a Kadcyla-exposed pregnancy and the first year of the infant's life. This will enable Roche to better understand the safety of Kadcyla and to provide appropriate information to Health Authorities, Healthcare Providers and patients.

Contraception in males and females

Women of childbearing potential should use effective contraception while receiving Kadcyla and for 7 months following the last dose of Kadcyla. Male patients or their female partners should also use effective contraception.

Pregnancy

There are no data from the use of Kadcyla in pregnant women. Trastuzumab, a component of Kadcyla, can cause foetal harm or death when administered to a pregnant woman. In the post-marketing setting, cases of oligohydramnios, some associated with fatal pulmonary hypoplasia, have been reported in pregnant women receiving trastuzumab. Animal studies of maytansine, a closely related chemical entity of the same maytansinoid class as DM1, suggest that DM1, the microtubule inhibiting cytotoxic component of Kadcyla, is expected to be teratogenic and potentially embryotoxic.

Administration of Kadcyla to pregnant women is not recommended and women should be informed of the possibility of harm to the foetus before they become pregnant. Women who become pregnant must immediately contact their doctor. If a pregnant woman is treated with Kadcyla, close monitoring by a multidisciplinary team is recommended.

Breast-feeding

It is not known whether Kadcyla is excreted in human milk. Since many medicinal products are excreted in human milk and because of the potential for serious adverse reactions in breast-feeding infants, women should discontinue breast-feeding prior to initiating treatment with Kadcyla. Women may begin breast-feeding 7 months after concluding treatment.

Fertility

No reproductive and developmental toxicology studies have been conducted with Kadcyla.