HER2-positive metastatic breast cancer: Dosing distinctions between
PrKADCYLA® (trastuzumab emtansine), as a single agent, is indicated for the treatment of patients with HER2-positive, metastatic breast cancer (mBC) who received both prior treatment with PrHERCEPTIN® (trastuzumab) and a taxane, separately or in combination. Patients should have either received prior therapy for metastatic disease, or developed disease recurrence during or within 6 months of completing adjuvant therapy.

HERCEPTIN is indicated for the treatment of patients with early stage breast cancer with ECOG 0-1 status, whose tumours overexpress HER2,
• following surgery and after chemotherapy
• following adjuvant chemotherapy consisting of doxorubicin and cyclophosphamide, in combination with paclitaxel or docetaxel
• in combination with adjuvant chemotherapy consisting of docetaxel and carboplatin.
The benefit of the adjuvant treatment with HERCEPTIN for low risk patients not given adjuvant chemotherapy are unknown.

HERCEPTIN is indicated for the treatment of patients with metastatic breast cancer whose tumours overexpress HER2.

HERCEPTIN can be used in combination with PrPERJETA® (pertuzumab) and docetaxel for the treatment of patients with HER2-positive metastatic breast cancer who have not received prior anti-HER2 therapy or chemotherapy for metastatic disease. For information on the use of HERCEPTIN in combination with PERJETA and docetaxel, consult the Product Monograph for PERJETA.

Roche Patient Assistance Program (RPAP)
To enrol patients into the RPAP, please call 1-855-224-2233 or fax 1-855-212-7977.

If you require this information in an accessible format, please contact Roche at 1-800-561-1759.

*Comparative clinical significance has not been established.
There is a risk of medication errors between KADCYLA (trastuzumab emtansine) and HERCEPTIN (trastuzumab). In order to minimize this risk, check the vial labels to ensure that the drug being prepared and administered is KADCYLA (trastuzumab emtansine) and not HERCEPTIN (trastuzumab).

KADCYLA (trastuzumab emtansine) should be prescribed using both the trade name and non-proprietary name.
- Do not substitute KADCYLA for or with HERCEPTIN
- Do not administer KADCYLA at doses greater than 3.6 mg/kg

Dosage Forms and Strengths
KADCYLA SINGLE-USE VIALS
Available vial sizes (mg)
- KADCYLA is supplied in 100 mg and 160 mg vials.
- Single-use vials contain sterile powder for concentrate for infusion solution.

Vials and Vial Cap Colors
Single-use 100 mg WHITE cap
Single-use 160 mg PURPLE cap

Reconstitution
Reconstitution volumes
- 100 mg vial reconstituted with 5 mL of Sterile Water for Injection (SWFI) to yield 5 mL of 20 mg/mL of KADCYLA.
- 160 mg vial reconstituted with 8 mL of SWFI to yield 8 mL of 20 mg/mL of KADCYLA.

Dilution
The volume of solution required should be determined based on the dose to be administered and added to an infusion bag containing 250 mL of 0.45% sodium chloride or 0.9% sodium chloride.
- 0.45% sodium chloride may be used without a 0.2-micron in-line (non-protein adsorptive)/0.22-micron polyethersulfone (PES) filter.
- With 0.9% sodium chloride, a 0.2-micron in-line (non-protein adsorptive)/0.22-micron polyethersulfone (PES) filter is required.
Dextrose (5%) solution should not be used since it causes aggregation of the protein. KADCYLA should not be mixed or diluted with other drugs.
Recommended Doses and Schedules for Breast Cancer

For 3-weekly schedule in metastatic breast cancer

Initial and subsequent doses
• The recommended dose is 3.6 mg/kg administered as an intravenous infusion every 3 weeks (21-day cycle). Patients should be treated until disease progression or unacceptable toxicity.
• Do not substitute KADCYLA for or with HERCEPTIN.
• Do not administer KADCYLA at doses greater than 3.6 mg/kg.
• Do not administer as an intravenous push or bolus.

Dosing schedule
• Initial dose should be administered as a 90-minute intravenous infusion.
• If prior infusion was well tolerated, subsequent doses may be administered as 30-minute infusions.

Monitoring
Observe patients for fever, chills, or other infusion-related reactions during each infusion.
• 90-minute infusions: patients should be observed for at least 90 minutes.
• 30-minute infusions if prior infusion was well tolerated: patients should be observed for at least 30 minutes.

For weekly schedule in early and metastatic breast cancer

Loading dose
• The recommended initial loading dose is 4 mg/kg HERCEPTIN.

Maintenance dose
• The recommended weekly maintenance dose is 2 mg/kg HERCEPTIN.

Dosing schedule
• Initial loading dose can be administered as a 90-minute infusion.
• Maintenance doses can be administered as 30-minute infusions if the initial loading dose was well tolerated.
• HERCEPTIN should not be administered as an IV push or bolus.

Monitoring
• Patients should be observed for fever and chills or other infusion-associated symptoms during the initial dose and subsequent weekly doses.

For 3-weekly schedule in early breast cancer only

Loading dose
• The recommended initial loading dose is 8 mg/kg HERCEPTIN.

Maintenance dose
• The recommended maintenance dose is 6 mg/kg HERCEPTIN.

Dosing schedule
• Initial loading dose can be administered as a 90-minute infusion.
• Maintenance doses can be administered as 30-minute infusions if the initial loading dose was well tolerated.
• HERCEPTIN should not be administered as an IV push or bolus.

Monitoring
• Patients should be observed for fever and chills or other infusion-associated symptoms during the initial dose and subsequent weekly doses.

Appropriate aseptic technique should be used to reconstitute and dilute KADCYLA. Please refer to the KADCYLA Product Monograph for the complete instructions for reconstitution and dilution.

KADCYLA is associated with adverse events (AEs) that may require dose modifications, dose holding or treatment discontinuation.

Please see the KADCYLA Product Monograph for dose adjustment information and additional important safety information.

Appropriate aseptic technique should be used to reconstitute and dilute HERCEPTIN. Please refer to the HERCEPTIN Product Monograph for the complete instructions for reconstitution and dilution.

When using HERCEPTIN in combination with PERJETA and docetaxel for treatment of patients with HER2-positive metastatic breast cancer, consult Product Monographs for PERJETA and docetaxel for further information, such as dose adjustment, sequence of administration of each medication and duration of treatment.

HERCEPTIN is associated with adverse events (AEs) that may require dose holding or treatment discontinuation.

Please see the HERCEPTIN Product Monograph for complete dosing information and additional important safety information.
**KADCYLA**

**Indications and clinical use:**
KADCYLA (trastuzumab emtansine), as a single agent, is indicated for the treatment of patients with HER2-positive, metastatic breast cancer (mBC) who received both prior treatment with HERCEPTIN (trastuzumab) and a taxane, separately or in combination. Patients should have either received prior therapy for metastatic disease, or developed disease recurrence during or within 6 months of completing adjuvant therapy.

**Most serious warnings and precautions:**
- Risk of Medication Errors between KADCYLA (trastuzumab emtansine) and HERCEPTIN (trastuzumab): In order to minimize this risk, check the vial labels to ensure that the drug being prepared and administered is KADCYLA (trastuzumab emtansine) and not HERCEPTIN (trastuzumab). KADCYLA should be prescribed using both the trade name and non-proprietary name.
- Liver Toxicity: Hepatotoxicity, liver failure and death have occurred in KADCYLA-treated patients. Monitor hepatic function prior to initiation and prior to each dose. Institute dose modifications or permanently discontinue as appropriate.
- Cardiotoxicity: KADCYLA may lead to reductions in left ventricular ejection fraction (LVEF). Assess LVEF prior to initiation. Monitor during treatment and withhold dosing or discontinue as appropriate.
- Embryo-fetal Toxicity: Exposure to KADCYLA can cause fetal harm or death of the fetus. Advise women of potential risk to the fetus.

**Other relevant warnings and precautions:**
- Hematologic: thrombocytopenia, bleeding, cases of bleeding events with a fatal outcome
- Infusion-related reactions
- Hypersensitivity reactions, including serious, anaphylactic-like reactions
- Temporary discontinuation of treatment with KADCYLA in patients experiencing Grade 3 or 4 peripheral neuropathy and consideration of dose reduction on retreatment
- Cases of interstitial lung disease (ILD), including pneumonia, some leading to acute respiratory distress syndrome or a fatal outcome. Signs and symptoms may or may not occur as part of an infusion-related reaction. It is recommended that treatment with KADCYLA be permanently discontinued in patients who are diagnosed with ILD or pneumonitis.
- Extravasation
- Use of contraception in women of childbearing potential who are taking KADCYLA and for at least 6 months after treatment has concluded.

**Nursing Women:** Women should discontinue nursing prior to initiating treatment with KADCYLA.

**Other warnings and precautions:**
- Less definitive benefit in PFS and OS in patients ≥65 years of age.
- Potential need for dose adjustment in patients with severe renal impairment cannot be determined due to insufficient data.
- Thrombocytopenia in Asian patients.

**For more information:**
Please consult the Product Monograph at [http://rochecanada.com/PMs/Kadcyla/Kadcyla_PM_E.pdf](http://rochecanada.com/PMs/Kadcyla/Kadcyla_PM_E.pdf) for important information relating to adverse reactions, drug interactions, and dosing information which have not been discussed in this piece.

The Product Monograph is also available by calling us at 1-888-762-4388.

**HERCEPTIN**

**Indications and clinical use:**
HERCEPTIN (trastuzumab) is indicated for the treatment of patients with early stage breast cancer with ECOG 0-1 status, whose tumours overexpress HER2,

- following surgery and after chemotherapy
- following adjuvant chemotherapy consisting of doxorubicin and cyclophosphamide, in combination with paclitaxel or docetaxel
- in combination with adjuvant chemotherapy consisting of docetaxel and carboplatin.

The benefit of the adjuvant treatment with HERCEPTIN for low risk patients not given adjuvant chemotherapy are unknown.

HERCEPTIN (trastuzumab) is indicated for the treatment of patients with metastatic breast cancer whose tumours overexpress HER2.

HERCEPTIN can be used in combination with PERJETA (pertuzumab) and docetaxel for the treatment of patients with HER2-positive metastatic breast cancer who have not received prior anti-HER2 therapy or chemotherapy for metastatic disease. For information on the use of HERCEPTIN in combination with PERJETA and docetaxel, consult the Product Monograph for PERJETA.

The safety and effectiveness of HERCEPTIN in pediatric patients have not been established.

**Contraindications:**
- Known hypersensitivity to trastuzumab, Chinese Hamster Ovary (CHO) cell proteins, or any component of this product.
- When using in combination with PERJETA (pertuzumab) and docetaxel, consult Product Monographs for PERJETA and docetaxel for further information on these drugs.

**Most serious warnings and precautions:**
- Cardiotoxicity: HERCEPTIN can result in the development of ventricular dysfunction and congestive heart failure. Evaluate left ventricular function in all patients prior to and during treatment with HERCEPTIN.
- Infusion Reactions; Pulmonary Toxicity: Discontinue HERCEPTIN for infusion reactions manifesting as anaphylaxis, angioedema, interstitial pneumonitis, or acute respiratory distress syndrome.
- Embryo-Fetal Toxicity: Exposure to HERCEPTIN during pregnancy can result in impairment of fetal renal growth and/or renal function impairment resulting in oligohydramnios and oligohydramnios sequence manifesting as pulmonary hypoplasia, skeletal abnormalities, intrauterine growth retardation and neonatal death.

See full Product Monograph for complete boxed warnings.

**Other relevant warnings and precautions:**
- Exacerbation of chemotherapy-induced neutropenia
- Thrombosis/Embolism
- Of 903 patients evaluated in MBC trials, human anti-human antibody (HAHA) to trastuzumab detected in 1 patient, who had no allergic manifestations
- Ability to Drive and Use Machines: Patients experiencing infusion-related symptoms should be advised not to drive or use machines until symptoms resolve completely.
- Pregnant Women: See full Product Monograph for complete warning. HERCEPTIN should not be used during pregnancy unless the potential benefit for the mother outweighs the potential risk to the fetus.
- Nursing Women: A decision should be made whether to discontinue nursing, or discontinue drug, taking into account the elimination half-life of trastuzumab and the importance of the drug to the mother.
- Geriatric patients.
- Selection of Patients / Diagnostic Tests (Breast Cancer): HERCEPTIN should only be used in patients whose tumours overexpress HER2 as determined by immunohistochemistry. For inclusion criteria in terms of HER2 expression in clinical trials in EBC see Clinical Trials section of the Product Monograph.
- Patients with a known hypersensitivity to benzyl alcohol. Benzyl alcohol has been associated with toxicity in neonates and children up to 3 years old.
- Hypersensitivity reactions including anaphylaxis, infusion-associated reactions and pulmonary events.
- When using in combination with PERJETA (pertuzumab) and docetaxel, consult Product Monographs for PERJETA and docetaxel for further information on these drugs.

**For more information:**
Please consult the Product Monograph at [http://www.rochecanada.com/PMs/Herceptin/Herceptin_PM_E.pdf](http://www.rochecanada.com/PMs/Herceptin/Herceptin_PM_E.pdf) for important information relating to warnings and precautions, adverse reactions, drug interactions, and dosing information (including administration and preparation for administration) which have not been discussed in this piece.

The Product Monograph is also available by calling us at 1-888-762-4388.

Please see KADCYLA and HERCEPTIN Product Monographs for dose modification information and additional important safety information.