Ado-trastuzumab emtansine: Drug information

(For additional information see "Ado-trastuzumab emtansine: Patient drug information ")

For abbreviations and symbols that may be used in Lexicomp (show table)

ALERT: US Boxed Warning

Do not interchange:

Do not substitute ado-trastuzumab emtansine (Kadcyla) for or with trastuzumab (Herceptin).

Hepatotoxicity:

Serious hepatotoxicity has been reported, including liver failure and death. Monitor serum transaminases and bilirubin prior to initiation of treatment and prior to each dose. Reduce the dose or discontinue ado-trastuzumab emtansine as appropriate in cases of increased serum transaminases or total bilirubin.

Cardiotoxicity:

Ado-trastuzumab emtansine administration may lead to reductions in left ventricular ejection fraction (LVEF). Evaluate left ventricular function in all patients prior to and during treatment. Withhold treatment for a clinically significant decrease in left ventricular function.

Pregnancy:

Exposure to ado-trastuzumab emtansine during pregnancy can result in embryo-fetal harm. Advise patients of these risks and the need for effective contraception.

Brand Names: US

Kadcyla

Brand Names: Canada

Kadcyla

Pharmacologic Category

Antineoplastic Agent, Anti-HER2; Antineoplastic Agent, Antibody Drug Conjugate; Antineoplastic Agent, Antimicrotubular; Antineoplastic Agent, Monoclonal Antibody

Dosing: Adult

Note: Do not substitute ado-trastuzumab emtansine (US) or trastuzumab emtansine (Canada) for or with conventional trastuzumab; products are different and are **NOT** interchangeable.

Breast cancer, metastatic, HER2+: IV: 3.6 mg/kg every 3 weeks until disease progression or unacceptable toxicity; Maximum dose: 3.6 mg/kg

Missed or delayed doses: If a planned dose is missed or delayed, administer as soon as possible (at the dose and rate most recently tolerated), do not wait until the next planned cycle. Then adjust schedule to maintain a 3-week interval between doses.

Dosing: Geriatric

Refer to adult dosing.

Dosing: Renal Impairment

CrCl ≥30 mL/minute: No dosage adjustment necessary.

CrCl <30 mL/minute: There are no dosage adjustments provided in the manufacturer's labeling (has not been studied).

Dosing: Hepatic Impairment

Hepatic impairment prior to treatment initiation:

Mild to moderate impairment (Child-Pugh class A or B): No dosage adjustment necessary; use with caution.

Severe impairment (Child-Pugh class C): There are no dosage adjustments provided in the manufacturer's labeling (has not been studied).

Hepatotoxicity during treatment: Refer to dosage adjustment for toxicity for dose level reductions:

Grade 2 ALT, AST elevations (>2.5 to ≤5 times ULN): Continue at same dose level.

Grade 3 ALT, AST elevations (>5 to ≤20 times ULN): Withhold until ALT, AST recover to ≤grade 2, then resume with one dose level reduction.

Grade 4 ALT, AST elevations (>20 times ULN): Permanently discontinue treatment.

Grade 2 hyperbilirubinemia (>1.5 to ≤3 times ULN): Withhold until bilirubin recovers to ≤grade 1 (≤1.5 times ULN), then resume at the same dose level.

Grade 3 hyperbilirubinemia (>3 to ≤10 times ULN): Withhold until bilirubin recovers to ≤grade 1, then resume with one dose level reduction.

Grade 4 hyperbilirubinemia (>10 times ULN): Permanently discontinue treatment.

Concomitant ALT, AST >3 times ULN and total bilirubin >2 times ULN: Permanently discontinue treatment.

Nodular regenerative hyperplasia: Permanently discontinue treatment.

Dosing: Adjustment for Toxicity

Note: After a dose reduction is implemented, do not re-escalate dose.

Infusion-related reaction: Slow infusion rate or interrupt infusion. Permanently discontinue if life-threatening infusion reactions occur.

Dose levels for dosage reductions and/or discontinuation:

Starting dose: 3.6 mg/kg

First dose reduction: Reduce dose to 3 mg/kg

Second dose reduction: Reduce dose to 2.4 mg/kg

Further reductions necessary: Discontinue treatment.

Hematologic toxicity:

Grade 3 thrombocytopenia (platelets 25,000/mm^3 to <50,000/mm^3): Withhold treatment until platelet count recovers to ≤ grade 1 (platelets ≥75,000/mm^3), then resume treatment at the same dose level.

Grade 4 thrombocytopenia (platelets <25,000/mm^3): Withhold treatment until platelet count recovers to ≤ grade 1 (platelets ≥75,000/mm^3), then resume treatment with one dose level reduction.

Cardiotoxicity:

LVEF >45%: Continue treatment.

LVEF 40% to ≤45% and decrease is <10% points from baseline: Continue treatment and repeat LVEF assessment within 3 weeks.

LVEF 40% to ≤45% and decrease is ≥10% points from baseline: Withhold treatment and repeat LVEF assessment within 3 weeks; if repeat LVEF has not recovered to within 10% points from baseline, discontinue treatment.

LVEF <40%: Withhold treatment and repeat LVEF assessment within 3 weeks; if repeat LVEF is confirmed <40%, discontinue treatment.

HF (symptomatic): Discontinue treatment.

Peripheral neuropathy, grade 3 or 4: Temporarily discontinue until resolves to ≤ grade 2.

Pulmonary toxicity: Interstitial lung disease or pneumonitis: Permanently discontinue.

Dosage Forms

Excipient information presented when available (limited, particularly for generics); consult specific product labeling.

Solution Reconstituted, Intravenous [preservative free]:

Kadcyla: 100 mg (1 ea); 160 mg (1 ea) [contains mouse (murine) and/or hamster protein]

Generic Equivalent Available (US)

No

Administration

Check label to ensure appropriate product is being administered (ado-trastuzumab emtansine [US] or trastuzumab emtansine [Canada] and conventional trastuzumab are different products and are **NOT** interchangeable).

Infuse over 90 minutes (first infusion) or over 30 minutes (subsequent infusions if prior infusions were well tolerated) through a 0.2 or 0.22 micron inline nonprotein adsorptive polyethersulfone filter. Do not administer IV push or bolus. Do not administer with other medications.

Closely monitor infusion site during administration. Monitor patient during infusion for signs of infusion-related

reactions (eg, fever, chills); monitor for at least 90 minutes following initial infusion and (if tolerated) for at least 30 minutes following subsequent infusions.

Hazardous Drugs Handling Considerations

Hazardous agent (NIOSH 2016 [group 1]).

Use appropriate precautions for receiving, handling, administration, and disposal. Gloves (single) should be worn during receiving, unpacking, and placing in storage.

NIOSH recommends double gloving, a protective gown, ventilated engineering controls (a class II biological safety cabinet or a compounding aseptic containment isolator), and closed system transfer devices (CSTDs) for preparation. Double gloving, a gown, and (if dosage form allows) CSTDs are required during administration (NIOSH 2016).

Use **Breast cancer, metastatic:** Treatment (single-agent) of HER2-positive, metastatic breast cancer in patients who previously received trastuzumab and a taxane, separately or in combination, and have either received prior therapy for metastatic disease or developed disease recurrence during or within 6 months of completing adjuvant therapy.

Medication Safety Issues

Sound-alike/look-alike issues:

Ado-trastuzumab emtansine may be confused with pertuzumab, trastuzumab

Other safety concerns:

In the US, ado-trastuzumab emtansine (Kadcyla) may be confused with conventional trastuzumab (Herceptin); products are **not** interchangeable.

In Canada, trastuzumab emtansine (Kadcyla) may be confused with conventional trastuzumab (Herceptin); products are **not** interchangeable.

Adverse Reactions

>10%:

Central nervous system: Fatigue (36%), headache (28%), peripheral neuropathy (21%; grades 3/4: 2%), insomnia (12%)

Dermatologic: Skin rash (12%)

Endocrine & metabolic: Decreased serum potassium (33%; grade 3: 3%)

Gastrointestinal: Nausea (40%), constipation (27%), diarrhea (24%), abdominal pain (19%), vomiting (19%), xerostomia (17%), stomatitis (14%)

Hematologic & oncologic: Decreased platelet count (83% [nadir by day 8]; grade 3: 14%; grade 4:

3%), decreased hemoglobin (60%; grade 3: 4%; grade 4: 1%), decreased neutrophils (39%; grade 3: 3%; grade 4: <1%), hemorrhage (32%; grades 3/4: 2%), thrombocytopenia (31%; grades 3/4: 15%; Asians grades 3/4: 45%), anemia (14%; grades 3/4: 4%)

Hepatic: Increased serum AST (98%; grades 3/4: <8%), increased serum ALT (82%; grades 3/4: <6%), increased serum transaminases (29%), increased serum bilirubin (17%)

Neuromuscular & skeletal: Musculoskeletal pain (36%), arthralgia (19%), weakness (18%), myalgia (14%)

Respiratory: Epistaxis (23%), cough (18%), dyspnea (12%)

Miscellaneous: Fever (19%)

1% to 10%:

Cardiovascular: Peripheral edema (7%), hypertension (5%; grades 3/4: 1%), left ventricular dysfunction (2%; grades 3/4: <1%)

Central nervous system: Dizziness (10%), chills (8%)

Dermatologic: Pruritus (6%)

Endocrine & metabolic: Hypokalemia (10%; grades 3/4: 3%)

Gastrointestinal: Dyspepsia (9%), dysgeusia (8%)

Genitourinary: Urinary tract infection (9%)

Hematologic & oncologic: Neutropenia (7%; grades 3/4: 2%)

Hepatic: Increased serum alkaline phosphatase (5%)

Hypersensitivity: Hypersensitivity (2%)

Immunologic: Antibody development (5%)

Ophthalmic: Blurred vision (5%), conjunctivitis (4%), dry eye syndrome (4%), increased lacrimation (3%)

Respiratory: Pneumonitis (≤1%)

Miscellaneous: Infusion related reaction (1%)

<1%: Anaphylactoid reaction, hepatic encephalopathy, hepatotoxicity, nodular regenerative hyperplasia, portal hypertension

Contraindications

US labeling: There are no contraindications in the manufacturer's labeling.

Canadian labeling: Hypersensitivity to trastuzumab emtansine or any component of the formulation.

Warnings/Precautions

Concerns related to adverse effects:

• Bone marrow suppression: Thrombocytopenia may occur (nadir achieved by day 8; generally resolves to ≤ grade 1 by the next scheduled dose). The incidence of thrombocytopenia may be higher in patients of Asian ancestry. Monitor platelet count at baseline and prior to each dose. May require treatment interruption or dose reduction. Monitor closely if at bleeding risk due to thrombocytopenia and/or concomitant anticoagulant use. Has not been studied in patients with platelets <100,000/mm^3 at treatment initiation. Neutropenia and anemia have also occurred.

• Cardiotoxicity: **[US Boxed Warning]: May result in left ventricular ejection fraction (LVEF) reductions. Evaluate left ventricular function (in all patients) prior to and at least every 3 months during treatment; withhold for clinically significant left ventricular function decreases.** Treatment interruption or dosage reductions are required inpatients who develop decreased LVEF. Use has not been studied in patients with LVEF <50% at baseline, with a history of symptomatic CHF, serious arrhythmia, or recent history (within 6 months) of MI, or unstable angina.

• Extravasation reactions: Local reactions (erythema, irritation, pain, swelling, or tenderness) secondary to extravasation have been noted. These were generally mild and typically occurred within 24 hours of infusion. Monitor infusion site during infusion for possible infiltration.

• Hemorrhage: Hemorrhagic events, including central nervous system, respiratory, and gastrointestinal hemorrhage, have been observed; some hemorrhages were fatal. Some events occurred in patients who were receiving anticoagulation or antiplatelet therapy, or in patients with thrombocytopenia, although bleeding also occurred in patients without additional risk factors. Use caution when administering with antiplatelet agents or anticoagulants; consider additional monitoring when indicated.

• Hepatotoxicity: **[US Boxed Warning]: Serious hepatotoxicity, including liver failure and death, has been reported. Monitor transaminases and bilirubin at baseline and prior to each dose. Increases (transaminases or total bilirubin) may require dose reductions or discontinuation.** Hepatotoxicity is typically manifested by asymptomatic and transient increases in transaminases, although fatal cases of drug induced liver injury and hepatic encephalopathy have occurred; may be confounded by comorbidities or concomitant hepatotoxic medications. Use with caution in patients with hepatic impairment (has not been studied in patients with baseline serum transaminases >2.5 times ULN or bilirubin >1.5 times ULN, or in patients with active hepatitis B or C virus). Cases of nodular regenerative hyperplasia (NRH), a rare liver disorder characterized by widespread benign transformation of hepatic parenchyma into small regenerative nodules, have been observed (by biopsy). NRH may develop into noncirrhotic portal hypertension. Consider NRH in patients with clinical symptoms of portal hypertension and/or cirrhosis-like pattern seen on liver CT scan, although without associated transaminase elevations or other manifestations of cirrhosis. Diagnosis of NRH is confirmed by histopathology; permanently discontinue if histopathology confirms NRH.

• Hypersensitivity/infusion-related reactions: Infusion reactions (flushing, chills, fever, bronchospasm, dyspnea, wheezing, hypotension, and/or tachycardia) have been reported. After termination of infusion, these reactions generally resolved within several hours to a day. Medications for the treatment of reactions should be available for immediate use. Monitor closely for infusion reactions, especially during initial infusion. If reaction occurs, decrease infusion rate; for severe infusion reactions, interrupt infusion; permanently discontinue for life-threatening reactions. Serious allergic/anaphylactic reaction was observed (rare). Use is not recommended in patients who had trastuzumab permanently discontinued due to infusion reaction or hypersensitivity (has not been

evaluated).

• Peripheral neuropathy: Sensory peripheral neuropathy has been reported, usually grade 1, although grade 3 peripheral neuropathy was also described. Monitor for signs and symptoms of neuropathy. May require treatment interruption and/or dose reduction.

• Pulmonary toxicity: Interstitial lung disease (ILD), including pneumonitis has been reported; some cases resulted in acute respiratory distress syndrome and/or fatalities. Permanently discontinue with diagnosis of ILD or pneumonitis. Signs and symptoms of pneumonitis include dyspnea, cough, fatigue, and pulmonary infiltrates; may or may not occur in correlation with infusion reaction. Patients with dyspnea at rest (due to advance malignancy complications or comorbidity) may be at increased risk for pulmonary toxicity.

Concurrent drug therapy issues:

• Drug-drug/drug-food interactions: Potentially significant interactions may exist, requiring dose or frequency adjustment, additional monitoring, and/or selection of alternative therapy. Consult drug interactions database for more detailed information.

Special populations:

• Asian ancestry: The incidence of thrombocytopenia may be higher in patients of Asian ancestry.

• Pregnancy: **[US Boxed Warning]: Exposure to ado-trastuzumab emtansine during pregnancy may cause embryo-fetal harm. Effective contraception must be used in women of reproductive potential.** Pregnancy status should be verified prior to therapy. Effective contraception is recommended during therapy and for 7 months after the last dose for women of childbearing potential and for 4 months after the last dose in males with female partners of reproductive potential.

Dosage form specific issues:

• Do not interchange: **[US Boxed Warning]: Ado-trastuzumab emtansine and conventional trastuzumab are NOT interchangeable.** Do not substitute. In Canada, the generic name for Kadcyla is trastuzumab emtansine (ie, lacks Ado- prefix) and may be confused with conventional trastuzumab. Verify product label prior to reconstitution and administration to prevent medication errors.

Other warnings/precautions:

• HER2 expression: Establish HER2 overexpression or gene amplification status prior to treatment; has only been studied in patients with evidence of HER2 overexpression, either as 3+ IHC (Dako Herceptest) or FISH amplification ratio ≥2 (Dako *HER2* FISH pharmDx test). There is only limited data on patients with breast cancer positive by FISH and 0 or 1+ by IHC.

Metabolism/Transport Effects

Substrate of CYP3A4 (major); **Note:** Assignment of Major/Minor substrate status based on clinically relevant drug interaction potential

Drug Interactions

(For additional information: Launch drug interactions program) Lexicomp®

Antineoplastic Agents (Anthracycline, Systemic): Ado-Trastuzumab Emtansine may enhance the cardiotoxic effect of Antineoplastic Agents (Anthracycline, Systemic). Management: When possible, patients treated with ado-trastuzumab emtansine should avoid anthracycline-based therapy for up to 7 months after stopping ado-trastuzumab emtansine. Monitor closely for cardiac dysfunction in patients receiving this combination. *Risk D: Consider therapy modification*

Aprepitant: May increase the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

BCG (Intravesical): Immunosuppressants may diminish the therapeutic effect of BCG (Intravesical). *Risk X: Avoid combination*

BCG (Intravesical): Myelosuppressive Agents may diminish the therapeutic effect of BCG (Intravesical). *Risk X: Avoid combination*

Belimumab: Monoclonal Antibodies may enhance the adverse/toxic effect of Belimumab. *Risk X: Avoid combination*

CloZAPine: Myelosuppressive Agents may enhance the adverse/toxic effect of CloZAPine. Specifically, the risk for neutropenia may be increased. *Risk C: Monitor therapy*

Coccidioides immitis Skin Test: Immunosuppressants may diminish the diagnostic effect of Coccidioides immitis Skin Test. *Risk C: Monitor therapy*

Conivaptan: May increase the serum concentration of CYP3A4 Substrates. *Risk X: Avoid combination*

CYP3A4 Inhibitors (Moderate): May decrease the metabolism of CYP3A4 Substrates. *Risk C: Monitor therapy*

CYP3A4 Inhibitors (Strong): May increase serum concentrations of the active metabolite(s) of Ado-Trastuzumab Emtansine. Specifically, strong CYP3A4 inhibitors may increase concentrations of the cytotoxic DM1 component. *Risk X: Avoid combination*

Dasatinib: May increase the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

Deferiprone: Myelosuppressive Agents may enhance the neutropenic effect of Deferiprone. *Risk X: Avoid combination*

Denosumab: May enhance the adverse/toxic effect of Immunosuppressants. Specifically, the risk for serious infections may be increased. *Risk C: Monitor therapy*

Dipyrone: May enhance the adverse/toxic effect of Myelosuppressive Agents. Specifically, the risk for agranulocytosis and pancytopenia may be increased *Risk X: Avoid combination*

Echinacea: May diminish the therapeutic effect of Immunosuppressants. *Risk D: Consider therapy modification*

Fingolimod: Immunosuppressants may enhance the immunosuppressive effect of Fingolimod. Management: Avoid the concomitant use of fingolimod and other immunosuppressants when possible. If combined, monitor patients closely for additive immunosuppressant effects (eg, infections). *Risk D: Consider therapy modification*

Fosaprepitant: May increase the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

Fusidic Acid (Systemic): May increase the serum concentration of CYP3A4 Substrates. *Risk X: Avoid*

combination

Idelalisib: May increase the serum concentration of CYP3A4 Substrates. *Risk X: Avoid combination*

Leflunomide: Immunosuppressants may enhance the adverse/toxic effect of Leflunomide. Specifically, the risk for hematologic toxicity such as pancytopenia, agranulocytosis, and/or thrombocytopenia may be increased. Management: Consider not using a leflunomide loading dose in patients receiving other immunosuppressants. Patients receiving both leflunomide and another immunosuppressant should be monitored for bone marrow suppression at least monthly. *Risk D: Consider therapy modification*

Natalizumab: Immunosuppressants may enhance the adverse/toxic effect of Natalizumab. Specifically, the risk of concurrent infection may be increased. *Risk X: Avoid combination*

Netupitant: May increase the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

Nivolumab: Immunosuppressants may diminish the therapeutic effect of Nivolumab. *Risk D: Consider therapy modification*

Ocrelizumab: May enhance the immunosuppressive effect of Immunosuppressants. *Risk C: Monitor therapy*

Palbociclib: May increase the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

Pimecrolimus: May enhance the adverse/toxic effect of Immunosuppressants. *Risk X: Avoid combination*

Promazine: May enhance the myelosuppressive effect of Myelosuppressive Agents. *Risk C: Monitor therapy*

Roflumilast: May enhance the immunosuppressive effect of Immunosuppressants. *Risk D: Consider therapy modification*

Simeprevir: May increase the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

Sipuleucel-T: Immunosuppressants may diminish the therapeutic effect of Sipuleucel-T. *Risk C: Monitor therapy*

Stiripentol: May increase the serum concentration of CYP3A4 Substrates. Management: Use of stiripentol with CYP3A4 substrates that are considered to have a narrow therapeutic index should be avoided due to the increased risk for adverse effects and toxicity. Any CYP3A4 substrate used with stiripentol requires closer monitoring. *Risk D: Consider therapy modification*

Tacrolimus (Topical): May enhance the adverse/toxic effect of Immunosuppressants. *Risk X: Avoid combination*

Tertomotide: Immunosuppressants may diminish the therapeutic effect of Tertomotide. *Risk C: Monitor therapy*

Tofacitinib: Immunosuppressants may enhance the immunosuppressive effect of Tofacitinib. Management: Concurrent use with antirheumatic doses of methotrexate or nonbiologic disease modifying antirheumatic drugs (DMARDs) is permitted, and this warning seems particularly focused on more potent immunosuppressants. *Risk X: Avoid combination*

Trastuzumab: May enhance the neutropenic effect of Immunosuppressants. *Risk C: Monitor therapy*

Vaccines (Inactivated): Immunosuppressants may diminish the therapeutic effect of Vaccines

(Inactivated). Management: Vaccine efficacy may be reduced. Complete all age-appropriate vaccinations at least 2 weeks prior to starting an immunosuppressant. If vaccinated during immunosuppressant therapy, revaccinate at least 3 months after immunosuppressant discontinuation. *Risk D: Consider therapy modification*

Vaccines (Live): Immunosuppressants may enhance the adverse/toxic effect of Vaccines (Live). Immunosuppressants may diminish the therapeutic effect of Vaccines (Live). Management: Avoid use of live organism vaccines with immunosuppressants; live-attenuated vaccines should not be given for at least 3 months after immunosuppressants. *Risk X: Avoid combination*

Pregnancy Implications Animal reproduction studies have not been conducted. **[US Boxed Warning]: Exposure to ado-trastuzumab emtansine during pregnancy may cause embryo-fetal harm. Effective contraception must be used in women of reproductive potential.** Oligohydramnios and oligohydramnios sequence (manifested as pulmonary hypoplasia, skeletal malformations and neonatal death) were observed following trastuzumab exposure during pregnancy (trastuzumab is the antibody component of ado-trastuzumab emtansine). Monitor for oligohydramnios if trastuzumab exposure occurs during pregnancy or within 7 months prior to conception; conduct appropriate fetal testing if oligohydramnios occurs. Based on the mechanism of action, the DM1 component of the ado-trastuzumab emtansine formulation may also cause fetal harm if administered during pregnancy. Verify pregnancy status (in females of reproductive potential) prior to therapy. Effective contraception is recommended during therapy and for 7 months after the last dose for women of childbearing potential. Males with female partners of reproductive potential should use effective contraception during therapy and for 4 months after the last dose. Ado-trastuzumab emtansine may impair fertility in females and males.

If ado-trastuzumab emtansine exposure occurs during pregnancy or within 7 months prior to conception, healthcare providers should report the exposure to the Genentech Adverse Event Line (888-835-2555). Women exposed to ado-trastuzumab emtansine during pregnancy or within 7 months prior to conception are encouraged to enroll in MotHER Pregnancy Registry (1-800-690-6720).

European Society for Medical Oncology (ESMO) guidelines for cancer during pregnancy recommend delaying treatment with HER-2 targeted agents until after delivery in pregnant patients with HER-2 positive disease (Peccatori 2013).

Breast-Feeding Considerations It is not known if ado-trastuzumab emtansine is excreted into breast milk. Endogenous immunoglobulins are found in breast milk. Due to the potential for serious adverse reactions in the nursing infant, women should not breast-feed during treatment and for 7 months following the last dose.

Monitoring Parameters Platelet count (at baseline and prior to each dose), transaminases and bilirubin (at baseline and prior to each dose); verify pregnancy status prior to treatment initiation; HER2 expression status. Evaluate left ventricular function (prior to and at least every 3 months during treatment; for LVEF <40% or 40% to 45% with ≥10% absolute decrease below baseline value, reassess within 3 weeks). Monitor infusion site during infusion for possible infiltration; monitor for infusion reactions (during infusion and for 90 minutes after initial infusion and for 30 minutes after subsequent infusions); signs and symptoms of bleeding, neuropathy, and/or pulmonary toxicity

Mechanism of Action Ado-trastuzumab emtansine is a HER2-antibody drug conjugate which incorporates the HER2 targeted actions of trastuzumab with the microtubule inhibitor DM1 (a maytansine

derivative). The conjugate, which is linked via a stable thioether linker, allows for selective delivery into HER2 overexpressing cells, resulting in cell cycle arrest and apoptosis.

Pharmacodynamics/Kinetics

Distribution: V_d: 3.13 L

Protein binding: DM1: 93%

Metabolism: DM1 undergoes hepatic metabolism via CYP3A4/5

Half-life elimination: ~4 days

Time to peak: Near the end of the infusion

Pricing: US

Solution (reconstituted) (Kadcyla Intravenous)

100 mg (1): $3428.87

160 mg (1): $5486.20

Disclaimer: The pricing data provide a representative AWP and/or AAWP price from a single manufacturer of the brand and/or generic product, respectively. The pricing data should be used for benchmarking purposes only, and as such should not be used to set or adjudicate any prices for reimbursement or purchasing functions. Pricing data is updated monthly.

International Brand Names

Kadccyla (LV); Kadcyla (AR, AT, AU, BE, BR, CH, CL, CR, CU, CY, CZ, DE, DK, DO, EC, EE, FI, FR, GB, GT, HK, HN, HR, HU, IL, IS, KR, LB, LT, LU, NI, NL, NO, NZ, PA, PL, PT, QA, RO, SE, SI, SK, SV, TR)

REFERENCES

1. *Burris HA 3rd, Rugo HS, Vukelja SJ, et al, "Phase II Study of the Antibody Drug Conjugate Trastuzumab-DM1 for the Treatment of Human Epidermal Growth Factor Receptor 2 (HER2)-Positive Breast Cancer After Prior HER2-Directed Therapy," J Clin Oncol, 2011, 29(4):398-405. [PubMed 21172893]*
2. *Girish S, Gupta M, Wang B, et al, "Clinical Pharmacology of Trastuzumab Emtansine (T-DM1): An Antibody-Drug Conjugate in Development for the Treatment of HER2-Positive Cancer," Cancer Chemother Pharmacol, 2012, 69(5):1229-40. [PubMed 22271209]*
3. *Giordano SH, Temin S, Kirshner JJ, et al. Systemic therapy for patients With advanced human epidermal growth factor receptor 2-positive breast cancer: American Society of Clinical Oncology clinical practice guideline. J Clin Oncol. 2014;32(19):2078-2099. [PubMed 24799465]*
4. *Hurvitz SA, Dirix L, Kocsis J, et al, "Phase II Randomized Study of Trastuzumab Emtansine versus Trastuzumab Plus Docetaxel in Patients With Human Epidermal Growth Factor Receptor 2-Positive Metastatic Breast Cancer," J Clin Oncol, 2013, 31(9):1157-63. [PubMed 23382472]*
5. *Kadcyla (ado-trastuzumab) [prescribing information]. South San Francisco, CA: Genentech Inc; July 2016.*
6. *Kadcyla (ado-trastuzumab) [product monograph]. Mississauga, ON, Canada: Hoffmann-La Roche Limited; March 2017.*
7. *Krop IE, LoRusso P, Miller KD, et al, "A Phase II Study of Trastuzumab Emtansine in Patients With Human Epidermal*

Growth Factor Receptor 2-Positive Metastatic Breast Cancer Who Were Previously Treated With Trastuzumab, Lapatinib, an Anthracycline, aTaxane, and Capecitabine," J Clin Oncol, 2012, 30(26):3234-41. [PubMed 22649126]

8. *Peccatori FA, Azim HA Jr, Orecchia R, et al. Cancer, pregnancy and fertility: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2013;24(Suppl 6):vi160-170. [PubMed 23813932]*
9. *Ramakrishna N, Temin S, Chandarlapaty S, et al. Recommendations on disease management for patients with advanced human epidermal growth factor receptor 2-positive breast cancer and brain metastases: American Society of Clinical Oncology clinical practice guideline. J Clin Oncol. 2014;32(19):2078-2099. [PubMed 24799487]*
10. *US Department of Health and Human Services; Centers for Disease Control and Prevention; National Institute for Occupational Safety and Health. NIOSH list of antineoplastic and other hazardous drugs in healthcare settings 2016. http://www.cdc.gov/niosh/topics/antineoplastic/pdf/hazardous-drugs-list_2016-161.pdf. Updated September 2016. Accessed October 5, 2016.*
11. *Verma S, Miles D, Gianni L, et al, "Trastuzumab Emtansine for HER2-positive Advanced Breast Cancer," N Engl J Med, 2012, 367(19):1783-91. [PubMed 23020162]*
12. *Welslau M, Diéras V, Sohn JH, et al. Patient-reported outcomes from EMILIA, a randomized phase 3 study of trastuzumab emtansine (T-DM1) versus capecitabine and lapatinib in human epidermal growth factor receptor 2-positive locally advanced or metastatic breast cancer. Cancer. 2014;120(5):642-651. [PubMed 24222194]*
13. *Wolff AC, Hammond ME, Hicks DG, et al. Recommendations for human epidermal growth factor receptor 2 testing in breast cancer: American Society of Clinical Oncology/College of American Pathologists clinical practice guideline update. J Clin Oncol. 2013;31(31):3997-4013. [PubMed 24101045]*

Topic 88427 Version 113.0