HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use PERJETA safely and effectively. See full prescribing information for PERJETA.

PERJETA® (pertuzumab)
Injection, for intravenous use
Initial U.S. Approval: 2012

WARNING: CARDIOMYOPATHY and EMBRYO-FETAL TOXICITY
See full prescribing information for complete boxed warning.

Cardiomyopathy: PERJETA can result in subclinical and clinical cardiac failure manifesting as CHF, and decreased LVEF. Evaluate cardiac function prior to and during treatment. Discontinue PERJETA treatment for a confirmed clinically significant decrease in left ventricular function. (2.2, 5.2, 6.1)

Embryo-fetal Toxicity: Exposure to PERJETA can result in embryo-fetal death and birth defects. Studies in animals have resulted in oligohydramnios, delayed renal development, and death. Advise patients of these risks and the need for effective contraception. (5.1, 8.1, 8.6)

----------RECENT MAJOR CHANGES----------

Indications and Usage (1.2)	09/2013
Dosage and Administration (2.1)	04/2013
Dosage and Administration (2.1, 2.2)	09/2013
Contraindications (4)	09/2013
Warnings and Precautions (5.2, 5.3, 5.4, 5.5)	09/2013

---------- INDICATIONS AND USAGE----------

PERJETA is a HER2/neu receptor antagonist indicated for:

- Use in combination with trastuzumab and docetaxel for treatment of patients with HER2-positive metastatic breast cancer (MBC) who have not received prior anti-HER2 therapy or chemotherapy for metastatic disease. (1.1)
- Use in combination with trastuzumab and docetaxel as neoadjuvant treatment of patients with HER2-positive, locally advanced, inflammatory, or early stage breast cancer (either greater than 2 cm in diameter or node positive) as part of a complete treatment regimen for early breast cancer. This indication is based on demonstration of an improvement in pathological complete response rate. No data are available demonstrating improvement in event-free survival or overall survival. (1.2, 2.1, 14.2)
  Limitations of Use:
  - The safety of PERJETA as part of a doxorubicin-containing regimen has not been established.
  - The safety of PERJETA administered for greater than 6 cycles for early breast cancer has not been established.

----------DOSAGE AND ADMINISTRATION----------

- **For intravenous infusion only.** Do not administer as an intravenous push or bolus. (2.3)
- The initial PERJETA dose is 840 mg administered as a 60-minute intravenous infusion, followed every 3 weeks thereafter by 420 mg administered as a 30 to 60 minute intravenous infusion. (2.1)
- MBC: Administer PERJETA, trastuzumab, and docetaxel by intravenous infusion every 3 weeks. (2.1)
- Neoadjuvant: Administer PERJETA, trastuzumab, and docetaxel by intravenous infusion preoperatively every 3 weeks for 3 to 6 cycles. (2.1)

---------- DOSAGE FORMS AND STRENGTHS ----------

- 420 mg/14 mL single-use vial. (3)

---------- CONTRAINDICATIONS ----------

PERJETA is contraindicated in patients with known hypersensitivity to pertuzumab or to any of its excipients. (4)

---------- WARNINGS AND PRECAUTIONS ----------

- Embryo-fetal toxicity: Fetal harm can occur when administered to a pregnant woman. (5.1, 8.1)
- Left Ventricular Dysfunction: Monitor LVEF and withhold dosing as appropriate. (5.2, 6.1)
- Infusion-Related Reactions: Monitor for signs and symptoms. If a significant infusion-associated reaction occurs, slow or interrupt the infusion and administer appropriate medical therapies. (5.3)
- Hypersensitivity Reactions/Anaphylaxis: Monitor for signs and symptoms. If a severe hypersensitivity reaction/anaphylaxis occurs, discontinue the infusion immediately and administer appropriate medical therapies. (5.4)
- HER2 testing: Perform using FDA-approved tests by laboratories with demonstrated proficiency. (5.5)

---------- ADVERSE REACTIONS ----------

Metastatic Breast Cancer

- The most common adverse reactions (> 30%) with PERJETA in combination with trastuzumab and docetaxel were diarrhea, alopecia, neutropenia, nausea, fatigue, rash, and peripheral neuropathy. (6.1)

Neoadjuvant Treatment of Breast Cancer

- The most common adverse reactions (> 30%) with PERJETA in combination with trastuzumab and docetaxel were alopecia, diarrhea, nausea, and neutropenia. (6.1)
- The most common adverse reactions (>30%) with PERJETA in combination with trastuzumab and docetaxel when given for 3 cycles following 3 cycles of FEC were fatigue, alopecia, diarrhea, nausea, vomiting, and neutropenia. (6.1)
- The most common adverse reactions (>30%) with PERJETA in combination with docetaxel, carboplatin, and trastuzumab (TCH) were fatigue, alopecia, diarrhea, nausea, vomiting, neutropenia, thrombocytopenia, and anemia. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Genentech at 1-888-835-2555 or FDA at 1-800-FDA-1088 or *www.fda.gov/medwatch*.

---------- USE IN SPECIFIC POPULATIONS ----------

- Nursing mothers: Discontinue nursing or discontinue PERJETA, taking into consideration the importance of the drug to the mother. (8.3)
- Females of Reproductive Potential: Counsel females on pregnancy prevention and planning. Encourage patient participation in the MotHER Pregnancy Registry by contacting 1-800-690-6720. (5.1, 8.1, 8.6, 17)

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 09/2013

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the Full Prescribing Information are not listed.

FULL PRESCRIBING INFORMATION

WARNING: CARDIOMYOPATHY AND EMBRYO-FETAL TOXICITY

Cardiomyopathy

PERJETA administration can result in subclinical and clinical cardiac failure. Evaluate left ventricular function in all patients prior to and during treatment with PERJETA. Discontinue PERJETA treatment for a confirmed clinically significant decrease in left ventricular function. (2.2, 5.2, 6.1)

Embryo-Fetal Toxicity

Exposure to PERJETA can result in embryo-fetal death and birth defects. Studies in animals have resulted in oligohydramnios, delayed renal development, and death. Advise patients of these risks and the need for effective contraception. (5.1, 8.1, 8.6)

1 INDICATIONS AND USAGE

1.1 Metastatic Breast Cancer (MBC)

PERJETA is indicated for use in combination with trastuzumab 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.

1.2 Neoadjuvant Treatment of Breast Cancer

PERJETA is indicated for use in combination with trastuzumab and docetaxel for the neoadjuvant treatment of patients with HER2-positive, locally advanced, inflammatory, or early stage breast cancer (either greater than 2 cm in diameter or node positive) as part of a complete treatment regimen for early breast cancer. This indication is based on demonstration of an improvement in pathological complete response rate. No data are available demonstrating improvement in event-free survival or overall survival *[see Clinical Studies (14.2) and Dosage and Administration (2.1)]*.

Limitations of Use:

- The safety of PERJETA as part of a doxorubicin-containing regimen has not been established.
- The safety of PERJETA administered for greater than 6 cycles for early breast cancer has not been established.

2 DOSAGE AND ADMINISTRATION

2.1 Recommended Doses and Schedules

The initial dose of PERJETA is 840 mg administered as a 60-minute intravenous infusion, followed every 3 weeks by a dose of 420 mg administered as an intravenous infusion over 30 to 60 minutes.

When administered with PERJETA, the recommended initial dose of trastuzumab is 8 mg/kg administered as a 90-minute intravenous infusion, followed every 3 weeks by a dose of 6 mg/kg administered as an intravenous infusion over 30 to 90 minutes.

PERJETA, trastuzumab, and docetaxel should be administered sequentially. PERJETA and trastuzumab can be given in any order. Docetaxel should be administered after PERJETA and trastuzumab. An observation period of 30 to 60 minutes is recommended after each PERJETA infusion and before commencement of any subsequent infusion of trastuzumab or docetaxel *[see Warnings and Precautions (5.3)]*.

Metastatic Breast Cancer (MBC)

When administered with PERJETA, the recommended initial dose of docetaxel is 75 mg/m^2 administered as an intravenous infusion. The dose may be escalated to 100 mg/m^2 administered every 3 weeks if the initial dose is well tolerated.

Neoadjuvant Treatment of Breast Cancer

PERJETA should be administered every 3 weeks for 3 to 6 cycles as part of one of the following treatment regimens for early breast cancer *[see Clinical Studies (14.2)]*:

- Four preoperative cycles of PERJETA in combination with trastuzumab and docetaxel followed by 3 postoperative cycles of fluorouracil, epirubicin, and cyclophosphamide (FEC) as given in Study 2
- Three preoperative cycles of FEC alone followed by 3 preoperative cycles of PERJETA in combination with docetaxel and trastuzumab as given in Study 3
- Six preoperative cycles of PERJETA in combination with docetaxel, carboplatin, and trastuzumab (TCH) (escalation of docetaxel above 75 mg/m^2 is not recommended) as given in Study 3

Following surgery, patients should continue to receive trastuzumab to complete 1 year of treatment. There is insufficient evidence to recommend continued use of PERJETA for greater than 6 cycles for early breast cancer. There is insufficient evidence to recommend concomitant administration of an anthracycline with PERJETA, and there are no safety data to support sequential use of doxorubicin with PERJETA.

2.2 Dose Modification

For delayed or missed doses, if the time between two sequential infusions is less than 6 weeks, the 420 mg dose of PERJETA should be administered. Do not wait until the next planned dose. If the time between two sequential infusions is 6 weeks or more, the initial dose of 840 mg PERJETA should be re-administered as a 60-minute intravenous infusion followed every 3 weeks thereafter by a dose of 420 mg administered as an intravenous infusion over 30 to 60 minutes.

PERJETA should be discontinued if trastuzumab treatment is discontinued.

Dose reductions are not recommended for PERJETA.

For docetaxel dose modifications, see relevant prescribing information.

Left Ventricular Ejection Fraction (LVEF):

Withhold PERJETA and trastuzumab dosing for at least 3 weeks for either:

- a drop in LVEF to less than 45% or
- LVEF of 45% to 49% with a 10% or greater absolute decrease below pretreatment values *[see Warnings and Precautions (5.2)]*

PERJETA may be resumed if the LVEF has recovered to greater than 49% or to 45% to 49% associated with less than a 10% absolute decrease below pretreatment values.

If after a repeat assessment within approximately 3 weeks, the LVEF has not improved, or has declined further, PERJETA and trastuzumab should be discontinued, unless the benefits for the individual patient are deemed to outweigh the risks *[see Warnings and Precautions (5.2)]*.

Infusion-Related Reactions

The infusion rate of PERJETA may be slowed or interrupted if the patient develops an infusion-related reaction *[see Warnings and Precautions (5.3)]*.

Hypersensitivity Reactions/Anaphylaxis

The infusion should be discontinued immediately if the patient experiences a serious hypersensitivity reaction *[see Warnings and Precautions (5.4)]*.

2.3 Preparation for Administration

Administer as an intravenous infusion only. Do not administer as an intravenous push or bolus. Do not mix PERJETA with other drugs.

Preparation

Prepare the solution for infusion, using aseptic technique, as follows:

- Parenteral drug products should be inspected visually for particulates and discoloration prior to administration.
- Withdraw the appropriate volume of PERJETA solution from the vial(s).
- Dilute into a 250 mL 0.9% sodium chloride PVC or non-PVC polyolefin infusion bag.
- Mix diluted solution by gentle inversion. Do not shake.
- Administer immediately once prepared.
- If the diluted infusion solution is not used immediately, it can be stored at 2°C to 8°C for up to 24 hours.
- Dilute with 0.9% Sodium Chloride injection only. Do not use dextrose (5%) solution.

3 DOSAGE FORMS AND STRENGTHS

PERJETA (pertuzumab) 420 mg/14 mL (30 mg/mL) in a single-use vial

4 CONTRAINDICATIONS

PERJETA is contraindicated in patients with known hypersensitivity to pertuzumab or to any of its excipients.

5 WARNINGS AND PRECAUTIONS

5.1 Embryo-Fetal Toxicity

PERJETA can cause fetal harm when administered to a pregnant woman. Treatment of pregnant cynomolgus monkeys with pertuzumab resulted in oligohydramnios, delayed fetal kidney development, and embryo-fetal death. If PERJETA is administered during pregnancy, or if the patient becomes pregnant while receiving this drug, the patient should be apprised of the potential hazard to a fetus *[see Use in Specific Populations (8.1)]*.

Verify pregnancy status prior to the initiation of PERJETA. Advise patients of the risks of embryo-fetal death and birth defects and the need for contraception during and after treatment. Advise patients to contact their healthcare provider immediately if they suspect they may be pregnant. If PERJETA is administered during pregnancy or if a patient becomes pregnant while receiving PERJETA, immediately report exposure to the Genentech Adverse Event Line at 1-888-835-2555. Encourage women who may be exposed during pregnancy to enroll in the

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