Pertuzumab: Drug information

(For additional information see "Pertuzumab: Patient drug information")

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

ALERT: US Boxed Warning

Cardiotoxicity:

Pertuzumab can result in subclinical and clinical cardiac failure manifesting as decreased left ventricular ejection fraction (LVEF) and congestive heart failure (CHF). Evaluate cardiac function prior to and during treatment. Discontinue pertuzumab treatment for a confirmed clinically significant decrease in left ventricular function.

Pregnancy:

Exposure to pertuzumab can result in embryo-fetal death and birth defects. Advise patients of these risks and the need for effective contraception.

Brand Names: US

Perjeta

Brand Names: Canada

Perjeta

Pharmacologic Category

Antineoplastic Agent, Anti-HER2; Antineoplastic Agent, Monoclonal Antibody

Dosing: Adult

Note: For pertuzumab, trastuzumab, and docetaxel combination regimens, pertuzumab and trastuzumab may be administered in any order; however, docetaxel should be given after pertuzumab and trastuzumab. Observe patients for 30 to 60 minutes after each pertuzumab infusion and before subsequent infusions of trastuzumab or docetaxel.

Breast cancer, metastatic HER2+: IV: 840 mg over 60 minutes followed by a maintenance dose of 420 mg over 30 to 60 minutes every 3 weeks until disease progression or unacceptable toxicity (in combination with trastuzumab and docetaxel) (Baselga, 2012; Swain, 2015).

Breast cancer, neoadjuvant treatment HER2+: Adults: IV: 840 mg over 60 minutes followed by a maintenance dose of 420 mg over 30 to 60 minutes every 3 weeks for 3 to 6 cycles; may be administered as one of the regimens below. Postoperatively, continue trastuzumab to complete 1 year of treatment.

Four preoperative cycles of pertuzumab, trastuzumab, and docetaxel, followed by 3 postoperative cycles of fluorouracil, epirubicin, and cyclophosphamide (FEC) (Gianni, 2012) **or**

Three preoperative cycles of FEC (alone) followed by 3 preoperative cycles of pertuzumab, trastuzumab, and docetaxel (Schneeweiss, 2013) **or**

Six preoperative cycles of pertuzumab, trastuzumab, docetaxel, and carboplatin (Schneeweiss, 2013)

Missed doses or delays: If <6 weeks has elapsed, administer the 420 mg maintenance dose; do not wait until the next planned dose. If ≥6 weeks has elapsed, readminister the 840 mg initial dose (over 60 minutes), and then follow with a maintenance dose of 420 mg (over 30 to 60 minutes) every 3 weeks.

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

There are no dosage adjustments provided in the manufacturer's labeling (has not been studied).

Dosing: Adjustment for Toxicity

Note: Dose reductions are not recommended for pertuzumab; if trastuzumab is withheld, pertuzumab should also be withheld; if trastuzumab is discontinued, pertuzumab should be discontinued; pertuzumab and trastuzumab may be continued if docetaxel is discontinued.

Infusion-related reaction: Slow or interrupt the infusion

Serious hypersensitivity: Discontinue immediately

Cardiotoxicity: Left ventricular ejection fraction (LVEF) declines to <45% **or** LVEF 45% to 49% with ≥10% absolute decrease below pretreatment values: Withhold treatment (pertuzumab and trastuzumab) for at least 3 weeks; may resume if LVEF returns to >49% **or** to 45% to 49% with <10% absolute decrease below pretreatment values. If after a repeat assessment within ~3 weeks, LVEF has not improved (or has declined further), discontinue pertuzumab and trastuzumab (unless the benefit of treatment outweighs risks).

Dosage Forms

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

Solution, Intravenous [preservative free]:

Perjeta: 420 mg/14 mL (14 mL) [contains mouse (murine) and/or hamster protein]

Generic Equivalent Available (US)

No

Administration

For IV infusion only, as a short infusion; infuse initial dose (840 mg) over 60 minutes; infuse maintenance dose (420 mg) over 30 to 60 minutes. Do not administer IV push or as a rapid bolus. Do

not mix with other medications. For pertuzumab, trastuzumab, and docetaxel combination regimens, pertuzumab and trastuzumab may be administered in any order; however, docetaxel should be given after pertuzumab and trastuzumab. Observe patients for 30 to 60 minutes after each pertuzumab infusion and before subsequent infusions of trastuzumab or docetaxel.

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 of human epidermal growth factor receptor 2 (HER2)-positive metastatic breast cancer (in combination with trastuzumab and docetaxel) in patients who have not received prior anti-HER2 therapy or chemotherapy to treat metastatic disease.

Breast cancer, neoadjuvant treatment: Neoadjuvant treatment of locally advanced, inflammatory, or early stage HER2-positive, breast cancer (either greater than 2 cm in diameter or node positive) in combination with trastuzumab and docetaxel (as part of a complete treatment regimen for early breast cancer).

Limitations of use: The safety of pertuzumab as part of a doxorubicin-containing regimen has not been established; the safety of pertuzumab administered for more than 6 cycles for early breast cancer has not been established.

Medication Safety Issues

Sound-alike/look-alike issues:

Pertuzumab may be confused with ado-trastuzumab emtansine, panitumumab, trastuzumab

High alert medication:

This medication is in a class the Institute for Safe Medication Practices (ISMP) includes among its list of drug classes which have a heightened risk of causing significant patient harm when used in error.

Adverse Reactions

Note: Reactions reported in combination therapy with trastuzumab and docetaxel unless otherwise noted.

>10%:

Central nervous system: Fatigue (26% to 38%), headache (11% to 21%), decreased left ventricular ejection fraction (8% to 16%), insomnia (8% to 13%), dizziness (3% to 13%)

Dermatologic: Alopecia (52% to 65%), skin rash (11% to 34%; grades 3/4: <1%), pruritus (4% to 14%), palmar-plantar erythrodysesthesia (11%), xeroderma (9% to 11%)

Gastrointestinal: Diarrhea (46% to 67%; grades 3/4: 5% to 8%), nausea (39% to 53%; monotherapy 24%), vomiting (13% to 36%; monotherapy 15%), decreased appetite (11% to 29%), constipation (23%), mucositis (20% to 28%), stomatitis (17% to 19%), dysgeusia (13% to 18%), abdominal pain (monotherapy 12%)

Hematologic & oncologic: Neutropenia (47% to 53%; grades 3/4: 43% to 49%), anemia (3% to 23%; grades 3/4: 3% to 4%), leukopenia (9% to 16%; grades 3/4: 5% to 12%), febrile neutropenia (8% to 14%; grades 3/4: 9% to 13%)

Hypersensitivity: Hypersensitivity (1% to 11%; grades 3/4: 2%)

Neuromuscular & skeletal: Weakness (15% to 26%), myalgia (11% to 23%), arthralgia (10% to 12%)

Respiratory: Upper respiratory tract infection (4% to 17%; grades 3/4: <1%), epistaxis (11%)

Miscellaneous: Fever (9% to 19%; grades 3/4: 1%), infusion reactions (13%; grades 3/4: <1%)

1% to 10%:

Cardiovascular: Left ventricular dysfunction (3% to 4%), peripheral edema (3% to 4%)

Central nervous system: Peripheral sensory neuropathy (8%; grades 3/4: 1%), peripheral neuropathy (1%)

Dermatologic: Nail disease (7%), paronychia (1% to 7%)

Gastrointestinal: Dyspepsia (8%), anorexia (monotherapy 5%)

Hematologic & oncologic: Thrombocytopenia (1%)

Hepatic: Increased serum ALT (3%)

Ophthalmic: Increased lacrimation (4% to 5%)

Respiratory: Dyspnea (5% to 8%), nasopharyngitis (7%), oropharyngeal pain (7%), cough (5%)

<1%, postmarketing, and/or case reports with combination therapy: Heart failure, pleural effusion, sepsis

Contraindications

Known hypersensitivity to pertuzumab or any component of the formulation

Warnings/Precautions

Concerns related to adverse effects:

• Cardiotoxicity: **[US Boxed Warning]: May result in cardiac failure (clinical and subclinical) manifesting as decreased left ventricular ejection fraction (LVEF) and heart failure (HF). Assess cardiac function at baseline and during treatment. Discontinue for confirmed clinically significant decline in left ventricular function.** Decreases in LVEF are associated with HER2 inhibitors, including pertuzumab. Patients who received prior anthracycline therapy or chest

irradiation may be at an increased risk for cardiotoxicity. In studies of pertuzumab (versus placebo) in combination with trastuzumab and docetaxel for the treatment of metastatic breast cancer, the rate of cardiotoxicity (LVEF decline or symptomatic LV systolic dysfunction) was not increased in the pertuzumab group when compared to placebo. In the neoadjuvant setting, the incidence of LV dysfunction was higher in patients treated with pertuzumab. In a study of pertuzumab, trastuzumab, and docetaxel, compared with trastuzumab and docetaxel, the incidence of LVEF decline (of >10% decrease from baseline or to <50%) was 8.4% and 1.9%, respectively; LVEF recovered to ≥50% in all patients. In another neoadjuvant study, LVEF declines (of >10% decrease from baseline or to <50%) were noted in 6.9% to 16% of patients receiving various combinations and sequences of pertuzumab plus trastuzumab with FEC (fluorouracil, epirubicin, and cyclophosphamide), docetaxel, and/or carboplatin; LVEF recovered to ≥50% in most patients. Of note, patients with pretreatment LVEF ≤50%, CHF, LVEF decreases to <50% during prior trastuzumab treatment, or conditions which could impair LV function (eg, uncontrolled hypertension, recent MI, serious arrhythmia requiring treatment, or cumulative lifetime anthracycline exposure >360 mg/m^2 doxorubicin or its equivalent) were excluded from studies. Assess LVEF at baseline, every 3 months during treatment (metastatic patients) or every 6 weeks during treatment (neoadjuvant setting), and every 6 months after therapy discontinuation up to 24 months after the last dose of pertuzumab and/or trastuzumab. Withhold pertuzumab and trastuzumab if LVEF <45% **or** 45% to 49% with a ≥10% absolute decline from baseline; repeat LVEF assessment in ~3 weeks; discontinue if LVEF has not improved or has declined further (unless potential benefits outweigh risks).

• Gastrointestinal adverse events: Diarrhea occurred more frequently in patients receiving pertuzumab in combination with trastuzumab and docetaxel, compared to patients receiving only trastuzumab and docetaxel.

• Hypersensitivity/infusion reaction: Infusion reactions (either during or on the day of infusion) have been associated with pertuzumab; commonly described as fever, chills, fatigue, headache, weakness, myalgia, hypersensitivity, abnormal taste or vomiting. The incidence of hypersensitivity/anaphylaxis was slightly higher in the group receiving pertuzumab (compared to placebo) in combination with trastuzumab and docetaxel. Monitor for 1 hour after the first infusion and for 30 minutes after subsequent infusions. For significant infusion reactions, interrupt or slow infusion rate; for severe infusion reactions, consider permanently discontinuing. Medications and equipment for the treatment of hypersensitivity should be available for immediate use during infusion.

Concomitant drug therapy issues:

• Drug-drug 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:

• Pregnancy: **[US Boxed Warning]: Pertuzumab exposure during pregnancy may result in embryo-fetal mortality and birth defects. Advise patients of the risks and the need for effective contraception.** Verify pregnancy status prior to treatment initiation. Effective contraception should be used by all patients receiving pertuzumab during therapy and for 7 months after the last dose (of pertuzumab in combination with trastuzumab) for women of childbearing potential.

Other warnings/precautions:

• HER2 expression: Establish HER2 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 *HER*2 FISH pharmDx test).

•Limitations of use: Safety of combination or sequential therapy with doxorubicin-containing regimens has not been established. For early breast cancer, the safety of treatment beyond 6 cycles has not been determined.

Metabolism/Transport Effects

None known.

Drug Interactions

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

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

Pregnancy Implications

[US Boxed Warning]: Pertuzumab exposure during pregnancy may result in embryo-fetal mortality and birth defects. Advise patients of the risks and the need for effective contraception. Verify pregnancy status prior to treatment initiation (in women of reproductive potential). Based on the mechanism of action of pertuzumab and data from similar agents, oligohydramnios or oligohydramnios sequence may occur resulting in pulmonary hypoplasia, skeletal anomalies, and neonatal death. Monitor for oligohydramnios if exposure occurs during pregnancy or within 7 months prior to conception; conduct appropriate fetal testing if oligohydramnios occurs. Effective contraception should be used during therapy and for 7 months after the last dose (of pertuzumab in combination with trastuzumab) for women of childbearing potential. Advise patients to immediately report to healthcare provider if pregnancy is suspected during treatment. If pertuzumab exposure occurs during pregnancy or exposure to pertuzumab in combination with trastuzumab occurs within 7 months prior to conception, healthcare providers should report the exposure to the Genentech Adverse Event Line (888-835-2555).

Women exposed to pertuzumab during pregnancy or exposed to pertuzumab in combination with trastuzumab within 7 months prior to conception are encouraged to enroll in MotHER Pregnancy Registry (1-800-690-6720 or www.motherpregnancyregistry.com).

European Society for Medical Oncology (ESMO) guidelines for cancer during pregnancy recommend delaying treatment with HER2-targeted agents until after delivery in pregnant patients with HER2-positive disease (Peccatori 2013).

Breast-Feeding Considerations

It is not known if pertuzumab is excreted in human milk. Because many immunoglobulins are excreted in human milk, and the potential for serious adverse reactions in the breast-feeding infant exists, the decision to discontinue breast-feeding or to discontinue pertuzumab should take into account the benefits of treatment to the mother. The extended half-life of pertuzumab and the 7-month wash out period for trastuzumab should be considered for decisions regarding breast-feeding after treatment is completed.

Monitoring Parameters

HER2 expression (either as 3+ IHC [Dako Herceptest™] or FISH amplification ratio ≥2 [Dako *HER*2 FISH pharmDx™ test]); pregnancy test; assess LVEF at baseline, every 3

months during treatment (more frequently for declines) in metastatic treatment and every 6 weeks for neoadjuvant treatment, and every 6 months following discontinuation for up to 24 months from the last dose of pertuzumab and/or trastuzumab); monitor for infusion reaction and hypersensitivity

Mechanism of Action Pertuzumab is a recombinant humanized monoclonal antibody which targets the extracellular human epidermal growth factor receptor 2 protein (HER2) dimerization domain. Inhibits HER2 dimerization and blocks HER downstream signaling halting cell growth and initiating apoptosis. Pertuzumab binds to a different HER2 epitope than trastuzumab so that when pertuzumab is combined with trastuzumab, a more complete inhibition of HER2 signaling occurs (Baselga, 2012).

Pharmacodynamics/Kinetics

Distribution: V_d: 5.12 L (Gianni, 2010)

Half-life elimination: Terminal: 18 days

Pricing: US

Solution (Perjeta Intravenous)

420 mg/14 mL (14 mL): $5504.64

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 Per'Yeta (UA); Perjeta (AR, AT, AU, BR, CH, CR, CU, CY, CZ, DE, DK, DO, EE, ES, FR, GB, GT, HK, HN, HR, HU, IE, IL, IS, JP, KR, LB, LT, LU, LV, MT, MX, MY, NI, NL, NO, NZ, PA, PH, PL, PT, QA, RO, SA, SE, SI, SK, SV, TH, TR)

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