

For your eligible patients with HER2+ breast cancer,

PHESGO is a faster way to administer PERJETA + trastuzumab-based treatment.*^{1,2}

PHESGO is a fixed-dose subcutaneous treatment with PERJETA and trastuzumab that's administered in ~5 minutes.*1

*Refers to actual PHESGO injection time of ~5 minutes for the maintenance dose. **The loading dose is ~8 minutes.** This does not account for observation time and other aspects of treatment. Actual clinic time may vary.

See the total administration time saved over the 18 cycles of EBC treatment.

EBC=early breast cancer; HER2=human epidermal growth factor receptor 2.

PHESGO Important Safety Information & Indications

Indications

Early Breast Cancer

PHESGO[®] (pertuzumab, trastuzumab, and hyaluronidase-zzxf) is indicated for use in combination with chemotherapy for

- the neoadjuvant treatment of adult 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 (EBC)
- the adjuvant treatment of adult patients with HER2-positive early breast cancer (EBC) at high risk of recurrence

Select patients for therapy based on an FDA-approved companion diagnostic test.

Important Safety Information

BOXED WARNINGS: Cardiomyopathy, Embryo-Fetal Toxicity, and Pulmonary Toxicity

- PHESGO administration can result in subclinical and clinical cardiac failure. The incidence and severity was highest in patients receiving PHESGO with anthracycline-containing chemotherapy regimens. Evaluate cardiac function prior to and during treatment with PHESGO. Discontinue PHESGO treatment in patients receiving adjuvant therapy and withhold PHESGO in patients with metastatic disease for clinically significant decrease in left ventricular function
- Exposure to PHESGO can result in embryo-fetal death and birth defects, including oligohydramnios and oligohydramnios sequence manifesting as pulmonary hypoplasia, skeletal abnormalities, and neonatal death. Advise patients of these risks and the need for effective contraception
- PHESGO administration can result in serious and fatal pulmonary toxicity. Discontinue PHESGO for anaphylaxis, angioedema, interstitial pneumonitis, or acute respiratory distress syndrome. Monitor patients until symptoms completely resolve





PERJETA Important Safety Information & Indications

Indications

Early Breast Cancer

PERJETA® (pertuzumab) is indicated for use in combination with Herceptin® (trastuzumab) and chemotherapy 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 (EBC)
- the adjuvant treatment of patients with HER2-positive early breast cancer (EBC) at high risk of recurrence

Important Safety Information

BOXED WARNINGS: Left Ventricular Dysfunction and Embryo-Fetal Toxicity

- PERJETA 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 PERJETA treatment for a confirmed clinically significant decrease in left ventricular function
- Exposure to PERJETA can result in embryo-fetal death and birth defects. Advise patients of these risks and the need for effective contraception
 - o Verify the pregnancy status of females of reproductive potential prior to the initiation of PERJETA. Advise pregnant women and females of reproductive potential that exposure to PERJETA in combination with trastuzumab during pregnancy or within 7 months prior to conception can result in fetal harm, including embryo-fetal death or birth defects. Advise females of reproductive potential to use effective contraception during treatment and for 7 months following the last dose of PERJETA in combination with trastuzumab
 - o There is a pregnancy pharmacovigilance program for PERJETA. If PERJETA is administered during pregnancy, or if a patient becomes pregnant while receiving PERJETA or within 7 months following the last dose of PERJETA in combination with trastuzumab, healthcare providers and patients should immediately report PERJETA exposure to Genentech at 1-888-835-2555

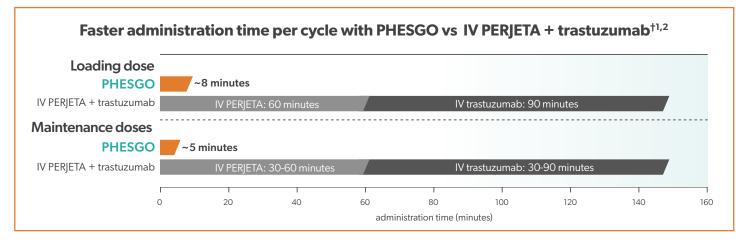
Please see Important Safety Information for PHESGO and PERJETA throughout and click <u>here</u> for full Prescribing Information for PHESGO, including BOXED WARNINGS, and click <u>here</u> for full Prescribing Information for PERJETA, including BOXED WARNINGS.





PHESGO administration may save up to 43.5 hours vs IV PERJETA + trastuzumab per patient receiving 18 cycles in early breast cancer*

*Due to variable IV infusion time, PHESGO administration time savings can range from 18 to 43.5 hours vs IV PERJETA + trastuzumab.



Faster administration time over 18 cycles with PHESGO vs IV PERJETA + trastuzumab $^{\pm1,2}$			
	Loading dose	Maintenance doses	Total admin time over 18 cycles§
PHESGO	1 cycle x ~8 minutes	17 cycles x ~5 minutes	~1.5 hours
IV PERJETA + trastuzumab (min time)	1 cycle x 150 minutes	17 cycles x 60 minutes	19.5 hours
IV PERJETA + trastuzumab (max time)	1 cycle x 150 minutes	17 cycles x 150 minutes	45 hours

• Patients should be observed for a minimum of 30 minutes after initial dose of PHESGO and 15 minutes after each maintenance dose of PHESGO for signs or hypersensitivity symptoms or administration-related reactions. Medications to treat such reactions, as well as emergency equipment, should be available for immediate use

• An observation period of 30 to 60 minutes is recommended after each PERJETA infusion and before commencement of any subsequent infusion of trastuzumab or chemotherapy

[†] Hypothetical example based on the recommended number of cycles (up to 18, or until disease recurrence or unmanageable toxicity, whichever occurs first) and administration time for patients found in the USPIs. Refer to individual product labeling for additional information.^{1,2}

[‡]Refers to actual injection time of PHESGO vs infusion time of IV PERJETA + trastuzumab and does not account for all aspects of treatment. PHESGO and IV PERJETA + trastuzumab are given with chemotherapy as part of a complete treatment regimen for early breast cancer. Actual clinic time may vary. PERJETA and trastuzumab can be given in any order.^{1,2} Please see the PERJETA full Prescribing Information for additional dosing information for PERJETA + trastuzumab.

[§]Total administration time = 1 loading dose + 17 maintenance doses.^{1,2}

What could this potential administration time savings mean for your patients and practice?

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PHESGO can be used anywhere that PERJETA is indicated¹⁻³

PHESGO is FDA-approved for all of the same HER2+ breast cancer indications as PERJETA.^{1,2}



NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)

NCCN Guidelines state that pertuzumab, trastuzumab and hyaluronidase-zzxf injection for subcutaneous use (PHESGO) may be substituted anywhere that IV pertuzumab (PERJETA) + trastuzumab are given as part of systemic therapy for HER2+ breast cancer.^{II3}

^{II}Pertuzumab, trastuzumab, and hyaluronidase-zzxf injection for subcutaneous use (PHESGO) has different dosing and administration instructions compared to the intravenous products.

Eligible patients currently receiving IV PERJETA + trastuzumab can be transitioned to PHESGO at the next scheduled dose of treatment.¹

PHESGO Important Safety Information (cont'd)

Contraindications

PHESGO is contraindicated in patients with known hypersensitivity to pertuzumab, or trastuzumab, or hyaluronidase, or to any of its excipients.

Additional Important Safety Information Cardiomyopathy and Cardiac Monitoring

- PHESGO administration can result in subclinical and clinical cardiac failure. The incidence and severity was highest in patients receiving PHESGO with anthracycline-containing chemotherapy regimens
- Discontinue PHESGO treatment in patients receiving adjuvant therapy and withhold PHESGO in patients with metastatic disease for clinically significant decrease in left ventricular function
- Evaluate cardiac function prior to and during treatment. For adjuvant therapy, also evaluate cardiac function after completion of PHESGO
- Monitor frequently for decreased left ventricular function during and after PHESGO treatment. Monitor more frequently if PHESGO is withheld for significant left ventricular cardiac dysfunction

Embryo-Fetal Toxicity

PHESGO can cause fetal harm when administered to a pregnant woman

PERJETA Important Safety Information (cont'd)

Additional Important Safety Information

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

Left Ventricular Dysfunction (LVD)

- Assess LVEF prior to initiation of PERJETA and at regular intervals during treatment to ensure that LVEF is within normal limits. If LVEF declines and has not improved, or has declined further at the subsequent assessment, discontinuation of PERJETA and trastuzumab should be strongly considered
- In the NeoSphere study, for patients receiving neoadjuvant treatment, a LVEF decline >10% and a drop to <50% occurred in 2% of patients treated with neoadjuvant trastuzumab and docetaxel as compared to 8% of patients in the PERJETA-treated group. LVD occurred in 0.9% of patients treated with neoadjuvant trastuzumab and docetaxel as compared to 3% of patients in the PERJETA-treated group. Symptomatic LVSD occurred in 0.9% of patients treated with neoadjuvant PERJETA in combination with trastuzumab and in no patients in the other 3 arms

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PHESGO Important Safety Information (cont'd)

Embryo-Fetal Toxicity (cont'd)

- Verify the pregnancy status of females of reproductive potential prior to the initiation of PHESGO. Advise pregnant women and females of reproductive potential that exposure to PHESGO during pregnancy or within 7 months prior to conception can result in fetal harm. Advise females of reproductive potential to use effective contraception during treatment and for 7 months following the last dose of PHESGO
- There is a pregnancy pharmacovigilance program for PHESGO. If PHESGO is administered during pregnancy, or if a patient becomes pregnant while receiving PHESGO or within 7 months following the last dose of PHESGO, health care providers and patients should immediately report PHESGO exposure to Genentech at 1-888-835-2555

Pulmonary Toxicity

- PHESGO can cause serious and fatal pulmonary toxicity. These adverse reactions have been reported with intravenous trastuzumab
- Pulmonary toxicity includes dyspnea, interstitial pneumonitis, pulmonary infiltrates, pleural effusions, non-cardiogenic pulmonary edema, pulmonary insufficiency and hypoxia, acute respiratory distress syndrome, and pulmonary fibrosis. Patients with symptomatic intrinsic lung disease or with extensive tumor involvement of the lungs, resulting in dyspnea at rest, appear to have more severe toxicity

Exacerbation of Chemotherapy-Induced Neutropenia

 PHESGO may exacerbate chemotherapy-induced neutropenia. In randomized controlled clinical trials with intravenous trastuzumab, Grade 3-4 neutropenia and febrile neutropenia were higher in patients receiving trastuzumab in combination with myelosuppressive chemotherapy as compared to those who received chemotherapy alone

Hypersensitivity and Administration-Related Reactions

- Severe administration-related reactions (ARRs), including hypersensitivity, anaphylaxis, and events with fatal outcomes, have been associated with intravenous pertuzumab and trastuzumab.
 Patients experiencing dyspnea at rest due to complications of advanced malignancy and comorbidities may be at increased risk of a severe or of a fatal ARR
- In the FeDeriCa study, the incidence of hypersensitivity was 1.2% in the PHESGO arm. ARRs occurred in 21% of patients who received PHESGO. In the PHESGO arm, the most common administrationrelated reactions were injection site reaction (15%) and injection site pain (2%)
- Closely monitor patients during and for 30 minutes after the injection of initial dose and during and for 15 minutes following subsequent injections of maintenance dose of PHESGO. If a significant injectionrelated reaction occurs, slow down or pause the injection and administer appropriate medical therapies. Evaluate and carefully monitor patients until complete resolution of signs and symptoms
- Permanently discontinue treatment with PHESGO in patients who experience anaphylaxis or severe injection-related reactions. Medications to treat such reactions, as well as emergency equipment, should be available for immediate use. For patients experiencing reversible Grade 1 or 2 hypersensitivity reactions, consider pre-medication with an analgesic, antipyretic, or an antihistamine prior to readministration of PHESGO

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PERJETA Important Safety Information (cont'd)

Left Ventricular Dysfunction (LVD) (cont'd)

- In the TRYPHAENA study, for patients receiving neoadjuvant treatment, in the overall treatment period, LVEF decline >10% and a drop to <50% occurred in 7% of patients treated with PERJETA plus trastuzumab and 5-fluorouracil, epirubicin, and cyclophosphamide (FEC), followed by PER|ETA plus trastuzumab and docetaxel; in 16% of patients treated with PERIETA plus trastuzumab and docetaxel following FEC; and in 11% of patients treated with PERJETA in combination with docetaxel, carboplatin, and trastuzumab (TCH). LVD occurred in 6% of patients treated with PERJETA plus trastuzumab and FEC, followed by PERJETA plus trastuzumab and docetaxel; in 4% of patients treated with PERJETA plus trastuzumab and docetaxel following FEC; and in 3% of patients treated with PERJETA in combination with TCH. Symptomatic LVSD occurred in 4% of patients treated with PERJETA plus trastuzumab and docetaxel following FEC, in 1% of patients treated with PERIETA in combination with TCH, and in none of the patients treated with PERJETA plus trastuzumab and FEC, followed by PERJETA plus trastuzumab and docetaxel
- In the BERENICE study, for patients receiving neoadjuvant PERJETA, LVEF decline ≥10% and a drop to <50% occurred in 7% of patients treated with PERJETA plus trastuzumab and paclitaxel following dosedense doxorubicin and cyclophosphamide (ddAC), and 2% of patients treated with PERJETA plus trastuzumab and docetaxel following FEC. Ejection fraction decrease (asymptomatic LVD) occurred in 7% of patients treated with PERJETA plus trastuzumab and paclitaxel following ddAC and in 4% of the patients treated with PERJETA plus trastuzumab and docetaxel following FEC. Symptomatic LVSD occurred in 2% of patients treated with PERJETA plus trastuzumab and paclitaxel following ddAC and in none of the patients treated with PERJETA plus trastuzumab and docetaxel following FEC
- In the APHINITY study, for patients treated in the adjuvant setting, the incidence of symptomatic heart failure with a LVEF decline ≥10% and a drop to <50% was <1% (0.6% of PERJETA-treated patients vs 0.2% of placebo-treated patients). Of the patients who experienced symptomatic heart failure, 47% of PERJETA-treated patients and 67% of placebo-treated patients had recovered (defined as 2 consecutive LVEF measurements above 50%) at the data cutoff. The majority of the events (86%) were reported in anthracycline-treated patients. Asymptomatic or mildly symptomatic declines in LVEF ≥10% and a drop to <50% were reported in 3% of PERJETA-treated patients and in 3% of placebo-treated patients, of whom 80% of PERJETA-treated patients and 81% of placebotreated patients recovered at the data cutoff

Infusion-Related Reactions

- PERJETA has been associated with infusion reactions, including fatal events
- In the NeoSphere, TRYPHAENA, and APHINITY studies, PERJETA was administered on the same day as the other study treatment drugs. For APHINITY, infusion-related reactions occurred in 21% of patients in the PERJETA-treated group and in 18% of patients in the placebo arm. The incidence of Grades 3-4 National Cancer Institute–Common Terminology Criteria for Adverse Events (NCI-CTCAE v4.0) reactions was 1% for the PERJETA arm and 0.7% for the placebo arm
- If a significant infusion reaction occurs, slow or interrupt the infusion and administer appropriate medical therapies. Monitor patients carefully until complete resolution of signs and symptoms. Consider permanent discontinuation in patients with severe infusion reactions

Hypersensitivity Reactions/Anaphylaxis

- In the CLEOPATRA study, the overall frequency of hypersensitivity reaction/anaphylaxis was 11% in the PERJETA-treated group and 9% in the placebo-treated group. The incidence of Grades 3-4 hypersensitivity reaction/anaphylaxis was 2% in the PERJETA-treated group and 3% in the placebo-treated group according to NCI-CTCAE v3.0
- In the NeoSphere, TRYPHAENA, BERENICE, and APHINITY studies, hypersensitivity/anaphylaxis events were consistent with those observed in CLEOPATRA





PHESGO Important Safety Information (cont'd)

Most Common Adverse Reactions Early Breast Cancer

The most common adverse reactions (>30%) with PHESGO were alopecia, nausea, diarrhea, anemia, and asthenia.

You are encouraged to report side effects to Genentech and the FDA. You may report side effects to the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch. You may also report side effects to Genentech at 1-888-835-2555.

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PERJETA Important Safety Information (cont'd)

Hypersensitivity Reactions/Anaphylaxis (cont'd)

 Patients should be observed closely for hypersensitivity reactions. Severe hypersensitivity, including anaphylaxis and fatal events, have been observed in patients treated with PERJETA. Angioedema has been described in post-marketing reports. Medications to treat such reactions, as well as emergency equipment, should be available for immediate use

Most Common Adverse Reactions Neoadjuvant Treatment of Breast Cancer

- The most common adverse reactions (>30%) with PERJETA in combination with trastuzumab and docetaxel administered for 4 cycles were alopecia, neutropenia, diarrhea, and nausea. The most common NCI-CTCAE v3.0 Grades 3-4 adverse reactions (>2%) were neutropenia, febrile neutropenia, leukopenia, and diarrhea
- The most common adverse reactions (>30%) with PERJETA in combination with trastuzumab and docetaxel administered for 3 cycles following 3 cycles of FEC were diarrhea, nausea, alopecia, neutropenia, vomiting, and fatigue. The most common NCI-CTCAE v3.0 Grades 3-4 adverse reactions (>2%) were neutropenia, leukopenia, febrile neutropenia, diarrhea, left ventricular dysfunction, anemia, dyspnea, nausea, and vomiting
- The most common adverse reactions (>30%) with PERJETA in combination with TCH administered for 6 cycles were diarrhea, alopecia, neutropenia, nausea, fatigue, vomiting, anemia, and thrombocytopenia. The most common NCI-CTCAE v3.0 Grades 3-4 adverse reactions (>2%) were neutropenia, febrile neutropenia, anemia, leukopenia, diarrhea, thrombocytopenia, vomiting, fatigue, alanine aminotransferase (ALT) increased, hypokalemia, and hypersensitivity
- The most common adverse reactions (>30%) with PERJETA in combination with trastuzumab and paclitaxel administered for 4 cycles following 4 cycles of ddAC were nausea, diarrhea, alopecia, fatigue, constipation, peripheral neuropathy, and headache. The most common Grades 3-4 adverse reactions (>2%) were neutropenia, febrile neutropenia, neutrophil count decreased, white blood cell count decreased, anemia, diarrhea, peripheral neuropathy, ALT increased, and nausea
- The most common adverse reactions (>30%) with PERJETA in combination with trastuzumab and docetaxel administered for 4 cycles following 4 cycles of FEC were diarrhea, nausea, alopecia, asthenia, constipation, fatigue, mucosal inflammation, vomiting, myalgia, and anemia. The most common Grades 3-4 adverse reactions (>2%) were febrile neutropenia, diarrhea, neutropenia, neutrophil count decreased, stomatitis, fatigue, vomiting, mucosal inflammation, neutropenic sepsis, and anemia

Adjuvant Treatment of Breast Cancer

- The most common adverse reactions (>30%) with PERJETA in combination with trastuzumab and chemotherapy were diarrhea, nausea, alopecia, fatigue, peripheral neuropathy, and vomiting. The most common Grades 3-4 adverse reactions (>2%) were neutropenia, febrile neutropenia, diarrhea, neutrophil count decreased, anemia, white blood cell count decreased, leukopenia, fatigue, nausea, and stomatitis
- The incidence of diarrhea, all Grades, was higher when chemotherapy was administered with targeted therapy (61% in the PERJETA-treated group vs 34% in the placebo-treated group) and was higher when administered with non–anthracycline-based therapy (85% in the PERJETA-treated group vs 62% in the placebo-treated group) than with anthracycline-based therapy (67% in the PERJETA-treated group vs 41% in the placebo-treated group). The incidence of diarrhea during the period that targeted therapy was administered without chemotherapy was 18% in the PERJETA-treated group vs 9% in the placebo-treated group

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Learn how you could help your patients spend less time in the clinic—with PHESGO.^{1,2}

VISIT PHESGO-HCP.COM

PHESGO Important Safety Information & Indications

Indications

Early Breast Cancer

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References: 1. PHESGO Prescribing Information. Genentech, Inc. 2020. **2.** PERJETA Prescribing Information. Genentech, Inc. 2021. **3.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines[®]) for Breast Cancer V.4.2023. © National Comprehensive Cancer Network, Inc. 2023. All rights reserved. Accessed March 23, 2023. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding the content, use or application of these guidelines and disclaims any responsibility for their application or use in any way.

