

Herceptin

ADMINISTRATION AND MONITORING

Please see page 20 and accompanying full Prescribing Information for **Boxed WARNINGS** and additional important safety information.



Herceptin[®]
t r a s t u z u m a b

indications,
regimens,
and dosing

adjuvant setting¹



Indications

Herceptin is indicated for adjuvant treatment of HER2-overexpressing node-positive or node-negative (ER/PR-negative or with one high-risk feature) breast cancer:

- As part of a treatment regimen containing doxorubicin, cyclophosphamide, and either paclitaxel or docetaxel
- With docetaxel and carboplatin
- As a single agent following multi-modality anthracycline-based therapy

Herceptin should be administered for a total of 12 months using 1 of the regimens on the following pages.

Please see page 20 and accompanying full Prescribing Information for **Boxed WARNINGS** and additional important safety information.

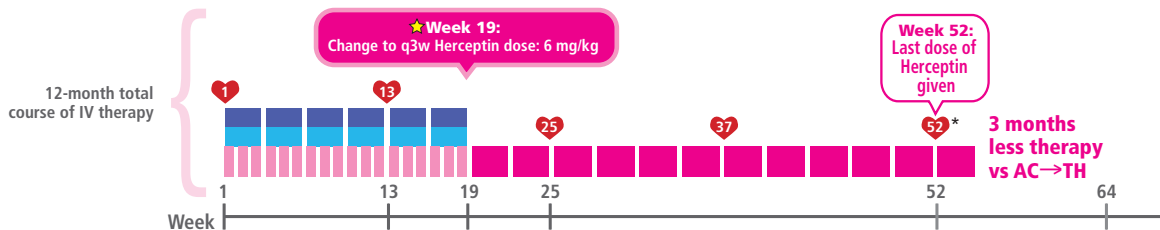


Herceptin[®]
trastuzumab

Indications,
regimens, and dosing

indications, regimens, and dosing (continued)

TCH regimen¹



- **TCH (weeks 1–18):** 4 mg/kg loading dose, as a 90-minute infusion, at week 1; 2 mg/kg at weeks 2–18, as a 30-minute infusion, weekly for 17 weeks
- **TCH (weeks 19–52):** 6 mg/kg, as a 30–90-minute infusion, every 3 weeks for 12 cycles
- **Taxotere^{®†} (docetaxel):** 75 mg/m² every 3 weeks for 6 cycles
- **Carboplatin:** at a target AUC of 6 mg/mL•min, as a 30- to 60-minute infusion, every 3 weeks for 6 cycles

Radiation therapy and/or hormonal therapy may be given after completion of chemotherapy if indicated.

★ **q3w Herceptin dose begins the week immediately following chemotherapy cycle.**

♥ **Week of cardiac assessment**

*Left ventricular ejection fraction (LVEF) should be measured at baseline immediately prior to initiation of Herceptin, every 3 months during and upon completion of Herceptin, and every 6 months for at least 2 years following completion of Herceptin as a component of adjuvant therapy.¹

[†]Taxotere is a registered trademark of sanofi-aventis U.S. LLC.

Herceptin dosing and administration guidelines

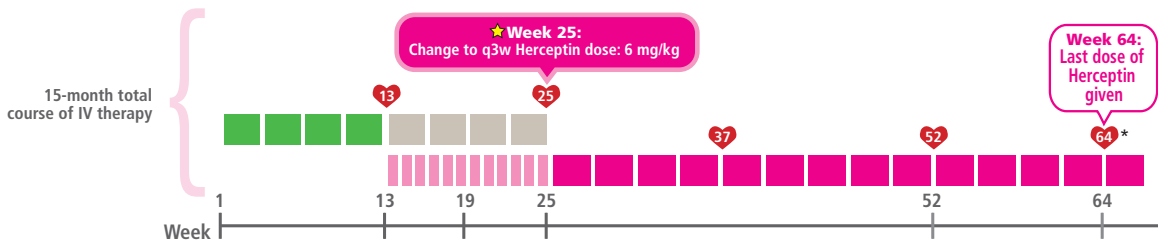
	Dosage	Infusion time
Loading dose	4 mg/kg	90 minutes
Subsequent weekly doses through week 18	2 mg/kg	30 minutes
Subsequent q3w doses from week 19 through end of Herceptin therapy	6 mg/kg	30–90 minutes

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indications, regimens, and dosing (continued)

AC→TH regimen¹



- **AC→TH (weeks 13–24):** 4 mg/kg loading dose, as a 90-minute infusion, at week 13; 2 mg/kg at weeks 14–24, as a 30-minute infusion, weekly for 11 weeks
- **AC→TH (weeks 25–64):** 6 mg/kg, as a 30–90-minute infusion, every 3 weeks for 14 cycles
- **AC:** doxorubicin 60 mg/m² and cyclophosphamide 600 mg/m² every 3 weeks for 4 cycles
- **T:** Taxane, either:
 - Taxotere 100 mg/m², every 3 weeks for 4 cycles, or
 - paclitaxel 175 mg/m², every 3 weeks for 4 cycles, or 80 mg/m² weekly for 12 weeks

Radiation therapy and/or hormonal therapy may be given after completion of chemotherapy if indicated.

★ **q3w Herceptin dose begins the week immediately following chemotherapy cycle.**

♥ **Week of cardiac assessment**

*Left ventricular ejection fraction (LVEF) should be measured at baseline immediately prior to initiation of Herceptin, every 3 months during and upon completion of Herceptin, and every 6 months for at least 2 years following completion of Herceptin as a component of adjuvant therapy.¹

¹Taxotere is a registered trademark of sanofi-aventis U.S. LLC.

Herceptin dosing and administration guidelines

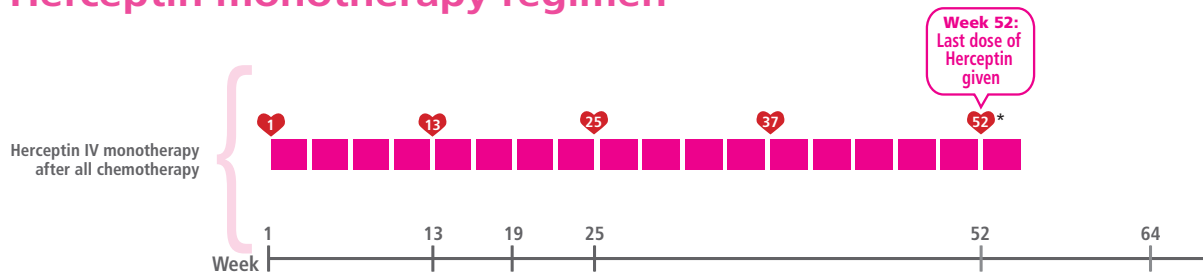
	Dosage	Infusion time
Loading dose	4 mg/kg	90 minutes
Subsequent weekly doses through week 12 of Herceptin therapy	2 mg/kg	30 minutes
Subsequent q3w doses from week 13 through end of Herceptin therapy	6 mg/kg	30–90 minutes

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Herceptin monotherapy regimen¹



■ **Herceptin monotherapy (weeks 1–52):** after completion of all chemotherapy regimens, 8 mg/kg loading dose, as a 90-minute infusion, at week 1; 6 mg/kg at weeks 4–52, as a 30–90-minute infusion, every 3 weeks for 18 cycles

Radiation therapy and/or hormonal therapy may be given after completion of chemotherapy if indicated.

♥ **Week of cardiac assessment**

*Left ventricular ejection fraction (LVEF) should be measured at baseline immediately prior to initiation of Herceptin, every 3 months during and upon completion of Herceptin, and every 6 months for at least 2 years following completion of Herceptin as a component of adjuvant therapy.¹

- Hormonal therapy may be given concurrently with Herceptin

Herceptin dosing and administration guidelines

	Dosage	Infusion time
Loading dose	8 mg/kg	90 minutes
Subsequent doses through end of Herceptin therapy	6 mg/kg	30–90 minutes

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metastatic setting¹

Indications

Herceptin is indicated:

- In combination with paclitaxel for first-line treatment of HER2-overexpressing metastatic breast cancer
- As a single agent for treatment of HER2-overexpressing breast cancer in patients who have received 1 or more chemotherapy regimens for metastatic disease

Herceptin should be administered, alone or in combination with paclitaxel, once weekly until disease progression using the following guidelines:

Herceptin dosing and administration guidelines		
	Dosage	Infusion time
Loading dose	4 mg/kg	90 minutes
Subsequent doses	2 mg/kg	30 minutes

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dosage calculation¹

- The recommended dosages of Herceptin are based on patient body weight
- To determine the correct number of milligrams of Herceptin needed for a given patient:

1

Convert patient weight into kilograms: 2.2 lb = 1 kg

$$\frac{\text{Patient weight in pounds}}{2.2 \text{ lb/kg}} = \text{Patient weight in kilograms}$$

2

Insert patient weight in kilograms into the dosage equation below, using the loading dose or the subsequent dose as the multiplier (see pages 5–11 for dosing information):

$$\frac{\text{Patient weight in kg} \times \text{multiplier (2, 4, 6, or 8 mg/kg)}}{21 \text{ mg/mL}} = \# \text{ mL reconstituted Herceptin solution}$$

- Please see pages 18–19 for treatment modifications

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Please see page 20 and accompanying full Prescribing Information for **Boxed WARNINGS** and additional important safety information.



Dosage
calculation

reconstitution¹

- **Reconstitution with 20 mL of the supplied Bacteriostatic Water for Injection (BWFI), USP**, containing 1.1% benzyl alcohol as a preservative, yields a multidose solution containing 21 mg/mL trastuzumab at a pH of approximately 6
- Keep the multidose solution refrigerated at 2°C–8°C (36°F–46°F). When reconstituted with BWFI, the multidose solution may be used for 28 days when stored at 2°C–8°C (36°F–46°F). **DO NOT FREEZE OR SHAKE RECONSTITUTED SOLUTION**
- If the patient has known sensitivity to benzyl alcohol, Herceptin must be reconstituted with Sterile Water for Injection (SWFI) (see DOSING AND ADMINISTRATION in accompanying full Prescribing Information)

HERCEPTIN THAT HAS BEEN RECONSTITUTED WITH SWFI MUST BE USED IMMEDIATELY AND ANY UNUSED PORTION DISCARDED. USE OF OTHER RECONSTITUTION DILUENTS SHOULD BE AVOIDED.

- Add calculated amount of reconstituted Herceptin solution to 250 mL of 0.9% Sodium Chloride Injection, USP. **DO NOT USE DEXTROSE (5%) SOLUTION**

additional administration information¹

- See pages 5–11 for information about Herceptin doses and infusion times
- Herceptin may be given in an outpatient setting
- **DO NOT ADMINISTER AS AN IV PUSH OR BOLUS**
- DO NOT MIX HERCEPTIN WITH OTHER DRUGS
- During the first infusion with Herceptin, a symptom complex most commonly consisting of chills and/or fever was observed in about 40% of patients in clinical trials
- The symptoms were usually mild to moderate in severity and were treated with acetaminophen, diphenhydramine, and meperidine (with or without reduction in the rate of Herceptin infusion)

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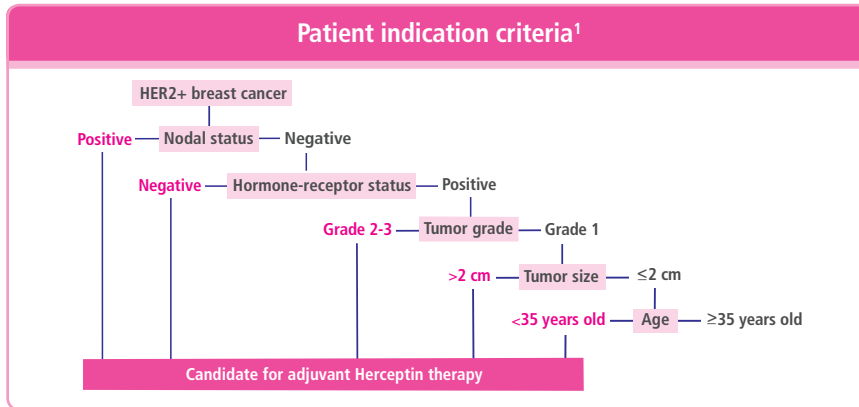
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Reconstitution &
Administration
information

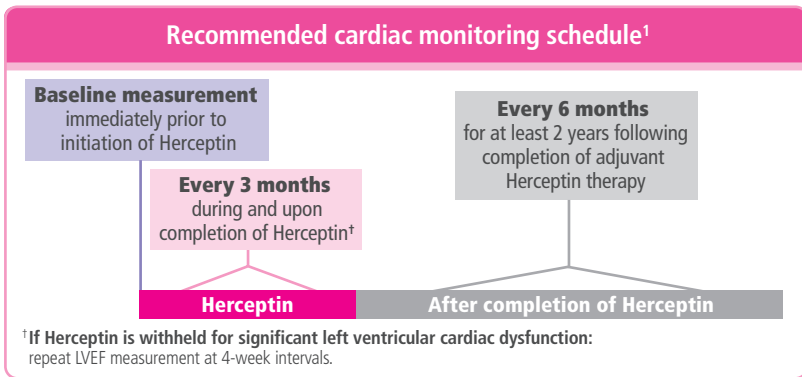
patient selection¹

- Herceptin is indicated for the adjuvant treatment of patients with node-positive or node-negative disease*:



*In the adjuvant clinical trials, eligible patients had a baseline left ventricular ejection fraction (LVEF) of >50%.

cardiac monitoring¹



- Conduct a thorough cardiac assessment, including history, physical examination, and determination of LVEF by echocardiogram or MUGA scan
- Patients should undergo monitoring for deteriorating left ventricular function prior to Herceptin treatment, and frequently during and after Herceptin treatment

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Patient selection &
Cardiac monitoring

treatment modifications¹

Cardiac issues

- Discontinue Herceptin for congestive heart failure or clinically significant asymptomatic decreases in left ventricular function
- In patients with asymptomatic declines in LVEF, Herceptin may be held and resumed **up to 3 times**, using the management protocol below

Herceptin administration for asymptomatic decreases in LVEF¹

Relationship of LVEF to LLN*	Absolute decrease from baseline (percentage points)		
	<10	10–15	≥16
Within normal limits	CONTINUE	CONTINUE	HOLD for ≥ 4 weeks
Below LLN	CONTINUE	HOLD for ≥ 4 weeks	HOLD for ≥ 4 weeks

*Lower limit of normal.

- When Herceptin is held, it may be resumed if, within 4–8 weeks:
 - The LVEF returns to normal limits, **and**
 - The absolute decrease from baseline is ≤15 percentage points
- Herceptin should be permanently discontinued if:
 - Persistent (>8 weeks) LVEF decline is observed, **or**
 - Herceptin dosing is held on more than 3 occasions for cardiomyopathy

Infusion reactions

- Treatment should be modified as follows for infusion reactions that occur during adjuvant treatment or treatment of metastatic disease:
 - Decrease the rate of infusion for mild or moderate infusion reactions
 - Interrupt the infusion in patients with dyspnea or clinically significant hypotension
 - Discontinue Herceptin for severe or life-threatening infusion reactions

These treatment modification guidelines should not be used as a substitute for independent medical judgment.

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Boxed WARNINGS and Additional Important Safety Information

Herceptin administration can result in sub-clinical and clinical cardiac failure manifesting as congestive heart failure and decreased left ventricular ejection fraction. Serious infusion reactions and pulmonary toxicity have occurred; fatal infusion reactions have been reported. Exacerbation of chemotherapy-induced neutropenia has also occurred. Herceptin can cause oligohydramnios and fetal harm when administered to a pregnant woman. The most common adverse reactions associated with Herceptin use were fever, nausea, vomiting, infusion reactions, diarrhea, infections, increased cough, headache, fatigue, dyspnea, rash, neutropenia, anemia, and myalgia.

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Herceptin[®]
trastuzumab

Important
Safety Information

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Reference: 1. Herceptin Prescribing Information. Genentech, Inc. March 2009.

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