

## Evidence Based Guideline

### Herceptin

**File Name:** herceptin  
**Guideline Number:** EBG.DRU4090  
**Origination:** 2/1999  
**Last Review:** 4/2009  
**Next Review:** 4/2011

#### Description of Procedure or Service

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Herceptin® also known as Trastuzumab, is a drug used to treat breast cancer that has spread to other parts of the body from its original site. Herceptin® is a monoclonal antibody, one of a group of drugs designed to attack specific cancer cells. It has been approved by the Food and Drug Administration (FDA) for the treatment of [metastatic](#) breast cancer in patients who overexpress HER2 (human epidermal growth factor receptor2). HER2 protein overexpression is seen in approximately 25-30% of women with [metastatic](#) breast cancer. HER2 overexpression is determined by an immunohistochemical test done on the tumor tissue or by FISH assay.

**Note: The clinical indications for this drug are complex and technical. If you have questions concerning use of the drug or the medical criteria for its use, please talk with your physician.**

#### Evidence Based Guideline for Herceptin

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Herceptin® may be appropriate for the treatment of [metastatic](#) breast cancer for one of the following clinical indications:

1. Overexpression of ( $\geq 2+$ ) HER2 has been detected and the patient has received one or more chemotherapy regimens for the [metastatic](#) breast disease; or
2. Overexpression of ( $\geq 2+$ ) HER2 has been detected in newly diagnosed [metastatic](#) breast disease, the patient has not received any chemotherapy and the patient will be receiving a combination of Herceptin® (trastuzumab) and other standard chemotherapy regimens.

Herceptin® in combination with adjuvant chemotherapy may be appropriate for patients who have had completely resected HER-2-positive breast cancer and have either of the following:

1. Node-positive disease; or
2. High-risk breast cancer, defined as either tumors greater than 1 cm if the tumor is estrogen receptor negative OR if the tumor is greater than 2 cm and is estrogen receptor positive.

Herceptin® as a component of preoperative (neoadjuvant or primary systemic) therapy, followed by additional post-operative adjuvant trastuzumab may be appropriate to complete a full year of treatment, for patients with HER2-positive breast cancer undergoing medically appropriate preoperative chemotherapy.

## Policy: Herceptin

### Medical Evidence regarding Herceptin indicates it is not recommended in the following situations:

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For indications other than those listed above, including the treatment of other malignancies such as osteosarcoma, non-small-cell lung, ovarian, prostate, head and neck, esophageal, gastric, pancreatic, colorectal, endometrial, or urothelial cancers.

#### **Relative Contraindications:**

- ◆ Patients with pre-existing cardiac dysfunction, cardiomyopathy, or anthracycline use in the past should use this drug cautiously.
- ◆ Concurrent anthracycline therapy (e.g., doxorubicin, epirubicin, daunorubicin) use.

### Benefits Application

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Please refer to certificate for availability of benefit. This guideline relates only to the services or supplies described herein. Benefits may vary according to benefit design; therefore certificate language should be reviewed before applying the terms of the policy.

### Billing/Coding/Physician Documentation Information

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This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at [www.bcbsnc.com](http://www.bcbsnc.com). They are listed in the Category Search on the Medical Policy search page.

*Applicable codes: J9355*

### Medical Term Definitions

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#### **Metastatic**

transfer of disease from one organ or part of the body to another not directly connected with it.

### Scientific Background and Reference Sources

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Genetech BioOncology product information

Blue Cross Blue Shield Association, Clearinghouse Update, September 1998, pp 1,3.

Oncology Consultant Review 11/98

Pegram MD, Lipton A. Phase II study of receptor-enhanced chemosensitivity using recumbent humanized anti-p185HER2/Neu monoclonal antibody plus cisplatin in patients with HER2/Neu overexpressing metastatic breast cancer refractory to chemotherapy treatment. *J Clin Oncol.* 1998; 16(8);2659-71.

Baselga J, Norton L. Recumbent humanized anti-HER2 antibody (Herceptin) enhances the antitumor activity of Paclitaxel and doxorubicin against HER2/neu overexpressing human breast cancer xenografts. *Cancer Res.* 1998; 58(13);2825-31.

Medical Policy Advisory Group 3/1/99

USPDI - 1999 - On-line Update Version - Developed 12/11/98 - 9/99

## Policy: Herceptin

USPDI - 2000 - On-line Update Version - Developed 12/11/98. Revised 07/24/2000

Specialty Matched Consultant Advisory Panel - 6/2001

BCBSA Medical Policy Reference Manual, 12/18/02; 5.01.12

Specialty Matched Consultant Advisory Panel - 6/2003

National Institute for Clinical Excellence (NCCN). (2002). Guidance on the use of trastuzumab for the treatment of advanced breast cancer. Retrieved 2/9/2005 from <http://www.nice.org.uk/page.aspx?o=29280>.

BCBSA Medical Policy Reference Manual [Electronic Version], 5.01.12, 11/9/2004

Specialty Matched Consultant Advisory Panel - 4/2005

BCBSA Medical Policy Reference Manual [Electronic Version], 5.01.12, 12/14/2005

Specialty Matched Consultant Advisory Panel - 4/2007

BCBSA Medical Policy Reference Manual [Electronic Version], 5.01.12, 12/11/08

Specialty Matched Consultant Advisory Panel - 4/2009

### Policy Implementation/Update Information

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- 2/99 Original policy developed. There appears to be little benefit in using Herceptin with 2+HER2 over-expressors. At the same time, the test for overexpression is somewhat subjective.
- 5/99 Reformatted, description of service changed, medical terms added.
- 9/99 Revised to include 2+ HER2 overexpression as per 1999 USPDI on-line update information.
- 1/00 Revised to add new HCPCS code J9355.
- 3/01 System changes.
- 6/01 Specialty Matched Consultant Advisory Panel review. No change in criteria.
- 6/03 Specialty Matched Consultant Advisory Panel review. No criteria changes. Format changes.
- 4/04 Benefits Application and Billing/Coding sections updated for consistency.
- 5/5/05 Specialty Matched Consultant Advisory Panel meeting 4/14/2005. No changes to criteria. References added.
- 9/18/06 Medical Policy changed to Evidence Based Guideline.
- 5/21/07 Specialty Matched Consultant Advisory Panel review 4/25/2007. Added additional indication under "Evidence Based Guideline for Herceptin" which states; "Herceptin® in combination with adjuvant chemotherapy may be appropriate for patients who have had completely resected HER-2-positive breast cancer and have either of the following: 1. Node-positive disease; or 2. High-risk breast cancer, defined as either tumors greater than 1 cm if the tumor is estrogen receptor negative OR if the tumor is greater than 2 cm and is estrogen receptor positive." References added.
- 5/18/09 The following statement was added to the guideline: "Herceptin as a component of preoperative (neoadjuvant or primary systemic) therapy, followed by additional postoperative adjuvant trastuzumab may be appropriate to complete a full year of treatment, for patients with HER2-positive breast cancer undergoing medically appropriate preoperative chemotherapy." Also added a statement to indicate Herceptin may not be appropriate for indications other than those listed in the guideline, including the treatment of other malignancies such as osteosarcoma, non-small-cell lung, ovarian, prostate, head and neck, esophageal, gastric, pancreatic, colorectal, endometrial, or urothelial cancers. Specialty Matched Consultant Advisory Panel review 4/21/09. (btw)

## **Policy: Herceptin**

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Medical policy is not an authorization, certification, explanation of benefits or a contract. Benefits and eligibility are determined before medical guidelines and payment guidelines are applied. Benefits are determined by the group contract and subscriber certificate that is in effect at the time services are rendered. This document is solely provided for informational purposes only and is based on research of current medical literature and review of common medical practices in the treatment and diagnosis of disease. Medical practices and knowledge are constantly changing and BCBSNC reserves the right to review and revise its medical policies periodically.