

<b>Trastuzumab (Herceptin™)</b>	
<input checked="" type="checkbox"/> Original	<b>Original Committee Approval: 12/3/08</b>
<input type="checkbox"/> Revised	<b>Last Committee Approval: 12/3/08</b>
	<b>Last Review: October 2008</b>

## **Background**

Trastuzumab (Herceptin®; Genentech Inc) is a recombinant DNA-derived humanized monoclonal antibody that selectively binds with high affinity to the extracellular domain of the human epidermal growth factor receptor 2 protein, HER2. After binding to HER2 on the tumor cell surface, trastuzumab induces an antibody-dependent cell-mediated cytotoxicity against tumor cells that over-express HER2. HER2 is over-expressed by many adenocarcinomas, particularly breast adenocarcinomas

Trastuzumab, administered by IV infusion, was originally approved by the U.S. Food and Drug Administration (FDA) for the treatment of metastatic breast cancer that is HER2 positive. The FDA approved this after several clinical trials demonstrated that trastuzumab was safe and effective in treating metastatic breast cancers that produced excess amounts of HER2

In 2005, the results of four clinical trials showed that trastuzumab is also effective in the treatment of early-stage breast cancer that over-expresses HER2. In all four studies, women who received this drug, in combination with chemotherapy, lived longer and had significantly less chance of breast cancer recurrence compared with those who received chemotherapy alone.

Subsequent to this, the FDA has approved and the National Comprehensive Cancer Care Network has recommended the additional indications for Trastuzumab as specified below.

## **Indications/Criteria**

**In all instances**, Trastuzumab should be used in patients whose tumors have been evaluated with an assay validated to predict HER2 protein over-expression.

**Trastuzumab is considered medically necessary for the following indications:**

- As a single agent for the treatment of patients with metastatic breast cancer whose tumors overexpress the HER2 protein and who have received one or more chemotherapy regimens for their metastatic disease.
- In combination with paclitaxel or docetaxel for the treatment of patients with metastatic breast cancer whose tumors over-express the HER2 protein and who have not received chemotherapy for their metastatic disease.

- In combination with doxorubicin, cyclophosphamide, and paclitaxel or docetaxel for adjuvant (i.e., post-surgical) treatment of patients with early (localized) breast cancer that over-expresses HER2 protein
- In combination with docetaxel and carboplatin for adjuvant (post-surgical) treatment of patients with early (localized) breast cancer that over-expresses HER2 protein.
- As a single agent following multi-modality anthracycline-based (e.g., doxorubicin) adjuvant therapy for patients with node-negative or node-positive breast cancer that over-expresses the HER2 protein.

### **Additional indications and treatment limitations:**

- Trastuzumab is considered medically necessary for up to one year of therapy for HER2-positive breast cancer with no distant metastatic disease.
- A repeat course of Trastuzumab is considered medically necessary for HER2-positive breast cancer with no distant metastatic disease if this has been in remission for more than one year after finishing the prior course of Trastuzumab therapy.
- Herceptin treatment is considered medically necessary for HER2-positive breast cancer with distant metastatic disease, unless disease progresses.

### **CHP considers Trastuzumab) experimental and investigational, alone or in combination with chemotherapy, for the following:**

- Neoadjuvant (i.e., pre-operative) therapy for early, localized breast cancer
- All other types of cancer (e.g., non-small cell lung cancer, ovarian cancer, prostate cancer, colorectal cancer, endometrial cancer, pancreatic cancer)
- All other indications

### **Special Considerations**

#### **Cardiotoxicity**

Patients treated with trastuzumab can demonstrate signs and symptoms of cardiac dysfunction, such as dyspnea, increased cough, paroxysmal nocturnal dyspnea, and peripheral edema. Congestive heart failure associated with this agent may be severe and has been associated with disabling cardiac failure, stroke, and death. Extreme caution should be exercised in treating patients with pre-existing cardiac dysfunction, and patients receiving trastuzumab should undergo frequent monitoring of cardiac status. The data suggest that advanced age may increase the probability of such dysfunction.

### **Limitations/Exclusions**

<b>Healthy Options:</b>	None; pre-authorization required.
<b>Basic Health Plan:</b>	None; pre-authorization required.
<b>GAU:</b>	None; pre-authorization required.
<b>Medicare Advantage:</b>	None; pre-authorization required.

**Required Review and Approvals:**

Trastuzumab (Herceptin®) infusions require prior authorization by the CHP Medical Director or his/her designee. Each authorization period will be for six months.

**References:**

1. National Cancer Institute ([www.cancer.gov](http://www.cancer.gov))
2. Federal Drug Administration ([www.fda.gov](http://www.fda.gov))
3. Facts and Comparisons 4.0 (<http://online.factsandcomparisons.com>)
4. National Comprehensive Cancer Network, Clinical Practice Guidelines in Oncology™ ([www.nccn.org](http://www.nccn.org))
5. UpToDate Online 16.2 ([www.uptodate.com](http://www.uptodate.com))
6. Hayes, Inc. ([www.hayesinc.com](http://www.hayesinc.com))
7. Premera Blue Cross Corporate Med. Policy CP.MP.PR.5.01.514 (rev. 10/9/07)
8. Aetna Clinical Policy Bulletin #0313 (rev. 6/27/08)