CareFirst Family of health care plans

CVS/caremark

# SPECIALTY GUIDELINE MANAGEMENT

## HERCEPTIN (trastuzumab)
## KADCYLA (ado-trastuzumab)

**POLICY**

### I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

**HERCEPTIN**

A. FDA-Approved Indications
   1. Adjuvant breast cancer
      a. Herceptin is indicated for adjuvant treatment of human epidermal growth factor receptor (HER)2-overexpressing node positive or node negative (estrogen receptor (ER)/progesterone receptor (PR) negative or with one high risk feature) breast cancer
      b. As part of a treatment regimen consisting of doxorubicin, cyclophosphamide, and either paclitaxel or docetaxel
      c. With docetaxel and carboplatin
      d. As a single agent following multi-modality anthracycline based therapy
   2. Metastatic breast cancer
      a. In combination with paclitaxel for first-line treatment of HER2-overexpressing metastatic breast cancer
      b. As a single agent for treatment of HER2-overexpressing breast cancer in patients who have received one or more chemotherapy regimens for metastatic disease
   3. Metastatic gastric cancer
      In combination with cisplatin and capecitabine or 5-fluorouracil, for the treatment of patients with HER2 overexpressing metastatic gastric or gastroesophageal junction adenocarcinoma, who have not received prior treatment for metastatic disease.

B. Compendial Uses
   1. HER2-positive breast cancer
      a. Preoperative (neoadjuvant) therapy, in combination with or as a component of:
         i. Paclitaxel or docetaxel with or without pertuzumab following AC (doxorubicin and cyclophosphamide)
         ii. TCH (docetaxel, carboplatin and trastuzumab) with or without pertuzumab
         iii. Docetaxel + cyclophosphamide
         iv. Pertuzumab + docetaxel or paclitaxel prior to or following FEC/CEF (fluorouracil, epirubicin, cyclophosphamide.
      b. Adjuvant treatment in combination with chemotherapy for tumors that are
         i. At least 0.6 cm
         ii. Less than, or equal to, 0.5 cm and node positive
         iii. Microinvasive and node positive
      c. Combination therapy with paclitaxel for low risk stage I, particularly for patients not eligible for other standard adjuvant regimens due to comorbidities.
      d. Recurrent or metastatic ER-positive disease, in combination with aromatase inhibition in postmenopausal women

e. Recurrent or metastatic disease that is hormone receptor (HR)-negative or HR-positive and endocrine refractory as:
   i. First-line chemotherapy in combination with pertuzumab with docetaxel or paclitaxel
   ii. First-line chemotherapy alone or in combination with docetaxel, vinorelbine, or capecitabine, or paclitaxel with or without carboplatin
   iii. Treatment for trastuzumab-exposed HER2-positive disease in combination with carboplatin, cisplatin, cyclophosphamide, eribulin, gemcitabine, ixabepilone lapatinib (without cytotoxic therapy) or capecitabine
   iv. May be considered in combination with pertuzumab with or without cytotoxic therapy (e.g., vinorelbine or taxane) for one line of therapy beyond first-line therapy in patients previously treated with chemotherapy and trastuzumab in the absence of pertuzumab
f. Leptomeningeal metastases from HER2-positive breast cancer

2. First-line palliative therapy for metastatic or locally advanced HER2-positive esophageal, esophagogastric junction, or gastric cancer, in combination with cisplatin and fluorouracil or capecitabine, for patients with Karnofsky performance score of at least 60% or an Eastern Cooperative Oncology Group (ECOG) performance score of 0-2.

**KADCYLA**

A. FDA-Approved Indications
Kadcyla, as a single agent, is indicated for the treatment of patients with *HER2*-positive, metastatic breast cancer who previously received trastuzumab and a taxane, separately or in combination. Patients should have either received prior therapy for metastatic disease, or developed disease recurrence during or within six months of completing adjuvant therapy.

B. Compendial Uses
Single-agent therapy for recurrent or metastatic HER2-positive disease with symptomatic visceral disease or visceral crisis that is hormone receptor-negative or hormone receptor-positive and endocrine therapy refractory

All other indications are considered experimental/investigational and are not a covered benefit.

## II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the prior authorization review:

**A. Breast cancer**
1. HER2 test results
2. HR test result (if applicable)

**B. Esophageal, gastric, or esophagogastric junction cancer:** HER2 test results

## III. CRITERIA FOR INITIAL APPROVAL

**HERCEPTIN**

**A. Breast cancer**
1. Authorization of 6 months may be granted for neoadjuvant treatment of HER2-positive breast cancer when Herceptin is used as a component of or in combination with a chemotherapy regimen that includes docetaxel or paclitaxel.
2. Authorization of up to 12 months total may be granted for adjuvant treatment of HER2-positive breast cancer when all of the following criteria are met [a and b]:
   a. Herceptin is used as a component of, in combination with, or following a chemotherapy regimen, with or without pertuzumab.
   b. If Herceptin is used in combination with pertuzumab, a pertuzumab-containing regimen was not used as neoadjuvant therapy.
3. Authorization of 12 months may be granted for treatment of leptomeningeal metastases from HER2-positive breast cancer.
4. Authorization of 12 months may be granted for treatment of HER2-positive metastatic or recurrent breast cancer when any of the following criteria sets is met [a, b, or c]:

a. Herceptin is used as a single agent in a member who has been previously treated with one or more chemotherapy regimens for metastatic disease.
b. Member has an ER-positive disease and Herceptin is used with an aromatase inhibitor (e.g., letrozole, anastrozole, exemestane) in a postmenopausal woman.
c. Member has an HR-negative or endocrine-therapy refractory disease and meets either of the following criteria sets [i or ii]:
    i. Herceptin is used in combination with chemotherapy with or without pertuzumab.
    ii. Herceptin is used in combination with lapatinib or pertuzumab, without chemotherapy, and the member has previously been treated with trastuzumab.

**B. Esophageal, gastric, or esophagogastric junction cancer**

Authorization of 12 months may be granted for treatment of HER2-positive metastatic or locally advanced esophageal, gastric, or esophagogastric junction cancer when Herceptin is used in combination with any of the following chemotherapy regimens:

1. Cisplatin and fluorouracil (5-FU)
2. Cisplatin and capecitabine

**KADCYLA**

Authorization of 12 months may be granted for treatment of HER2-positive recurrent or metastatic breast cancer when Kadcyla is used as a single agent.

## IV. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

## V. DOSAGE AND ADMINISTRATION

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

## VI. REFERENCES


1. Herceptin [package insert]. South San Francisco, CA: Genentech, Inc.; March 2016.
2. Kadcyla [package insert]. South San Francisco, CA: Genentech, Inc.; April 2016.
3. The NCCN Drugs & Biologics Compendium™ © 2015 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed July 19, 2016.
4. National Comprehensive Cancer Network. NCCN clinical practice guidelines in oncology: breast cancer. Version 2.2016. http://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed July 19, 2016.
5. National Comprehensive Cancer Network. NCCN clinical practice guidelines in oncology: gastric cancer. Version 2.2016. http://www.nccn.org/professionals/physician_gls/pdf/gastric.pdf. Accessed July 19, 2016.
6. National Comprehensive Cancer Network. NCCN clinical practice guidelines in oncology: esophageal and esophagogastric junction cancer. Version 2.2016. http://www.nccn.org/professionals/physician_gls/pdf/esophageal.pdf. Accessed July 19, 2016.