Pertuzumab
ACG: A-0898 (AC)
Link to Codes

Clinical Indications
- Pertuzumab may be indicated when ALL of the following are present(1)(2)(3):
  - Age 18 years or older
  - Breast cancer, and disease activity and treatment scenario include 1 or more of the following:
    - Metastatic disease and need for initial treatment, administered in combination with trastuzumab and either docetaxel or paclitaxel[3](6)(7)(8)(9)
    - Nonmetastatic disease and 1 or more of the following[15](16)(17)(18)(19):
      - Preoperative (ie, neoadjuvant) multiagent treatment regimen needed for patient with 1 or more of the following:
        - Lymph-node positive
        - Tumor size greater than 2 cm in diameter
        - Inflammatory disease
        - Locally advanced disease
      - Postoperative (ie, adjuvant) multiagent treatment regimen (ie, in combination with chemotherapy) needed for patient with 1 or more of the following:
        - Lymph-node positive
        - Tumor size greater than 2 cm in diameter
    - HER2 overexpression, as indicated by 1 or more of the following[22](23)(24):
      - Immunohistochemistry showing 3+ positivity for HER2
      - Positive test for HER2 via gene amplification with fluorescence in situ hybridization
      - Positive test for HER2 with chromogenic in situ hybridization
    - Patient not pregnant

Evidence Summary
Background
Pertuzumab is a recombinant monoclonal antibody that binds to the HER2 protein, thereby inhibiting cell proliferation.(1)(2) (EG 2)
HER2 overexpression (HER2 positivity) occurs in approximately 15% to 20% of primary breast cancers.(4)(5) (EG 2)

Criteria
For metastatic breast cancer that is HER2 positive, evidence demonstrates at least moderate certainty of at least moderate net benefit.
(RG A1) A network meta-analysis of 8 randomized trials (3976 patients) evaluating the efficacy of combinations of HER2-targeted agents for first-line treatment of metastatic HER2-positive breast cancer concluded that the combination of pertuzumab, docetaxel, and trastuzumab was the only regimen that was associated with improved overall and progression-free survival.(10) (EG 1) A randomized controlled trial of 808 patients with HER2-positive metastatic breast cancer found that first-line therapy consisting of the addition of pertuzumab to a regimen of trastuzumab and docetaxel significantly improved median overall survival from 40.8 months to 56.5 months.(8) (EG 1) Furthermore, addition of pertuzumab to trastuzumab and docetaxel increased the median time to development of central nervous system metastases from 11.9 months to 15 months.(11) (EG 1) Expert consensus guidelines and review articles recommend pertuzumab in combination with trastuzumab and either docetaxel or paclitaxel for patients with HER2-positive metastatic breast cancer.(3)(12)(13)(14) (EG 2)

For nonmetastatic breast cancer that is HER2 positive, evidence demonstrates at least moderate certainty of at least moderate net benefit. (RG A1) A prospective, multicenter, multinational, double-blind, placebo-controlled trial involving 4805 patients with early...
HER2-positive breast cancer reported a significantly lower disease recurrence (7.1% vs 8.7%, respectively) in patients randomized to chemotherapy and 1 year of treatment with trastuzumab plus pertuzumab as compared with patients randomized to chemotherapy and 1 year of treatment with trastuzumab plus placebo. The invasive disease-free survival at 36 months was significantly improved (92% vs 90.2%, respectively) only in the cohort with node-positive disease. (15) (EG 1) A network meta-analysis of 13 randomized trials (3160 patients) evaluating the effectiveness of neoadjuvant therapies for HER2-positive breast cancer concluded that the combination of pertuzumab, trastuzumab, and chemotherapy had the highest probability of success in terms of pathologic complete response (defined as the absence of invasive neoplastic cells in the breast tissue or lymph nodes at the time of surgery). (20) (EG 1) An open-label phase II trial randomly assigned 417 treatment-naive women with nonmetastatic HER2-positive breast cancer to 4 different multiagent treatment regimens. Pathologic complete response was achieved in 45.8% of patients treated with the combination of pertuzumab, trastuzumab, and docetaxel, as compared with 29% of those treated with trastuzumab plus docetaxel, 24% of those treated with pertuzumab plus docetaxel, and 16.8% of those treated with pertuzumab plus trastuzumab. (17) (EG 2) A subsequent 5-year analysis revealed a greater progression-free survival rate in patients who had achieved a pathologic complete response as compared with patients who did not achieve a pathologic complete response. (21) (EG 2) In an open-label phase II trial, 225 patients with HER2-positive operable, locally advanced, or inflammatory breast cancer were randomly assigned to receive 1 of 3 treatment regimens, all of which included pertuzumab, trastuzumab, and docetaxel. Pathologic complete response was noted in 57% to 66% of patients, depending on the treatment regimen. (18) (EG 2) An expert consensus guideline recommends that a pertuzumab-containing regimen be given preoperatively to patients with HER2-positive early-stage breast cancer and either positive lymph nodes or tumors larger than 2 cm. (3) (EG 2)

References


Footnotes

[A] For metastatic breast cancer, pertuzumab is administered as an initial 60-minute intravenous infusion, followed by a 30-minute to 60-minute intravenous infusion every 3 weeks. (1) [A in Context Link 1]

[B] For nonmetastatic breast cancer, neoadjuvant treatment with pertuzumab is administered as an initial 60-minute intravenous infusion, followed by a 30-minute to 60-minute intravenous infusion every 3 weeks for 3 to 6 cycles. For adjuvant treatment, pertuzumab is administered every 3 weeks for up to 1 year, or until disease recurrence or unacceptable toxicity occurs. (1) [B in Context Link 1]

[C] HER2 testing should be performed by a laboratory with documented proficiency in the testing technology. (1)(3)(22) [C in Context Link 1]

[D] Left ventricular ejection fraction should be measured before starting pertuzumab and then every 12 weeks thereafter. Deterioration in ejection fraction may require temporary or permanent discontinuation of pertuzumab. (1)(18) [D in Context Link 1]

Codes

HCPCS: J9306