# Pertuzumab

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

MCG Health
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## 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[A](3)(6)(7)(8)(9) N
    - Nonmetastatic disease and **1 or more** of the following[B](15)(16)(17)(18)(19): N
      - Preoperative (ie, neoadjuvant) multiagent treatment regimen needed for patient with **1 or more** of the following:
        - Early-stage disease and **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[C](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
  - Left ventricular ejection fraction measured prior to administration and at regular intervals during therapy[D](18)
  - Patient not pregnant(25)

## 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


1. Perjeta (pertuzumab) injection. Physician Prescribing Information [Internet] Genentech, Inc. 2018 Sep Accessed at: http://www.perjeta.com/. [created 2012; accessed 2018 Nov 20] [ Context Link 1, 2, 3, 4, 5, 6 ]
2. Blumenthal GM, et al. First FDA approval of dual anti-HER2 regimen: pertuzumab in combination with trastuzumab and docetaxel for HER2-positive metastatic breast cancer. Clinical Cancer Research 2013;19(18):4911-6. DOI: 10.1158/1078-0432.CCR-13-1212. [ Context Link 1, 2 ] View abstract...
3. Gradishar WJ, et al. Breast Cancer. NCCN Clinical Practice Guideline in Oncology [Internet] National Comprehensive Cancer Network (NCCN). v. 2.2018; 2018 Oct Accessed at: http://www.nccn.org/professionals/physician_gls/f_guidelines.asp. [accessed 2018 Oct 15] [ Context Link 1, 2, 3, 4, 5 ]
4. Loibl S, Gianni L. HER2-positive breast cancer. Lancet 2017;389(10087):2415-29. DOI: 10.1016/S0140-6736(16)32417-5. [ Context Link 1 ] View abstract...
5. Wuerstlein R, Harbeck N. Neoadjuvant therapy for HER2-positive breast cancer. Reviews on Recent Clinical Trials 2017;12(2):81-92. DOI: 10.2174/1574887112666170202165049. [ Context Link 1 ] View abstract...
6. Baselga J, et al. Pertuzumab plus trastuzumab plus docetaxel for metastatic breast cancer. New England Journal of Medicine 2012;366(2):109-19. DOI: 10.1056/NEJMoa1113216. [ Context Link 1 ] View abstract...
7. Swain SM, et al. Pertuzumab, trastuzumab, and docetaxel for HER2-positive metastatic breast cancer (CLEOPATRA study): overall survival results from a randomised, double-blind, placebo-controlled, phase 3 study. Lancet Oncology 2013;14(6):461-71. DOI: 10.1016/S1470-2045(13)70130-X. [ Context Link 1 ] View abstract...
8. Swain SM, et al. Pertuzumab, trastuzumab, and docetaxel in HER2-positive metastatic breast cancer. New England Journal of Medicine 2015;372(8):724-34. DOI: 10.1056/NEJMoa1413513. [ Context Link 1, 2 ] View abstract...
9. Pertuzumab with Trastuzumab and Docetaxel for Treating HER2-Positive Breast Cancer. NICE Technology Appraisal Guidance TA 509 [Internet] National Institute for Health and Care Excellence. 2018 Mar 7 Accessed at: http://www.nice.org.uk/guidance. [accessed 2018 Oct 10] [ Context Link 1 ]
10. Leung HWC, Leung JH, Chan ALF. Efficacy and safety of a combination of HER2-targeted agents as first-line treatment for metastatic HER2-positive breast cancer: a network meta-analysis. Expert Opinion on Drug Safety 2018;17(1):1-7. DOI: 10.1080/14740338.2018.1394454. [ Context Link 1 ] View abstract...
11. Swain SM, et al. Incidence of central nervous system metastases in patients with HER2-positive metastatic breast cancer treated with pertuzumab, trastuzumab, and docetaxel: results from the randomized phase III study CLEOPATRA. Annals of Oncology 2014;25(6):1116-21. DOI: 10.1093/annonc/mdu133. [ Context Link 1 ] View abstract...
12. Giordano SH, et al. Systemic therapy for patients with advanced human epidermal growth factor receptor 2-positive breast cancer: ASCO clinical practice guideline update. Journal of Clinical Oncology 2018;36(26):2736-2740. DOI: 10.1200/JCO.2018.79.2697. [ Context Link 1 ] View abstract...
13. Boix-Perales H, et al. The European medicines agency review of pertuzumab for the treatment of adult patients with HER2-positive metastatic or locally recurrent unresectable breast cancer: Summary of the scientific assessment of the Committee for medicinal products for human use. Oncologist 2014;19(7):766-73. DOI: 10.1634/theoncologist.2013-0348. [ Context Link 1 ] View abstract...
14. O'Sullivan CC, Swain SM. Pertuzumab : evolving therapeutic strategies in the management of HER2-overexpressing breast cancer. Expert Opinion on Biological Therapy 2013;13(5):779-90. DOI: 10.1517/14712598.2013.783007. [ Context Link 1 ] View abstract...
15. von Minckwitz G, et al. Adjuvant pertuzumab and trastuzumab in early HER2-positive breast cancer. New England Journal of Medicine 2017;377(2):122-31. DOI: 10.1056/NEJMoa1703643. [ Context Link 1, 2 ] View abstract...
16. Nagayama A, et al. Comparative effectiveness of neoadjuvant therapy for HER2-positive breast cancer: a network meta-analysis. Journal of the National Cancer Institute 2014;106(9):Online. DOI: 10.1093/jnci/dju203. [ Context Link 1 ] View abstract...

17. Gianni L, et al. Efficacy and safety of neoadjuvant pertuzumab and trastuzumab in women with locally advanced, inflammatory, or early HER2-positive breast cancer (NeoSphere): a randomised multicentre, open-label, phase 2 trial. Lancet Oncology 2012;13(1):25-32. DOI: 10.1016/S1470-2045(11)70336-9. [ Context Link 1, 2 ] View abstract...

18. Schneeweiss A, et al. Pertuzumab plus trastuzumab in combination with standard neoadjuvant anthracycline-containing and anthracycline-free chemotherapy regimens in patients with HER2-positive early breast cancer: a randomized phase II cardiac safety study (TRYPHAENA). Annals of Oncology 2013;24(9):2278-84. DOI: 10.1093/annonc/mdt182. [ Context Link 1, 2, 3, 4 ] View abstract...

19. Pertuzumab for the Neoadjuvant Treatment of HER2-Positive Breast Cancer. NICE Technology Appraisal TA424 [Internet] National Institute for Health and Care Excellence. 2016 Dec Accessed at: http://www.nice.org.uk/guidance. [accessed 2018 Oct 10] [ Context Link 1 ]

20. Nakashoji A, et al. The updated network meta-analysis of neoadjuvant therapy for HER2-positive breast cancer. Cancer Treatment Reviews 2018;62:9-17. DOI: 10.1016/j.ctrv.2017.10.009. [ Context Link 1 ] View abstract...

21. Gianni L, et al. 5-year analysis of neoadjuvant pertuzumab and trastuzumab in patients with locally advanced, inflammatory, or early-stage HER2-positive breast cancer (NeoSphere): a multicentre, open-label, phase 2 randomised trial. Lancet Oncology 2016;17(6):791-800. DOI: 10.1016/S1470-2045(16)00163-7. [ Context Link 1 ] View abstract...

22. Wolff AC, et al. Recommendations for human epidermal growth factor receptor 2 testing in breast cancer: American Society of Clinical Oncology/College of American Pathologists clinical practice guideline update. Journal of Clinical Oncology 2013;31(31):3997-4013. DOI: 10.1200/JCO.2013.50.9984. (Reaffirmed 2017 May) [ Context Link 1, 2 ] View abstract...

23. Ballinger TJ, Sanders ME, Abramson VG. Current HER2 testing recommendations and clinical relevance as a predictor of response to targeted therapy. Clinical Breast Cancer 2015;15(3):171-180. DOI: 10.1016/j.clbc.2014.11.009. [ Context Link 1 ] View abstract...

24. Rakha EA, et al. Updated UK Recommendations for HER2 assessment in breast cancer. Journal of Clinical Pathology 2015;68(2):93-99. DOI: 10.1136/jclinpath-2014-202571. [ Context Link 1 ] View abstract...

25. Amant F, Loibl S, Neven P, Van Calsteren K. Breast cancer in pregnancy. Lancet 2012;379(9815):570-9. DOI: 10.1016/S0140-6736(11)61092-1. [ Context Link 1 ] View abstract...

# 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

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