Submitted by:
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NCCN Guidelines Panel: Breast Cancer

On behalf of Genentech, Inc., I respectfully request the NCCN Breast Cancer Guideline Panel to review the enclosed recent key publications and presentations for:

- **Perjeta® (pertuzumab)**

  Swain SM, Kim S-B, Cortes J, et al. Final overall survival (OS) analysis from the CLEOPATRA study of first-line (1L) pertuzumab (Ptz), trastuzumab (T), and docetaxel (D) in patients with HER2-positive metastatic breast cancer (MBC). Presented at the European Society for Medical Oncology in Madrid, Spain; September 26-30, 2014. ESMO Oral presentation #3500_PR.

- **Herceptin® (trastuzumab)**

  Perez EA, Romond EH, Suman VJ, et al. Trastuzumab plus adjuvant chemotherapy for human epidermal growth factor receptor 2-positive breast cancer: planned joint analysis of overall survival from NSABP B-31 and NCCTG N9831. J Clin Oncol. E-pub date: [published online ahead of print] 2014. DOI# 10.1200/JCO.2014.55.5730.
  http://www.ncbi.nlm.nih.gov/pubmed/?term=25332249

Specific Changes:

There are no specific changes being requested. Please consider the Swain et al. Perjeta presentation and the Perez et al. Herceptin publication for your updating purposes.

FDA Clearance:

- Perjeta is FDA-approved for use in combination with trastuzumab and docetaxel for treatment of patients with HER2-positive metastatic breast cancer (MBC) who have not received prior anti-HER2 therapy or chemotherapy for metastatic disease.
- Herceptin is FDA-approved for the adjuvant treatment of HER2 overexpressing node positive or node negative (ER/PR negative or with one high risk feature) breast cancer.

Please refer to the enclosed Perjeta and Herceptin prescribing information for the full FDA-approved indications and safety information.

Rationale:

- **Perjeta:**

  The CLEOPATRA study was a Phase III trial that supported the FDA approval of Perjeta in patients with previously untreated HER2-positive MBC. The final overall survival (OS) analysis showed that adding Perjeta to Herceptin and docetaxel chemotherapy extended the lives of patients with previously untreated HER2-positive MBC by 15.7 months compared with patients treated with Herceptin and docetaxel alone (median OS: 56.5 vs. 40.8 months; HR=0.68 [95% CI 0.56-0.84; p=0.0002]). Safety was consistent with that observed previously in the study.

- **Herceptin:**

  The NSABP B-31 and NCCTG N9831 clinical trials supported the FDA-approval of Herceptin in the adjuvant setting for early HER2+ breast cancer. The final joint analysis of OS showed adding Herceptin to chemotherapy resulted in a 37% reduction in the risk of death (84% vs 75.2%; HR=0.63; 95% CI, 0.54-0.73; p<0.0001). This planned joint analysis did not include extensive discussion of safety which has been reported in earlier analyses.

Respectfully submitted,