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Submitted by:
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Date of request: September 15, 2017
NCCN Guidelines Panel: NCCN Esophageal/Gastric Cancers Panel

On behalf of Genentech, Inc., I respectfully request the NCCN Esophageal/Gastric Cancers Panel to review the enclosed data for:

- **Perjeta® (pertuzumab)**

  Tabernero J, Hoff PM, Shen L, et al. Pertuzumab(P) + trastuzumab(H) + chemotherapy (CT) for HER2-positive metastatic gastric or gastro-oesophageal junction cancer (mGC/GEJC): Final analysis of a Phase III study (JACOB). Presented at the ESMO 2017 Congress in Madrid, Spain; September 8–12, 2017. ESMO Oral Presentation #616O.
  https://cslide.ctimeetingtech.com/library/esmo/browse/search/2bxL#2Bb5i0Ft

Specific Changes:
There are no specific changes being requested. We are providing data on Perjeta in combination with trastuzumab and chemotherapy in patients with HER2-postitive metastatic gastric or gastroesophageal junction cancer.

FDA Clearance:
- Perjeta is not FDA-approved for treatment of patients with HER2-positive metastatic gastric or gastroesophageal junction cancer.
- Herceptin is FDA-approved for use 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.

Please refer to the product prescribing information for the full FDA-approved indications and safety information.
- Full Perjeta® prescribing information available at: http://www.gene.com/download/pdf/perjeta_prescribing.pdf
- Full Herceptin® prescribing information available at: https://www.gene.com/download/pdf/herceptin_prescribing.pdf

Rationale:
JACOB was a Phase 3, double-blind, placebo-controlled, randomized, multicenter, international study conducted to evaluate the effect of adding Perjeta to trastuzumab and chemotherapy (cisplatin plus 5-fluorouracil or capecitabine) in patients with HER2-positive metastatic gastric or gastroesophageal junction adenocarcinoma. The primary endpoint of overall survival (OS) was not met. The median OS observed in the study was 17.5 months vs. 14.2 months in the Perjeta-containing arm vs. control arm respectively (HR=0.84, 95% CI: 0.71-1.00, p=0.0565). The safety profile was comparable between the two arms except for diarrhea. All-grade diarrhea occurred in 61.6% vs. 35.1% and Grade 3-5 diarrhea occurred in 13.2% vs. 6.4% of Perjeta-treated vs. placebo-treated patients, respectively.

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To date, JACOB is the only Phase 3 trial that evaluated the addition of Perjeta to trastuzumab and chemotherapy for the treatment of HER2-postive metastatic gastric or gastroesophageal junction adenocarcinoma.

Respectfully submitted,

Susie Kim, Pharm.D.

Supplemental References:

1. Kang K, Rha Y, Tassone P, et al. A Phase IIa dose-finding and safety study of first-line pertuzumab in combination with trastuzumab, capecitabine and cisplatin in patients with HER2- positive advanced gastric cancer. Br J Cancer. E-pub Date: [published online ahead of print] June 2014. DOI # 10.1038/bjc.2014.356. http://www.ncbi.nlm.nih.gov/pubmed/24960402

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