Name: Suzana Giffin, AVP
Company/Organization: Merck & Co., Inc.
Address: 2000 Galloping Hill Rd. Kenilworth, NJ 07033
Phone: 908-740-6708
Email: suzana.giffin@merck.com
Date of Request: 06/04/2021
NCCN Guidelines Panel: Esophageal/Gastric Cancers

On behalf of Merck & Co., Inc., I respectfully request the NCCN Esophageal/Gastric Cancers Panel to review the enclosed information for KEYTRUDA® (pembrolizumab), in reference to use in patients with gastric or gastroesophageal junction (GEJ) cancer.

Specific Changes: As a follow up to the letter submitted on May 6, 2021, we respectfully request the inclusion of pembrolizumab, in combination with trastuzumab, fluoropyrimidine- and platinum-containing chemotherapy, as a first-line treatment option for patients with locally advanced unresectable or metastatic HER2-positive gastric or GEJ adenocarcinoma under "Preferred Regimens, HER2 overexpression positive adenocarcinoma" as a Category 2A recommendation in the NCCN Gastric Cancer Guidelines v2.2021 (page GAST-F 3 of 15) based on the FDA-approved indication of KEYTRUDA[1] and the data from KEYNOTE-811 presented by Janjigian et al.[2] at the 2021 American Society of Clinical Oncology (ASCO) Annual Meeting.

FDA Clearance:
Gastric Cancer

- KEYTRUDA, in combination with trastuzumab, fluoropyrimidine- and platinum-containing chemotherapy, is indicated for the first-line treatment of patients with locally advanced unresectable or metastatic HER2-positive gastric or gastroesophageal junction (GEJ) adenocarcinoma.

This indication is approved under accelerated approval based on tumor response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials.

Please refer to the KEYTRUDA (pembrolizumab) prescribing information for other FDA-approved indications.[1]

Rationale: KEYTRUDA in combination with trastuzumab, fluoropyrimidine- and platinum-containing chemotherapy is FDA-approved for the first-line treatment of patients with locally advanced unresectable or metastatic HER2-positive gastric or GEJ adenocarcinoma, based on the results from KEYNOTE-811, a phase 3, randomized, multicenter, double-blind, placebo-controlled study.[1]

In a protocol-specified first interim analysis by Janjigian et al., ORR (overall response rate) and DOR (duration of response) were assessed in the first 264 patients enrolled, with 133 patients randomized to the pembrolizumab arm and 131 patients randomized to the placebo arm. A statistically significant and clinically meaningful improvement in ORR with durable responses was demonstrated in patients receiving pembrolizumab in combination with trastuzumab and chemotherapy (74.4%, 95% CI: 66.2 – 81.6) vs. placebo in combination with trastuzumab and chemotherapy (51.9%, 95% CI: 43.0 – 60.7), with an ORR difference of 22.7% (95% CI: 11.2-33.7, p = 0.00006). The complete response rate was 11% (15/133) in the pembrolizumab

arm and 3% (4/131) in the placebo arm. The partial response rate was 63% (84/133) in the pembrolizumab arm and 49% (64/131) in the placebo arm. The median DOR was 10.6 months (range 1.1+ to 16.5+ months) in the pembrolizumab arm and 9.5 months (range 1.4+ to 15.4+ months) in the placebo arm. Out of the 99 responding patients in the pembrolizumab arm, 70.3% had ≥6-month duration of response and 58.4% had ≥9-month duration of response. Out of the 68 responding patients in the placebo arm, 61.4% had ≥6-month duration of response and 51.1% had ≥9-month duration of response. The safety analysis of KEYNOTE-811 included 217 patients who received pembrolizumab and 216 patients in the placebo arm. The all-cause adverse events (AEs) for Grade 3-5 were 57% in both groups. The immune-mediated AEs and infusion reactions for Grade 3-5 were 10% in the pembrolizumab arm and 3% in the placebo arm.[2]

Overall, the totality of the KEYNOTE-811 data presented by Janjigian et al. and the FDA-approved indication of KEYTRUDA support our request for the recommendation for pembrolizumab, in combination with trastuzumab, fluoropyrimidine- and platinum-containing chemotherapy, as a first-line treatment option for patients with locally advanced unresectable or metastatic HER2-positive gastric or GEJ adenocarcinoma under "Preferred Regimens, HER2 overexpression positive adenocarcinoma" as a Category 2A recommendation in the NCCN Gastric Cancer Guidelines.[1,2]

The following resources are submitted to assist the committee with their review.

1. KEYTRUDA (pembrolizumab) prescribing information. Merck & Co., Inc.
2. Janjigian Y, Kawazoe A, Yanez P et al. Pembrolizumab plus trastuzumab and chemotherapy for HER2+ metastatic gastric or gastroesophageal junction cancer: initial findings of the global phase 3 KEYNOTE-811 study. Presented at the 2021 ASCO Annual Meeting; June 4-8; Online Meeting.

Thank you for considering this request. Below is my contact information should you need to contact me for additional information.

Sincerely,

Suzana Giffin, AVP
Merck & Co., Inc.
2000 Galloping Hill Rd
Kenilworth, NJ 07033
908-740-6708
suzana.giffin@merck.com