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: 03/31/2021
NCCN Guidelines Panel: Esophageal/Gastric Cancers

NCCN Esophageal /Gastric Cancers Panel: 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 NCCN Esophageal and Esophagogastric Junction Cancers Guidelines, v2.2021.

Specific Changes: We respectfully request the recommendation that pembrolizumab, in combination with oxaliplatin and fluoropyrimidine based chemotherapy, for metastatic or locally advanced esophageal or gastroesophageal cancer as a first-line treatment option be changed from Category 2A to Category 1, and we also request the removal of PD-L1 CPS ≥ 10 testing requirement on the use of pembrolizumab in combination with oxaliplatin/cisplatin and fluoropyrimidine based chemotherapy as first-line treatment option in the NCCN Esophageal and Esophagogastric Junction Cancers Guidelines, v2.2021 (page ESOPH-F 3 of 16) based on the FDA approved indication of KEYTRUDA supported by the KEYNOTE-590 study data.

FDA Clearance:

Esophageal Cancer

KEYTRUDA is indicated for the treatment of patients with locally advanced or metastatic esophageal or gastroesophageal junction (GEJ) (tumors with epicenter 1 to 5 centimeters above the GEJ) carcinoma that is not amenable to surgical resection or definitive chemoradiation either:

- In combination with platinum- and fluoropyrimidine-based chemotherapy, or
- As a single agent after one or more prior lines of systemic therapy for patients with tumors of squamous cell histology that express PD-L1 (CPS ≥ 10) as determined by an FDA-approved test.

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

Rationale:

A previous request was submitted on March 23, 2021 following the FDA approval of KEYTRUDA, in combination with platinum and fluoropyrimidine based chemotherapy, for the first-line treatment of patients with metastatic or locally advanced esophageal or GEJ cancer, based on the results from KEYNOTE-590 study (NCT03189719), a phase 3, randomized, double-blind, placebo-controlled, international study which enrolled 749 patients with metastatic or locally advanced esophageal or GEJ cancer.[1] Additionally, the KEYNOTE-590 study data by Kato et al.[2], was previously submitted (on September 21, 2020) to this Panel for consideration.

In the KEYNOTE-590 study, pre-specified analyses were conducted on overall survival (OS) and progression free survival (PFS) based on squamous cell histology, CPS ≥ 10 and in all patients. In an exploratory analysis in patients with PD-L1 CPS < 10 (n=347), the median OS was 10.5 months (95% CI: 9.7, 13.5) for the pembrolizumab arm and 10.6 months (95% CI: 8.8, 12.0) for the placebo arm, with a HR of 0.86 (95% CI: 0.68, 1.10), with 271 events observed in 347 patients.[1,2] In an additional analysis of PFS in patients with PD-L1 CPS < 10, the pembrolizumab arm versus the placebo arm had a HR of 0.80 (95% CI: 0.64, 1.01), with 302 events observed in 347 patients.[2]

The FDA approved indication of KEYTRUDA as a first-line treatment option for patients with metastatic or locally advanced esophageal or GEJ carcinoma also supports our request to change the recommendation for pembrolizumab in combination with platinum (oxaliplatin/cisplatin) and fluoropyrimidine based chemotherapy to Category 1 without biomarker testing.[1]

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

1. KEYTRUDA (pembrolizumab) prescribing information. Merck & Co., Inc.
2. Kato K., Sun JM., Shah M. et al. Pembrolizumab plus chemotherapy versus chemotherapy as first-line therapy in patients with advanced esophageal cancer: the phase 3 KEYNOTE-590 study. Presented at: ESMO Annual Meeting; September 19-21, 2020; *Annals of Oncology* 2020;31(suppl_4):S1192-S1193.

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