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Date of Request: 06/30/2020
NCCN Guidelines Panel: Colon/Rectal/Anal Cancers

NCCN Colon/Rectal/Anal Cancers Panel: On behalf of Merck & Co., Inc., I respectfully request the NCCN Colon/Rectal/Anal Cancers Panel to review the enclosed information for KEYTRUDA® (pembrolizumab), in reference to NCCN Colon Cancer Guidelines v4.2020.

Specific Changes:

We respectfully request the recommendation for pembrolizumab as a first-line therapy option for patients with MSI-H/dMMR unresectable or metastatic colon cancer be changed from category 2A to category 1 in the NCCN Colon Cancer Guidelines v4.2020 (pages COL-D 1 of 13, and MS-49) based on the FDA approved indication of KEYTRUDA in MSI-H/dMMR colorectal cancer. We also request the removal of the associated footnote "Patients should be followed closely for 10 weeks to assess for response." on page COL-D 1 of 13.

FDA Clearance:

Microsatellite Instability-High or Mismatch Repair Deficient Colorectal Cancer

- KEYTRUDA is indicated for the first-line treatment of patients with unresectable or metastatic MSI-H or dMMR colorectal cancer (CRC).

Microsatellite Instability-High or Mismatch Repair Deficient Cancer

- KEYTRUDA is indicated for the treatment of adult and pediatric patients with unresectable or metastatic, microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR)
    - solid tumors that have progressed following prior treatment and who have no satisfactory alternative treatment options, or
    - colorectal cancer that has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan.

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

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

Rationale:

KEYTRUDA is now FDA approved for the first-line treatment of patients with unresectable or metastatic MSI-H or dMMR CRC, based on the results from KEYNOTE-177 (NCT02563002), a multicenter, randomized, open-label, active-controlled trial that enrolled 307 patients with previously untreated unresectable or metastatic MSI-H or dMMR CRC.[1]

Additionally, the KEYNOTE-177 study data from the Andre et al. presentation at the American Society for Clinical Oncology (ASCO) 2020 Virtual Scientific Program, which was previously submitted to this Panel, supports our

request to change the recommendation from category 2A to category 1 for pembrolizumab as a first-line therapy option for patients with MSI-H/dMMR metastatic colon cancer.[2]

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

1. KEYTRUDA (pembrolizumab) prescribing information. Merck & Co., Inc.
2. Andre T., Shiu K., Kim T. et al. Pembrolizumab versus chemotherapy for microsatellite instability-high/mismatch repair deficient metastatic colorectal cancer: the phase 3, KEYNOTE-177 study. Presented at: ASCO Virtual Scientific Program. *J Clin Oncol* 2020;38(suppl);abstr LBA4.

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

Sincerely,

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