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NCCN Guidelines Panel: Colon Cancer

On behalf of Merck & Co., Inc. we respectfully request the NCCN Colon Cancer Panel review the enclosed data and consider inclusion of KEYTRUDA® (pembrolizumab) for the treatment of patients with mismatch-repair deficient colorectal cancer.

FDA Clearance:

Melanoma
KEYTRUDA (pembrolizumab) is indicated for the treatment of patients with unresectable or metastatic melanoma.

Non-Small Cell Lung Cancer
KEYTRUDA is indicated for the treatment of patients with metastatic non-small cell lung cancer whose tumors express PD-L1 as determined by an FDA-approved test with disease progression on or after platinum-containing chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving KEYTRUDA.
This indication is approved under accelerated approval based on tumor response rate and durability of response. An improvement in survival or disease-related symptoms has not yet been established. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

Rationale:
In an article published in the *New England Journal of Medicine*, June 25, 2015, Le et al reported interim results from a phase 2 study which assessed the clinical activity of pembrolizumab in patients with progressive metastatic carcinoma with or without mismatch repair deficiency (MMR). At the data cutoff (May, 2015) the immune-related objective response rate (ORR) and immune-related progression free survival rate were 40% (4 of 10 patients) and 78% (7 of 9 patients), respectively, for mismatch repair-deficient colorectal cancers. The median progression free survival (PFS) and overall survival (OS) were not reached. At the annual *Society of Immunotherapy of Cancer* meeting, Le presented updated results for this cohort; as of September, 2015, the ORR for patients with MMR-deficient colorectal cancer (N=20) was 55% with a disease control rate of 90%. Responses were durable with the median PFS and OS not reached as of October, 2015, with a median follow up time of 37 weeks (11 - 93). Based on data from KEYNOTE 016, Merck has received breakthrough therapy designation from the FDA for KEYTRUDA in patients with microsatellite instability high metastatic colorectal cancer.

To assist the committee with their review, I have included the following resources:

1. KEYTRUDA (pembrolizumab) prescribing information. Merck & Co., Inc.
2. Le D et al. PD-1 Blockade in Patients with Mismatch-Repair Deficiency. *The New England Journal of Medicine. 2015. 372:2509-2520.*

3. Le D et al. Oral Presentation at the *Society of Immunotherapy of Cancer*, 4-8 November 2015: National Harbor, Maryland.

Thank you for your consideration of this request.

Sincerely,

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