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NCCN Guidelines Panel: Malignant Pleural Mesothelioma

Specific Changes:
On behalf of Merck & Co., Inc., we respectfully request the NCCN Malignant Pleural Mesothelioma panel review the enclosed publication and consider adding pembrolizumab as an option for patients with PD-L1 positive advanced or metastatic malignant pleural mesothelioma who have progressed on standard therapy.

FDA Clearance:
Melanoma
KEYTRUDA is indicated for the treatment of patients with unresectable or metastatic melanoma.

Non-Small Cell Lung Cancer
KEYTRUDA is indicated for the first-line treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have high PD-L1 expression [Tumor Proportion Score (TPS) ≥50%)] as determined by an FDA-approved test, with no EGFR or ALK genomic tumor aberrations.

KEYTRUDA is indicated for the treatment of patients with metastatic NSCLC whose tumors express PD-L1 (TPS ≥1%) 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.

Head and Neck Cancer
KEYTRUDA is indicated for the treatment of patients with recurrent or metastatic head and neck squamous cell carcinoma with disease progression on or after platinum-containing chemotherapy.

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.

Classical Hodgkin Lymphoma
KEYTRUDA is indicated for the treatment of adult and pediatric patients with refractory classical Hodgkin lymphoma (cHL), or who have relapsed after 3 or more prior lines of therapy.

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.

Rationale:
Interim results of the KEYNOTE-028 trial in the malignant pleural mesothelioma cohort were first published online in the *Lancet Oncology* on March 10th, 2017. In summary, pembrolizumab demonstrated anti-tumor activity in patients with PD-L1-positive (defined as membranous PD-L1 staining in ≥1% of tumor and associated inflammatory cells, or positive staining in the stroma) locally advanced or metastatic malignant pleural mesothelioma who had

failed standard therapy or were unable to receive standard therapy. As of June 20, 2016, 25 patients received pembrolizumab. Five (20%) had a partial response, for an objective response of 20% (95% CI 6.8-40.7). Thirteen (52%) of 25 had stable disease. The median follow-up duration was 18.7 months. The median duration of response was 12 months (3.7-NR). Two patients remained on treatment at data cutoff. Sixteen (64%) patients reported a treatment-related adverse event; the most common were fatigue (6[24%]), nausea 6[24%]) and arthralgia (5[20%]). No treatment-related deaths or discontinuations occurred.

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

1. KEYTRUDA (pembrolizumab) prescribing information. Merck & Co., Inc.
2. Alley EW, et al. Clinical safety and activity of pembrolizumab in patients with malignant pleural mesothelioma (KEYNOTE-028): preliminary results from a non-randomised, open-label, phase 1b trial. *Lancet Oncology*, 2017; http://dx.doi.org/10.1016/S1470-2045(17)30169-9.

Thank you for your consideration of this request.

Sincerely,

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Merck & Co., Inc.