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NCCN Guidelines Panel: Non-Small Cell Lung Cancer

Specific Changes:
On behalf of Merck & Co., Inc. we respectfully request the NCCN NSCLC Panel review the enclosed data and consider inclusion of KEYTRUDA® (pembrolizumab) in combination with carboplatin and pemetrexed as initial therapy for previously untreated, advanced non-squamous non-small cell lung cancer (NSCLC) patients whose tumors lack epidermal growth factor receptor sensitizing mutations or anaplastic lymphoma kinase translocations.

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 treatment of patients with metastatic NSCLC 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.

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.

Rationale:
In an article published online in *The Lancet Oncology* on October 9, 2016, Langer et al., published the results from a randomized, open-label, phase 2 cohort of a multicohort study (KEYNOTE-021). Patients with chemotherapy-naïve, stage IIIB or IV, non-squamous NSCLC without targetable EGFR or ALK genetic aberrations were randomly assigned to pembrolizumab plus carboplatin and pemetrexed or to carboplatin and pemetrexed alone. The primary endpoint was the proportion of patients who achieved an objective response. 33 of 60 patients in the pembrolizumab plus chemotherapy group achieved an objective response (55%; 95% CI 42-68) compared with 18 (29%; CI 18-41) of 63 patients in the chemotherapy alone group (estimated treatment difference 26% [95%; CI 9-42%]; p=0.0016). Median progression-free survival was 13.0 months (95% CI 8.3 to not reached) for pembrolizumab plus chemotherapy and 8.9 months (4.4-10.3) for chemotherapy alone. The incidence of grade 3 or worse treatment-related adverse events was similar between groups (23 [39%] of 59 patients in the pembrolizumab plus chemotherapy group and 16 [26%] of 62 in the chemotherapy alone group.

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

1. KEYTRUDA (pembrolizumab) prescribing information. Merck & Co., Inc.

2. Langer et al., Carboplatin and pemetrexed with or without pembrolizumab for advanced, non-squamous non-small-cell lung cancer: a randomized, phase 2 cohort of the open label KEYNOTE-021 study. *The Lancet Oncology.* Published online October 9, 2016 http://dx.doi.org/S1470-2045(16)30498-3.

Thank you for your consideration of this request.

Sincerely,

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