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NCCN Guidelines Panel: Non-Small Cell Lung Cancer

On behalf of Merck & Co., Inc., we respectfully request the NCCN Non-Small Cell Lung Cancer Panel to review the enclosed information for KEYTRUDA (pembrolizumab), in reference to NCCN Guidelines V3.2018 for Non-Small Cell Lung Cancer.

Specific Changes Requested:

We respectfully request that KEYTRUDA in combination with pemetrexed and platinum-containing chemotherapy be recommended as first-line therapy for patients with metastatic nonsquamous non-small cell lung cancer (NSCLC) (Category 1). We also request that a footnote be added to pemetrexed maintenance to specify that if given with pembrolizumab and platinum combination therapy that pembrolizumab should be given with pemetrexed for up to 35 cycles.

FDA Approval (NSCLC indications):

Non-Small Cell Lung Cancer
KEYTRUDA, as a single agent, is indicated for the first-line treatment of patients with metastatic 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, as a single agent, 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.

KEYTRUDA, in combination with pemetrexed and carboplatin, is indicated for the first-line treatment of patients with metastatic nonsquamous NSCLC. This indication is approved under accelerated approval based on tumor response rate and progression-free survival. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials.

Rationale:

A double-blind, phase 3 trial (KEYNOTE-189; NCT02578680) was conducted in patients with untreated, metastatic nonsquamous NSCLC without sensitizing *EGFR* or *ALK* alterations to receive pembrolizumab 200 mg or placebo plus pemetrexed and platinum every 3 weeks for 4 cycles, then maintenance with pembrolizumab or placebo (for up to 35 cycles) plus pemetrexed. Primary endpoints were overall survival and progression-free survival assessed by blinded, independent central radiologic review. After a 10.5-month median follow-up, median overall survival was not reached in the pembrolizumab-pemetrexed-platinum group and was 11.3 months for the placebo-pemetrexed-platinum group (hazard ratio for death, 0.49; 95% CI, 0.38-0.64; P<0.00001). The hazard ratio for death was 0.59 [95% CI, 0.38-0.92] in patients with a PD-L1 TPS<1%, 0.55 [95% CI, 0.34-0.90] in patients with a TPS 1-49%, and 0.42 [95% CI, 0.26-0.68] in patients with a TPS≥50%. Median progression-free survival was 8.8 months in the pembrolizumab-pemetrexed-platinum group and 4.9 months in the placebo-pemetrexed-platinum group

(hazard ratio for progression or death, 0.52; 95% CI, 0.43-0.64; P<0.00001). Grade ≥3 adverse events occurred in 67.2% of the patients in the pembrolizumab-pemetrexed-platinum group and 65.8% of patients in the placebo-pemetrexed-platinum group. Adverse events led to death in 27 (6.7%) patients in the pembrolizumab-pemetrexed-platinum group and 12 (5.9%) patients in the placebo-pemetrexed-platinum group.

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

1. KEYTRUDA (pembrolizumab) Prescribing Information. Merck & Co., Inc.

2. Gandhi L, Rodriguez-Abreu D, Gadgeel S, et al. Pembrolizumab plus chemotherapy in metastatic non-small-cell lung cancer. *N Engl J Med*. 2018. doi: 10.1056/NEJMoa1801005. Epub ahead of print.

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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