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NCCN Guidelines Panel: Head and Neck Cancers

On behalf of Merck & Co., Inc., I respectfully request the NCCN Head and Neck Cancer Panel to review the enclosed information for KEYTRUDA (pembrolizumab), in reference to NCCN Guidelines V1.2018 for Head and Neck Cancers.

Specific changes requested:

We respectfully request the category of evidence and consensus for KEYTRUDA (pembrolizumab) to be changed from category 2A to category 1 recommendation in patients with non-nasopharyngeal, recurrent or metastatic head and neck squamous cell carcinoma with disease progression on or after platinum-containing chemotherapy (section CHEM-A).

FDA Approval:

KEYTRUDA (pembrolizumab) is approved for the treatment of patients with recurrent or metastatic head and neck squamous cell carcinoma (HNSCC) 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.

Please refer to the KEYTRUDA Prescribing Information for other FDA-approved indications.[1]

Rationale:

A multicenter, open-label, randomized phase III study (KEYNOTE-040; NCT02252042) of pembrolizumab versus standard of care (SOC) was conducted in patients with recurrent or metastatic head and neck squamous cell carcinoma (R/M HNSCC). Key eligibility criteria included SCC of the oral cavity, oropharynx, hypopharynx or larynx; progressive disease (PD) after platinum-containing chemotherapy for R/M HNSCC or recurrence or PD within 3-6 months of multimodal therapy using platinum; ECOG PS 0 or 1. Patients received pembrolizumab every 3 weeks for up to 24 months or SOC (methotrexate, docetaxel or cetuximab). The primary endpoint was overall survival (OS) in the ITT population with a pre-specified significance boundary α=0.0175 (one-sided). There were 247 patients randomized in the pembrolizumab arm and 248 patients in the SOC arm. Overall patient baseline characteristics were similar across treatment arms. Primary analysis presented at ESMO 2017 (data cut-off date: 15 May 2017; 380 deaths) showed OS HR: 0.81 (95% CI: 0.66-0.99), P=0.0204.[2] Updated OS data presented at AACR 2018 (same data cut-off date: 15 May 2017; 388 deaths) showed OS HR: 0.80 (95% CI: 0.65-0.98), P=0.0161. Treatment effect for pembrolizumab continued to be greater in PD-L1 expressing tumors. The apparent confounding effect of subsequent immune checkpoint inhibitors in the SOC arm continued to be observed. Treatment-related adverse events (TR-AEs) of any grade occurred in 155 patients (63%) and 196 patients (83.8%) in the pembrolizumab and SOC arms, respectively; Grade 3-5 TR-AEs occurred in 13.4% vs 36.3% of patients in the pembrolizumab and SOC arms, respectively. Discontinuation rates were 6.1% and 5.1%, and death rates were 1.6% and 0.9% for

pembrolizumab and SOC, respectively. Along with more durable responses and favorable safety profile, updated survival data provide additional evidence for the benefit of pembrolizumab in patients with R/M HNSCC.[3]

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

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

2. Cohen EEW, Harrington KJ, Le Tourneau C, et al. Pembrolizumab vs Standard of Care for Recurrent or Metastatic Head and Neck Squamous Cell Carcinoma: Phase 3 KEYNOTE-040 Trial. Presented at European Society for Medical Oncology (ESMO); September 8-12, 2017; Madrid Spain.

3. Soulières D, Cohen EEW, Le Tourneau C et al. Updated Survival Results of the KEYNOTE-040 Study of Pembrolizumab vs Standard-of-Care Chemotherapy for Recurrent or Metastatic Head and Neck Squamous Cell Carcinoma. Presented at American Association for Cancer Research (AACR); April 14-18, 2018; Chicago IL, USA

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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