Keytruda® (pembrolizumab) – Expanded indication

- On May 5, 2021, Merck announced the FDA approval of Keytruda (pembrolizumab), in combination with trastuzumab, fluoropyrimidine- and platinum-containing chemotherapy, for the first-line treatment of patients with locally advanced unresectable or metastatic HER2-positive gastric or gastroesophageal junction (GEJ) adenocarcinoma.
    - Keytruda was previously approved as a single agent for the treatment of patients with recurrent locally advanced or metastatic gastric or GEJ adenocarcinoma whose tumors express PD-L1 (CPS ≥ 1) as determined by an FDA-approved test, with disease progression on or after 2 or more prior lines of therapy including fluoropyrimidine- and platinum-containing chemotherapy and if appropriate, HER2/neu-targeted therapy.
    - These indications are approved under accelerated approval based on tumor response rate and durability of response. Continued approval of these indications may be contingent upon verification and description of clinical benefit in the confirmatory trials.

- Keytruda is also approved for melanoma, non-small cell lung cancer, head and neck squamous cell cancer, classical Hodgkin lymphoma, primary mediastinal large B-cell lymphoma, urothelial carcinoma, microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) cancer, MSI-H or dMMR colorectal cancer, esophageal cancer, cervical cancer, hepatocellular carcinoma, Merkel cell carcinoma, renal cell carcinoma, endometrial carcinoma, tumor mutational burden-high cancer, cutaneous squamous cell carcinoma, and triple-negative breast cancer.

- The approval of Keytruda for the expanded indication was based on KEYNOTE-811, a randomized, double-blind, placebo-controlled study in patients with HER2-positive advanced gastric or GEJ adenocarcinoma who had not previously received systemic therapy for metastatic disease. At the time of the interim analysis, efficacy was assessed in the first 264 patients randomized in the trial. Patients were randomized to Keytruda plus trastuzumab plus chemotherapy or trastuzumab plus chemotherapy alone. The primary endpoints were objective response rate (ORR) and duration of response (DOR).
    - The ORR was 74% (95% CI: 66, 82) for Keytruda plus trastuzumab plus chemotherapy vs. 52% (95% CI: 43, 61) for trastuzumab plus chemotherapy alone ($p < 0.0001$).
    - The median DOR was 10.6 months (range: 1.1+, 16.5+) for Keytruda plus trastuzumab plus chemotherapy vs. 9.5 months (95% CI: 1.4+, 15.4+) for trastuzumab plus chemotherapy alone.

- The recommended dose of Keytruda, when used in combination therapy for the treatment of gastric cancer, is 200 mg intravenously every 3 weeks or 400 mg every 6 weeks. Keytruda should be administered prior to trastuzumab and chemotherapy when given on the same day. Keytruda is administered until disease progression, unacceptable toxicity, or up to 24 months
    - Refer to the Keytruda drug label for dosing for all its other indications