Keytruda® (pembrolizumab) – New indication

- On March 14, 2017, Merck announced the FDA approval of Keytruda (pembrolizumab) injection, 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 new 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.

- Keytruda is also approved for the following indications:
    - Treatment of patients with unresectable or metastatic melanoma.
    - First-line treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have high programmed death ligand-1 (PD-L1) expression [Tumor Proportion Score (TPS) ≥ 50%)] as determined by an FDA-approved test, with no epidermal growth factor receptor (EGFR) or anaplastic lymphoma kinase (ALK) genomic tumor aberrations.
    - 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.
    - Treatment of patients with recurrent or metastatic head and neck squamous cell carcinoma with disease progression on or after platinum-containing chemotherapy.

- Hodgkin disease is a type of lymphoma, a cancer that affects lymphocytes. Lymphocytes are part of the body's immune system.
    - The American Cancer Society estimates that there will be 8,260 new cases and 1,070 deaths from Hodgkin disease in 2017.

- Keytruda's new indication was approved based on a non-randomized, open-label study involving 210 patients with relapsed or refractory cHL. The major endpoints were objective response rate (ORR), complete remission rate (CRR) and duration of response (DOR).
    - The ORR was 69% (95% CI: 62, 75) with a CRR of 22%.
    - Furthermore, among the 145 responding patients, the median DOR was 11.1 months (range: 0.0+ to 11.1 months).
    - The efficacy of Keytruda in pediatric patients was extrapolated from the results in the adult cHL population.

- The safety profile in pediatric patients was similar to that seen in adults treated with Keytruda. However, the toxicities that occurred at a higher rate (≥ 15% difference) in these patients vs. adults under 65 years of age were fatigue (45%), vomiting (38%), abdominal pain (28%), hypertransaminasemia (28%), and hyponatremia (18%).

- In addition, a new safety concern was added to the *Warnings and Precautions* section of the Keytruda label, regarding complications of allogeneic hematopoietic stem cell transplantation (HSCT).

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  - Immune-mediated complications, including fatal events, occurred in patients who underwent HSCT after being treated with Keytruda.
  - Of 23 patients with cHL who proceeded to allogeneic HSCT after treatment with Keytruda on any trial, 6 patients (26%) developed graft-versus-host-disease (GVHD), one of which was fatal, and 2 patients (9%) developed severe hepatic veno-occlusive disease (VOD) after reduced-intensity conditioning, one of which was fatal.
  - Cases of fatal hyperacute GVHD after allogeneic HSCT have also been reported in patients with lymphoma who received a PD-1 receptor blocking antibody before transplantation. These complications may occur despite intervening therapy between PD-1 blockade and allogeneic HSCT.
  - Patients should be followed closely for early evidence of transplant-related complications such as hyperacute GVHD, severe (Grade 3 to 4) acute GVHD, steroid-requiring febrile syndrome, hepatic VOD, and other immune-mediated adverse reactions, and intervened promptly.

- In adults with cHL, the recommended dose of Keytruda is 200 mg administered as an intravenous (IV) infusion every 3 weeks until disease progression or unacceptable toxicity, or up to 24 months in patients without disease progression.

- In pediatric patients with cHL, the recommended dose of Keytruda is 2 mg/kg (up to a maximum of 200 mg) administered as an IV infusion every 3 weeks until disease progression or unacceptable toxicity, or up to 24 months in patients without disease progression.

- For the recommended dose of Keytruda in other indications, refer to the product label.