Opdivo® (nivolumab) – New Warnings

- On October 4, 2016, the FDA approved new updates to the *Warnings and Precautions* section of the Opdivo (nivolumab) drug label, regarding new adverse reactions identified through Bristol Myers Squibb's pharmacovigilance program or in study CA209017: Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), histiocytic necrotizing lymphadenitis (Kikuchi lymphadenitis), myositis, myocarditis, and rhabdomyolysis.

- Opdivo is indicated for the treatment of the following:

    - BRAF V600 wild-type unresectable or metastatic melanoma, as a single agent.
    - BRAF V600 mutation-positive unresectable or metastatic melanoma, as a single agent.
    - Unresectable or metastatic melanoma, in combination with Yervoy® (ipilimumab).
    - Metastatic non-small cell lung cancer (NSCLC) with progression on or after platinum-based chemotherapy.
    - Advanced renal cell carcinoma in patients who have received prior anti-angiogenic therapy.
    - Classical Hodgkin lymphoma (cHL) that has relapsed or progressed after autologous hematopoietic stem cell transplantation (HSCT) and post-transplantation Adcetris® (brentuximab vedotin).

- The new safety update states: Opdivo can cause immune-mediated rash, including SJS and TEN, some cases with fatal outcome.

    - For symptoms or signs of SJS or TEN, withhold Opdivo and refer the patient for specialized care for assessment and treatment. If SJS or TEN is confirmed, permanently discontinue Opdivo.

- In addition, across clinical trials of Opdivo administered as a single agent or in combination with Yervoy, the following clinically significant immune-mediated adverse reactions occurred in < 1.0% of patients: uveitis, iritis, pancreatitis, facial and abducens nerve paresis, demyelination, polymyalgia rheumatica, autoimmune neuropathy, Guillain-Barré syndrome, hypopituitarism, systemic inflammatory response syndrome, gastritis, duodenitis, sarcoidosis, histiocytic necrotizing lymphadenitis (Kikuchi lymphadenitis), myositis, myocarditis, rhabdomyolysis, motor dysfunction, vasculitis, and myasthenic syndrome.

    - For any suspected immune-mediated adverse reactions, exclude other causes. Based on the severity of the adverse reaction, permanently discontinue or withhold Opdivo, administer high-dose corticosteroids, and if appropriate, initiate hormone-replacement therapy.

- Other updates to the drug label:

    - Results for progression-free survival, overall response rate, and response duration from study CA209017 were added to the *Clinical Studies* section.
    - Data were pooled in the *Adverse Reactions* subsection for squamous and non-squamous NSCLC.
    - Disease-specific information was replaced with the results of pooled analysis across multiple randomized trials conducted in patients with metastatic NSCLC, melanoma, renal cell cancer, or cHL to describe the risks of serious immune-mediated adverse reactions with nivolumab, administered either as a single agent or with Yervoy.

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- Dose modifications in the *Dosage and Administration* section of the drug label were added for suspected or confirmed SJS and TEN.

- Other warnings and precautions of Opdivo include immune-mediated pneumonitis, immune-mediated colitis, immune-mediated hepatitis, immune-mediated endocrinopathies, immune-mediated nephritis and renal dysfunction, immune-mediated encephalitis, infusion reactions, complications of allogeneic HSCT after Opdivo, and embryo-fetal toxicity.