Bristol-Myers Squibb

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NCCN Guidelines® Panel: Bladder Cancer

Dear Panel Members:

On behalf of Bristol-Myers Squibb Company, I respectfully submit to the panel the prescribing information for OPDIVO® (nivolumab) with an updated indication. With this update, nivolumab is now approved for the treatment of patients with locally advanced or metastatic urothelial carcinoma who have disease progression during or following platinum-containing chemotherapy or have disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy. This indication is approved under accelerated approval based on tumor response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.[1]

I am also submitting OPDIVO® clinical data from the registrational Phase 2 study CA209-275 (Nivolumab in metastatic urothelial carcinoma after platinum therapy (CheckMate 275): a multicentre, single-arm, phase 2 trial) that was recently published in Lancet Oncology on January 25, 2017.[2]

Specific Changes: I respectfully request you to consider adding nivolumab monotherapy in the NCCN Guidelines for Bladder Cancer as a second-line systemic therapy for locally advanced or metastatic bladder cancer (page BL-H 2 of 4)

FDA Clearance: The FDA-approved OPDIVO® (nivolumab) on February 2, 2017 for the treatment of locally advanced or metastatic urothelial carcinoma who have disease progression during or following platinum-containing chemotherapy or have disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy. This indication is approved under accelerated approval based on tumor response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials. Nivolumab is also approved in the treatment of patients with:

- BRAF V600 wild-type unresectable or metastatic melanoma, as a single agent.
- BRAF V600 mutation-positive unresectable or metastatic melanoma, as a single agent. This indication is approved under accelerated approval based on progression-free survival. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials.
- Unresectable or metastatic melanoma, in combination with ipilimumab. This indication is approved under accelerated approval based on progression-free survival. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials.
- Metastatic non-small cell lung cancer and progression on or after platinum based chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving nivolumab.
- Advanced renal cell carcinoma 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 brentuximab vedotin
- Recurrent or metastatic squamous cell carcinoma of the head and neck (SCCHN) with disease progression on or after a platinum-based therapy.

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Rationale: Data from the registrational Phase 2 CA209-275 study was previously submitted to NCCN on October 10, 2016.

The following resources are included for your review:

1. Opdivo Prescribing Information.
2. Sharma P, Retz M, Siefker-Radtke A, et al. Nivolumab in metastatic urothelial carcinoma after platinum therapy (CheckMate 275): a multicentre, single-arm, phase 2 trial. Lancet Oncol. 2017. doi: 10.1016/S1470-2045(17)30065-7.

Thank you for your consideration of this request.

Sincerely,

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