



Submitted by:

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March 6, 2018

NCCN Guidelines® Panel: Kidney Cancer

Dear Panel Members,

On behalf of Bristol-Myers Squibb Company, I respectfully submit the enclosed OPDIVO® (nivolumab) prescribing information and clinical data which supports the most recent label change, that occurred on March 5, 2018 to reflect the new dosing for nivolumab to 240mg administered intravenously every 2 weeks or 480mg administered intravenously every 4 weeks over 30 minutes.¹ This information is being sent to the NCCN® Kidney Cancer Panel for your consideration.

Specific Changes: Request for the inclusion as a footnote to KID-4 and KID-5, the following: nivolumab FDA approved dose is 240mg IV every 2 weeks or 480mg IV every 4 weeks administered over 30 minutes until disease progression or unacceptable toxicity.¹

FDA Clearance of OPDIVO® (nivolumab) (indication in Kidney Cancer):

- On November 23, 2015, the FDA approved the use of nivolumab as monotherapy for the treatment of patients with advanced renal cell carcinoma who have received prior anti-angiogenic therapy.

Rationale: The Opdivo Prescribing Information was updated to reflect the new dosing of Opdivo to 240mg administered intravenously every 2 weeks or 480mg administered intravenously every 4 weeks over 30 minutes for all indications, except for metastatic colorectal cancer which is to be dosed at 240mg administered intravenously every 2 weeks over 30 minutes.¹ The dosing recommendations stated in the product label are different than the dose that was administered in the original protocol of the registrational clinical studies that support the current approved FDA indications.

As part of this submission, the published literature that support the pharmacokinetic analyses for the dosing of 240mg every 2 weeks, 480mg every 4 weeks, and a 30 minute infusion time are enclosed for your review.²⁻⁴

1. Product Information, OPDIVO® (nivolumab) injection for intravenous infusion. Bristol-Myers Squibb Company, Princeton, NJ. March 2018.
2. Zhao X, Suryawanshi S, Hruska M, et al. Assessment of nivolumab benefit-risk profile of a 240-mg flat dose relative to a 3-mg/kg dosing regimen in patients with advanced tumors. *Ann Oncol.* 2017;28:2002-2008.
3. Zhao X, Ivaturi V, Gopalakrishnan M, et al. A model-based exposure-response (ER) assessment of a nivolumab (NIVO) 4-weekly (Q4W) dosing schedule across multiple tumor types. Poster presentation at the American Association for Cancer Research (AACR), April 1-5, 2017; Washington, DC.
4. Waterhouse D, Horn L, Reynolds C, et al. Safety profile of nivolumab administered as 30-min infusion: analysis of data from CheckMate 153. *Cancer Chemotherapy and Pharmacology.* 2018; DOI: 10.1007/s00280-018-3527-6.

Thank you for your consideration.
Sincerely,

A handwritten signature in black ink, appearing to read 'Awny Farajallah', with a stylized, flowing script.

Awny Farajallah, MD, FACP
Vice President, Head US Medical Oncology
Bristol-Myers Squibb Company