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September 8, 2014
NCCN Melanoma Panel



On behalf of Merck & Co., Inc., I respectfully request the NCCN Melanoma Panel review the enclosed information for inclusion of KEYTRUDA® (pembrolizumab) on the NCCN Melanoma Treatment Guidelines of unresectable or metastatic melanoma in patients whose disease progressed on or following ipilimumab and, if BRAF V600 mutation positive, a BRAF inhibitor.

Specific changes requested:

In section ME-E we respectfully request that KEYTRUDA be added as systemic therapy for patients with unresectable or metastatic melanoma and disease progression following ipilimumab and, if BRAF V600 positive, a BRAF inhibitor. (NCCN category 1)

FDA Clearance:

The FDA approved KEYTRUDA for treatment for the above indication on September 4, 2014. This indication was approved under accelerated approval based on tumor response rate and durability of response. An improvement in survival or disease-related symptoms has not yet been established. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials

Rationale:

In support of the requested change, FDA approval was based on an uncontrolled, open-label study involving 173 patients with unresectable or metastatic melanoma with progression of disease; refractory to two or more doses of ipilimumab and, if BRAF V600 mutation-positive, a BRAF or MEK inhibitor; and disease progression within 24 weeks following the last dose of ipilimumab: the overall response rate was 24% (95% CI: 15, 34) in the 2 mg/kg arm, consisting of 1 complete response and 20 partial responses; responses were ongoing in 18 out of 21 (86%) patients.

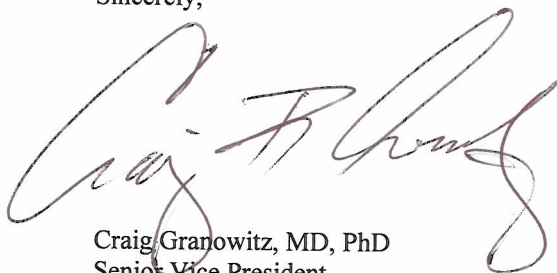
To assist the committee with their review, I have included the following resources:

1. KEYTRUDA® Prescribing information. Merck & Co., Inc. Whitehouse Station, NJ. September 2014
2. Robert C, Ribas A, Wolchok J, Hodi F, Hamid O, Kefford R, et al. Anti-programmed-death-receptor-1 treatment with pembrolizumab in ipilimumab-refractory advanced melanoma: a randomised dose-comparison cohort of a phase 1 trial. *Lancet*. 2014 Jul 14. pii: S0140-6736(14)60958-2. [Epub ahead of print].



Thank you for considering this request. Below is my contact information should you need to contact me for additional information.

Sincerely,

A handwritten signature in dark ink, appearing to read "Craig Granowitz", written in a cursive style.

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