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Submitted by:
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Date of request: November 10, 2015
NCCN Guidelines Panel: Melanoma

On behalf of Genentech, Inc., I respectfully request the NCCN Melanoma Guideline Panel to review the enclosed recent information for:

- Cotellic™ (Cobimetinib)**:** a selective allosteric inhibitor that targets MEK1 and MEK 2 in the mitogen-activated protein kinanse (MAPK)/extracellular signal regulated kinases (MEK) pathway.

1. Larkin J, Ascierto PA, Dreno B. Combined vemurafenib and cobimetinib in BRAF-mutated melanoma [protocol appears online at: http://www.nejm.org/doi/suppl/10.1056/NEJMoa1408868/suppl_file/nejmoa1408868_protocol.pdf]. N Engl J Med 2013;20:1 - 179. http://www.ncbi.nlm.nih.gov/pubmed/25265494
2. Larkin JMG, Yan Y, McArthur GA, et al. Update of progression-free survival (PFS) and correlative biomarker analysis from coBRIM: Phase III study of cobimetinib (cobi) plus vemurafenib (vem) in advanced BRAF-mutated melanoma.. Presented at the American Society of Clinical Oncology 2015 Annual Meeting in Chicago, Illinois; 2015 May 29 - June 2. ASCO Abstract #9006. http://www.asco.org.
3. Larkin J, Yan Y, McArthur G, et al. Update of progression-free survival and correlative biomarker analysis from coBRIM: Phase 3 study of cobimetinib plus vemurafenib in advanced BRAF-mutated melanoma. Presented at the American Society of Clinical Oncology 2015 Annual Meeting in Chicago, Illinois; 2015 May 29 - June 2. ASCO Oral Presentation .

Specific Changes:

Notification of the approval of Cotellic™, a kinase inhibitor, in combination with Zelboraf® (vemurafenib) for the treatment of patients with unresectable or metastatic melanoma with a BRAF V600E or V600K mutation.
Limitation of use: Cotellic is not indicated for treatment of patients with wild-type BRAF melanoma.

FDA Clearance:

- Cotellic™ was approved for use by the FDA on November 10, 2015.

Please refer to the product prescribing information for the full FDA-approved indications and safety information.

- Full Cotellic™ prescribing information available at: http://www.gene.com/download/pdf/cotellic_prescribing.pdf

Rationale:

- Cotellic™: The approval of Cotellic is based on results from the pivotal Phase III study, CoBRIM, an international, multicenter, randomized study which evaluated the efficacy and safety of Cotellic and Zelboraf in patients with previously untreated, unresectable, stage IIIC or stage IV

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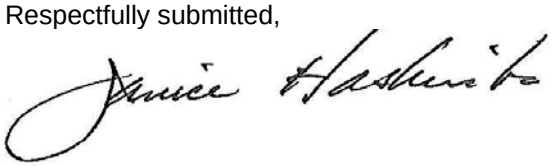
melanoma with a BRAF V600 mutation[1]. Updated efficacy data from a post-hoc analysis of the CoBRIM trial have also been provided for your review.[2,3]

Respectfully submitted,



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