To Whom It May Concern:

As the NCCN NSCLC Panel reviews the Clinical Practice Guidelines in Oncology® (NCCN Guidelines) for Non-small Cell Lung Cancer version 4.2016, we have enclosed data relating to treatment with the combination of Tafinlar® (dabrafenib) and Mekinist® (trametinib):

- Data supporting the combination of dabrafenib and trametinib for the treatment of advanced or metastatic NSCLC with a BRAF V600E mutation

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Dabrafenib and trametinib for BRAF V600E advanced or metastatic NSCLC

This request is for the Panel to consider amending the Systemic Therapy for Metastatic Disease section (NSCL-16) and associated discussion to include testing for BRAF V600E as part of broad molecular profiling and to include the combination of dabrafenib and trametinib as a preferred treatment option for previously treated patients with advanced or metastatic NSCLC who test positive for BRAF V600E. The combination of dabrafenib and trametinib is currently listed under Emerging Targeted Agents For Patients with Genetic Alterations (NSCL-H).

In a Phase II, multicenter, non-randomized, open-label study (N=57), previously treated patients receiving the combination of dabrafenib and trametinib achieved an investigator-assessed overall response rate of 63.2% (95% CI 49.3-75.6) and duration of response of 9.0 months (95% CI 6.9-18.3). Most common (≥30%) adverse events of any grade included: pyrexia (46%), nausea (40%), vomiting (35%), diarrhea (33%), asthenia (32%) and decreased appetite (30%).

Specific changes recommended for the Guidelines & Compendium

Please consider modifying sections NSCL-16 and NSCL-H, and relevant discussion and reference, of the NCCN Guidelines® for NSCLC to include the combination of dabrafenib and
trametinib as a preferred treatment option for previously treated patients with advanced or metastatic NSCLC who test positive for a BRAF V600E mutation.

**FDA status**
Dabrafenib, trametinib and the combination of dabrafenib and trametinib are not FDA approved for the treatment of patients with advanced or metastatic NSCLC with BRAF V600E mutation.

**Rationale for recommended change**
The results of this study have demonstrated the safety and efficacy of the combination of dabrafenib and trametinib in previously treated patients with advanced or metastatic NSCLC with a BRAF V600E mutation.

**Literature support**

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We appreciate the opportunity to provide this additional information for consideration by the NCCN NSCLC Panel. If you have any questions or require additional information, please do not hesitate to contact me at 862-778-5494 or via e-mail at neilda.baron@novartis.com. Thank you for your time and consideration.

Sincerely,

Neilda Baron, MD
Executive Director and Head, US Oncology Medical Information
Novartis Pharmaceuticals Corporation

Enclosures: Copy of referenced publication and Tafinlar and Mekinist Prescribing Information