January 9, 2018

Submission Request
National Comprehensive Cancer Network® (NCCN®)

RE: Clinical Evidence in Support of Tafinlar® (dabrafenib) Plus Mekinist® (trametinib) in Patients With Locally Advanced or Metastatic BRAF *V600E*-Mutant Anaplastic Thyroid Carcinoma (ATC)

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Date of request:	January 9, 2018
NCCN Guidelines Panel:	Thyroid Carcinoma

To Whom It May Concern:

As the NCCN Thyroid Carcinoma Panel reviews the NCCN Clinical Practice Guidelines in Oncology® (NCCN Guidelines®) for Thyroid Carcinoma v.2.2017 and the associated Drugs and Biologics Compendium™, we have enclosed data relating to treatment with dabrafenib and trametinib for your consideration:

- Data to support the use of dabrafenib plus trametinib in patients with locally advanced or metastatic BRAF *V600E*-mutant ATC

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Dabrafenib plus trametinib in locally advanced or metastatic BRAF *V600E*-mutant ATC

This request is for the Panel to consider the addition of dabrafenib plus trametinib as a treatment option in patients with *BRAF V600E*-mutant ATC in the Thyroid Carcinoma Guidelines® and the associated NCCN Drugs and Biologics Compendium™.

During a multicenter, open-label, Phase II trial in patients with predefined BRAF *V600E*-mutated cancers (N = 100), patients received dabrafenib 150 mg twice daily plus trametinib 2 mg once daily until unacceptable toxicity, disease progression, or death. The study included 16 patients with ATC. After a median follow-up of 47 weeks (range, 4-120), the confirmed overall response rate (primary endpoint) in these patients was 69% (11/16, 95% CI: 41-89%).[1]

In the overall safety population (N = 100), common adverse events (AEs) included fatigue (38%), pyrexia (37%) and nausea (35%), and the most commonly reported grade 3/4 AEs were fatigue, anemia and neutropenia (5% each).[1]

Specific changes recommended for the Guidelines & Compendium

Please consider including dabrafenib plus trametinib as a systemic treatment option in patients with locally advanced or metastatic BRAF *V600E*-mutant ATC.

FDA status

Dabrafenib and trametinib are not approved for the treatment of patients with *BRAF V600*-mutant ATC.

Dabrafenib and trametinib are approved in combination for the treatment of patients with unresectable or metastatic melanoma with *BRAF V600E* or *V600K* mutations as detected by an FDA-approved test. Dabrafenib and trametinib are also approved as single agents for the treatment of unresectable or metastatic melanoma with *BRAF V600E* or *V600E/K* mutation, respectively.

Rationale for recommended change
The results of this study have demonstrated safety and efficacy of dabrafenib plus trametinib in patients with *BRAF V600*-mutant ATC.

Literature support
1. Subbiah V, Kreitman RJ, Wainberg ZA, et al. Dabrafenib and trametinib treatment in patients with locally advanced or metastatic BRAF V600-mutant anaplastic thyroid cancer. *J Clin Oncol*. 2017. Oct 26 [Epub ahead of print]

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We appreciate the opportunity to provide this additional information for consideration by the NCCN Thyroid Carcinoma Panel. If you have any questions or require additional information, please do not hesitate to contact me at 1-862-778-5494 or via e-mail at neilda.baron@novartis.com.

Thank you for your time and consideration.

Sincerely,

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

Enclosures: Copy of Prescribing Information and referenced primary literature; author disclosures included within references