

March 22, 2018



Submission Request

National Comprehensive Cancer Network® (NCCN®)

RE: Clinical Evidence in Support of Treatment Discontinuation With Tasigna® (nilotinib) in Eligible Patients With Chronic-Phase Philadelphia Chromosome-Positive Chronic Myeloid Leukemia (Ph+ CML-CP)

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Date of request: March 22, 2018
NCCN Guidelines Panel: Chronic Myeloid Leukemia (CML)

To Whom It May Concern:

As an addendum to the submission to the NCCN Clinical Practices Guidelines in Oncology® (NCCN Guidelines®) for CML and the associated Drugs and Biologics Compendium™ dated January 18, 2018, we have enclosed the peer-reviewed manuscripts containing data in support of treatment discontinuation with Tasigna® (nilotinib) in eligible patients with Ph+ CML-CP.

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Treatment-free remission with nilotinib in eligible patients with Ph+ CML-CP

This request is for the Panel to consider including the peer-reviewed, published data from the ENESTfreedom and ENESTop trials in support of treatment discontinuation with nilotinib in eligible CML patients.^{1,2}

Specific changes recommended for the Guidelines & Compendium

- Please consider modifying the discussion section and associated references to include the 96-week data from both ENESTfreedom and ENESTop in support of TKI discontinuation with nilotinib for eligible CML patients (MS-18 and MS-28)
 - Please consider including ENESTop in Table 2: Summary of TKI discontinuation trials
- Please consider amending the recommended criteria for CML-E bullet regarding “access to a reliable qPCR test with...within 2 weeks” with the addition of footnote to include an FDA-authorized test per the Tasigna Prescribing Information (PI).

FDA status

Tasigna is a kinase inhibitor indicated for the treatment of:

- Adult and pediatric patients greater than or equal to 1 year of age with newly diagnosed Ph+ CML-CP
- Adult patients with chronic phase and accelerated phase Ph+ CML resistant to or intolerant to prior therapy that included imatinib
- Pediatric patients greater than or equal to 1 year of age with Ph+ CML-CP resistant or intolerant to prior TKI therapy

Rationale for recommended change

The peer-reviewed, published clinical evidence from the 96-week updates from ENESTfreedom and ENESTop has demonstrated that treatment discontinuation with nilotinib may be considered as the preferred TKI in eligible first- or second-line patients with Ph+ CML-CP who have achieved a sustained

molecular response (MR4.5).

Literature support

1. Ross D, Masszi T, Gomez Casares M, et al. Durable treatment-free remission in patients with chronic myeloid leukemia in chronic phase following frontline nilotinib: 96-week update of the ENESTfreedom study. *J Cancer Res Clin Oncol*. 2018 Feb 22. [Epub ahead of print].
2. Mahon FX, Boquimpani C, Kim DW, et al. Treatment-free remission after second-line nilotinib treatment in patients with chronic myeloid leukemia in chronic phase: results from a single-group, phase 2, open-label study. *Ann Intern Med*. 2018 Feb 20. [Epub ahead of print].
3. Tasigna [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals Corp; 2018.

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We appreciate the opportunity to provide this additional information specific to nilotinib for consideration by the NCCN CML 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
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Novartis Pharmaceuticals Corporation

Enclosures: Copy of Tasigna PI and referenced primary literature; author disclosures included within references