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February 24, 2014

Submission Request
National Comprehensive Cancer Network

RE: Clinical Evidence in Support of Farydak® (panobinostat) Cutaneous T-cell Lymphoma (CTCL)

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Date of request:	February 24, 2015
NCCN Guidelines Panel:	Cutaneous T-cell Lymphoma

To Whom It May Concern:

As the NCCN Panel reviews the NCCN Clinical Practice Guidelines in Cutaneous T-cell Lymphoma (CTCL), and the associated Drugs and Biologics Compendium™, we have enclosed data relating to treatment with panobinostat. This information is highlighted below:

- Data to support the use of panobinostat in cutaneous T-cell lymphoma

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Panobinostat for the treatment of Cutaneous T-cell Lymphoma
This request is for the NCCN Panel to consider the addition of panobinostat use of panobinostat Cutaneous T-cell Lymphoma based on results of a Phase II study that examined the use of panobinostat 20 mg three times a week, over a 28-day cycle, in patients with CTCL subtypes mycosis fungoides and Sézary syndrome who had previously received treatment with two or more systemic regimens. Patients could be either bexarotene-exposed (n = 79) or bexarotene-naïve (n = 60) and received panobinostat treatment until disease progression, intolerance or discontinuation. The primary objective was overall response rate (ORR), determined by a combined evaluation of skin disease, lymph node and viscera involvement. Secondary objectives included the measurement of response rate using various response criteria including PGA, modified Severity Weighted Assessment Tool (mSWAT) alone or in combination with CT scan, blood counts, duration of response (DOR), progression-free survival (PFS), safety and tolerability. In this study, disease progression was defined as an unconfirmed, ≥25% increase in mSWAT compared to baseline. The ORR was 17.3% for all patients and 15.2% and 20% in the bexarotene-exposed and –naïve groups, respectively. A reduction in baseline mSWAT scores were observed in 103 patients. The median PFS was 4.2 months and 3.7 months, respectively and the median duration of response was 5.6 months in bexarotene-exposed patients; yet was not reached at data cutoff in the bexarotene-naïve patients.[1]

The most common AEs suspected to be related to study drug were thrombocytopenia (47.5%), diarrhea (42.4%), fatigue (33.1%), nausea (32.4%) and decreased appetite (20.9%). Most of these events were grades 1–2, with thrombocytopenia (13.7% and 2.9%) and neutropenia (9.4% and 0%) observed as grade 3 and grade 4 events, respectively in ≥5% (overall) of patients. Seven deaths occurred; six of which occurred within 28 days of study discontinuation. However, only one death in a patient with a history of hypertension and hyperlipidemia was considered related to study drug. This patient experienced cardiac arrest and died within two days. No acute injury or QT prolongation was noted during the hospital stay.[1] Farydak can cause serious side effects, including severe diarrhea which occurred in 25% of FARYDAK-treated patients, and Severe and fatal cardiac ischemic events, severe arrhythmias, and ECG changes.[2]

Specific changes recommended for the Guidelines & Compendium
Please add panobinostat for the treatment of cutaneous T-cell lymphoma.

FDA Status
FARYDAK, a histone deacetylase inhibitor, in combination with bortezomib and dexamethasone, is indicated for the treatment of patients with multiple myeloma who have received at least 2 prior regimens, including bortezomib and an immunomodulatory agent. This indication is approved under accelerated approval based on progression free survival. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.[2]

Rationale for recommended change
Efficacy and safety of panobinostat in cutaneous T-cell lymphoma has been assessed in Phase II study that examined the use of panobinostat 20 mg three times a week, over a 28-day cycle, in patients with CTCL subtypes mycosis fungoides and Sézary syndrome who had previously received treatment with two or more systemic regimens.[1]

Literature support

1. Duvic M, Dummer R, Becker JC, et al. Panobinostat activity in both bexarotene-exposed and -naive patients with refractory cutaneous T-cell lymphoma: Results of a Phase II trial. *Eur J Cancer*. 2013;49(2):386-394.

2. Farydak [package insert]. East Hanover, NJ; Novartis Pharmaceuticals Corporation; 2015.

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We appreciate the opportunity to provide this additional information for consideration by the NCCN Cutaneous T-cell Lymphoma 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, Medical Information Oncology
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Enclosures: Copies of referenced primary literature; Author disclosures included within references