CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

200582Orig1s000

CROSS DISCIPLINE TEAM LEADER REVIEW

Memorandum

To: NDA 200-582

From: Sarah Pope Miksinski, Ph.D.

Date: 2/2/2011

Re: CDTL Memo Update - Addendum

Reference is made to the 26-NOV-2010 CDTL memo and the corresponding CDTL memo update dated 01-FEB-2011. The purpose of this addendum is to provide confirmation of the expiration dating period to be granted in the forthcoming action letter. According to the Chemist's 09-JUL-2010 review, "based on the stability data provided, an 18-month expiration dating period is granted for the drug product when stored at 2°C-8°C (36°F-46°F) and protected from light." This assessment was based on the stability data package submitted as part of the initial NDA submission (submitted 29-OCT-2009). Note that the 26-NOV-2010 CDTL memo contains a typographical error in that the 18-month expiration dating period is specified under room temperature conditions. The granted expiration dating period applies to storage under refrigerated conditions, as is correctly stated in the Chemist's 26-NOV-2010 review and as reiterated in the current memo.

The 03-DEC-2010 resubmission did not include any new stability data for review and assessment. Therefore, the expiration dating period, as initially captured in the Chemist's review, remains the same. The expiration dating period granted for this NDA is 18 months, when the drug product is stored at 2°C-8°C (36°F-46°F) and protected from light.

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/s/

SARAH P MIKSINSKI
02/02/2011

Memorandum

To: NDA 200-582

From: Sarah Pope Miksinski, Ph.D.

Date: 2/1/2011

Re: CDTL Memo Update

NDA 200582 was initially submitted on 29-OCT-2009 as a 505(b)(2) application. During the initial review cycle, DMF deficiencies were noted by the Chemistry reviewer (see Chemistry Review #1 and documents referenced therein). The Applicant's response to these deficiencies was noted on 18-AUG-2010, and the Agency subsequently extended the PDUFA date by three months. In a 26-NOV-2010 letter, the Agency took a "Complete Response" action for NDA 200582, based on an overall withhold recommendation from the Office of Compliance issued on 11-AUG-2010. Final labeling was not issued as part of the Agency's 11-AUG-2010 action letter. Reference is also made to the 26-NOV-2010 CDTL memo, which recommended a "Complete Response" action based on the overall "withhold" recommendation for the NDA.

In a 03-DEC-2010 submission, the Applicant responded to the Agency's 26-NOV-2010 letter. The submission was classified as a Class 1 resubmission. In order to address the overall withhold recommendation from the Office of Compliance, the Applicant withdrew the non-cGMP-compliant site (Hospira Worldwide, Inc., Rocky Mount, NC) from the application. All listed sites were re-submitted to the Office of Compliance for an updated recommendation during the current review clock, and an updated overall "acceptable" recommendation was received on 04-JAN-2011. This updated recommendation resolves the cGMP deficiency issued in the previous action letter.

The 03-DEC-2010 resubmission also included updated PI and container/carton labeling. Chemistry Review #3 (19-NOV-2010) captures the majority of the recommended container/carton and PI labeling revisions, which were resolved and captured during the previous review cycle. Two outstanding CMC labeling comments were captured in the 26-NOV-2010 CDTL review, which were addressed and resolved during the current review cycle. An updated 17-DEC-2010 review by Irene Chan, Pharm.D. (DMEPA) resulted in one additional comment regarding the proposed container/carton labeling; this comment was resolved with the Applicant's 18-JAN-2011 submission of updated container/carton labeling. The container/carton labels received on 18-JAN-2011 were subsequently determined to be acceptable as the final container/carton labeling.

With the exception of the updated proposed PI, the resubmission did not include any new and/or updated Clinical, Pharmacology/Toxicology, Clinical Pharmacology, or

Biopharmaceutics information. All disciplines were included in the negotiation and internal discussion of final PI labeling, and all disciplines concur with the final PI and container/carton labeling.

An updated Clinical review (Michael Brave, M.D.) captures one outstanding labeling deficiency, which needs to be resolved before an approval action can be conducted (see Clinical Review dated 25-JAN-2011):

(b) (4)

In a 31-JAN-2011 addendum, the Clinical reviewer stated a reconsideration of the deficiency and concurred with the strategy of removing (b) (4) The reviewer also confirms that these revisions will provide clinicians with sufficient safety information, and that the revisions will maintain sufficient consistency between the currently-proposed and innovator (Hycamtin) drugs. This addendeum effectively resolves the previous deficiency.

The proposed labeling was recirculated to all disciplines on 30-JAN-2011. All disciplines agreed with the final proposed labeling, and the final labeling was sent to the Applicant on 01-FEB-2011.

There are no remaining deficiencies for this application, and approval is recommended (proposed indication = small-cell lung cancer).

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/s/

SARAH P MIKSINSKI
02/01/2011