CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

206545Orig1s000

PHARMACOLOGY REVIEW(S)

MEMORANDUM

Date: May 1, 2014
From: Haleh Saber, Ph.D.
Pharmacology/Toxicology Supervisor
Division of Hematology Oncology Toxicology (DHOT)
Office of Hematology and Oncology Products (OHOP)
Re: Approvability for Pharmacology and Toxicology
NDAs: 206545 and 205858
Drug: ZYDELIG (idelalisib)
Indications: Indolent non-Hodgkin lymphoma (iNHL) and chronic lymphocytic leukemia (CLL); see the label for detailed information
Applicant: Gilead Sciences, Inc.

Idelalisib is a small molecule PI3K inhibitor with selectivity toward PI3Kδ. NDA 205858 was submitted in September 2013 for the NHL indication; NDA 206545 was submitted in December 2013 for the CLL indication. The nonclinical studies submitted to and reviewed under NDA 205858 cover both indications.

For detailed pharmacology/toxicology findings, see the primary review by Drs. Ramadevi Gudi and Natalie Simpson and for an overview of the nonclinical package see my Team Leader Memorandum, both archived under NDA 205858.

Recommendation: From a pharmacology/toxicology perspective, ZYDELIG may be approved for the proposed indications. There are no outstanding pharmacology/ toxicology issues. Also see Dr. John Leighton's concurrence, archived under NDA 205858.

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/s/

HALEH SABER
05/01/2014

PHARMACOLOGY/TOXICOLOGY FILING CHECKLIST FOR NDA

NDA Number: 206545 **Applicant: Gilead Sciences Inc.** **Stamp Date: Dec. 6, 2013**

Drug Name: Idelalisib (GS-1101) **NDA Type: 505(b)(1); new molecular entity**

On **initial** overview of the NDA application for filing:

	Content Parameter	Yes	No	Comment
1	Is the pharmacology/toxicology section organized in accord with current regulations and guidelines for format and content in a manner to allow substantive review to begin?	✓		NDA is submitted in the eCTD format.
2	Is the pharmacology/toxicology section indexed and paginated in a manner allowing substantive review to begin?	✓		
3	Is the pharmacology/toxicology section legible so that substantive review can begin?	✓		
4	Are all required (*) and requested IND studies (in accord with 505 b1 and b2 including referenced literature) completed and submitted (carcinogenicity, mutagenicity, teratogenicity, effects on fertility, juvenile studies, acute and repeat dose adult animal studies, animal ADME studies, safety pharmacology, etc)?	✓		All studies needed for this indication have been conducted. In addition, other studies (for example: fertility studies) have been conducted.
5	If the formulation to be marketed is different from the formulation used in the toxicology studies, have studies by the appropriate route been conducted with appropriate formulations? (For other than the oral route, some studies may be by routes different from the clinical route intentionally and by desire of the FDA).	✓		Oral formulations were used in clinical and nonclinical studies.
6	Does the route of administration used in the animal studies appear to be the same as the intended human exposure route? If not, has the applicant submitted a rationale to justify the alternative route?	✓		
7	Has the applicant submitted a statement(s) that all of the pivotal pharm/tox studies have been performed in accordance with the GLP regulations (21 CFR 58) or an explanation for any significant deviations?	✓		
8	Has the applicant submitted all special studies/data requested by the Division during pre-submission discussions?	✓		

File name: 9_Pharmacology_Toxicology Filing Checklist for NDA 206545

PHARMACOLOGY/TOXICOLOGY FILING CHECKLIST FOR NDA

	Content Parameter	Yes	No	Comment
9	Are the proposed labeling sections relative to pharmacology/toxicology appropriate (including human dose multiples expressed in either mg/m2 or comparative serum/plasma levels) and in accordance with 201.57?	✓		
10	Have any impurity – etc. issues been addressed? (New toxicity studies may not be needed.)	✓		The Applicant has provided a justification (e.g. based on nonclinical studies) for the proposed specifications and the acceptability of the levels will be a review issue.
11	Has the applicant addressed any abuse potential issues in the submission?			Not Applicable
12	If this NDA is to support a Rx to OTC switch, have all relevant studies been submitted?			Not Applicable

IS THE PHARMACOLOGY/TOXICOLOGY SECTION OF THE APPLICATION FILEABLE? ____Yes____

If the NDA is not fileable from the pharmacology/toxicology perspective, state the reasons and provide comments to be sent to the Applicant.

Please identify and list any potential review issues to be forwarded to the Applicant for the 74-day letter.

Reviewing Pharmacologist Date

Team Leader/Supervisor Date

File name: 9_Pharmacology_Toxicology Filing Checklist for NDA 206545

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/s/

NATALIE E SIMPSON
01/31/2014

HALEH SABER
02/03/2014