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RESEARCH**

APPLICATION NUMBER:

204016Orig1s000

PHARMACOLOGY REVIEW(S)

Memorandum

NDA 204,016

Submission Date: January 30, 2012

Brand Name: Zometa®

Generic Name: zoledronic acid

Formulation: Aqueous Solution, (b) (4) bag for intravenous infusion

Strength: 4 mg/100 mL

Reviewer: Wei Chen, Ph.D.

Acting Team Leader: Todd Palmby, Ph.D.

Applicant: Hospira, Inc.

Submission Type: 505(b)(2)

Dosing regimen: 4 mg administered by intravenous infusions (b) (4)

Indications: Hypercalcemia of malignancy; multiple myeloma and bone metastasis from solid tumors

This 505(b)(2) submission is for a new formulation of a 4 mg strength of zoledronic acid dissolved in 100 mL infusion solution in a (b) (4) bag. The basis of submission for this application is the reference listed drug (RLD) product Zometa® (Zoledronic Acid) Injection, 4mg /5mL and 4 mg/100 mL (Novartis Pharmaceuticals Corporation). No nonclinical study reports were submitted or are needed to support approval at this time. No changes to the Reference Listed Drug's package insert were recommended in sections containing nonclinical data. There are no issues from the Pharmacology/Toxicology discipline that would preclude approval of this zoledronic acid product for the proposed indications.

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/s/

WEI CHEN
10/17/2012

TODD R PALMBY
10/17/2012

I concur with Dr. Wei Chen's conclusion that there are no Pharmacology/Toxicology issues that would preclude approval of NDA 204016.

PHARMACOLOGY/TOXICOLOGY FILING CHECKLIST FOR NDA/BLA or Supplement

NDA/BLA Number:
204,016

Applicant: Hospira, Inc.

Stamp Date: January 30, 2012

Drug Name: Zometa®
(zoledronic acid)

NDA/BLA Type: commercial

On **initial** overview of the NDA/BLA 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?	n/a		No pharmacology/toxicology data is submitted.
2	Is the pharmacology/toxicology section indexed and paginated in a manner allowing substantive review to begin?	n/a		No pharmacology/toxicology data is submitted.
3	Is the pharmacology/toxicology section legible so that substantive review can begin?	n/a		No pharmacology/toxicology data is submitted.
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)?	x		
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).	n/a		No new nonclinical studies submitted
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 <u>submitted</u> a rationale to justify the alternative route?	n/a		No new nonclinical studies submitted
7	Has the applicant <u>submitted</u> a statement(s) that all of the pivotal pharm/tox studies have been performed in accordance with the GLP regulations (21 CFR 58) <u>or</u> an explanation for any significant deviations?	n/a		No new nonclinical studies submitted

File name: 5_Pharmacology_Toxicology Filing Checklist for NDA_BLA or Supplement
010908

**PHARMACOLOGY/TOXICOLOGY FILING CHECKLIST FOR
NDA/BLA or Supplement**

	Content Parameter	Yes	No	Comment
8	Has the applicant submitted all special studies/data requested by the Division during pre-submission discussions?	n/a		No new nonclinical studies submitted
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?		x	Needs to be updated based on the recent labeling modification with zoledronic acid under NDA 21,386 (adjuvant treatment of breast cancer) and NDA 21,223 (4 mg/100mL)
10	Have any impurity – etc. issues been addressed? (New toxicity studies may not be needed.)	n/a		This will be a review issue
11	Has the applicant addressed any abuse potential issues in the submission?	n/a		
12	If this NDA/BLA is to support a Rx to OTC switch, have all relevant studies been submitted?	n/a		

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

If the NDA/BLA 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.

Wei Chen, Ph.D. 03/08/2012

 Reviewing Pharmacologist Date

Anne M. Pilaro, Ph.D. 03/08/2012

 Team Leader/Supervisor Date

File name: 5_Pharmacology_Toxicology Filing Checklist for NDA_BLA or Supplement 010908

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/s/

WEI CHEN
03/08/2012

ANNE M PILARO
03/08/2012

I concur with the reviewer's conclusion that the nonclinical sections of the NDA support filing of this application. No additional action is indicated at the present time from the nonclinical discipline.