

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**203231Orig1s000**

**PHARMACOLOGY REVIEW(S)**

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

**NDA/BLA Number:**  
203,231

**Applicant:** Sagent

**Stamp Date:** January 9, 2012

**Drug Name:** (b) (4)  
(zoledronic acid)

**NDA/BLA Type:** commercial

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

	<b>Content Parameter</b>	<b>Yes</b>	<b>No</b>	<b>Comment</b>
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**

	<b>Content Parameter</b>	<b>Yes</b>	<b>No</b>	<b>Comment</b>
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. 02/22/2012  
 \_\_\_\_\_  
 Reviewing Pharmacologist Date

Anne M. Pilaro, Ph.D. 02/22/2012  
 \_\_\_\_\_  
 Team Leader/Supervisor Date

File name: 5\_Pharmacology\_Toxicology Filing Checklist for NDA\_BLA or Supplement  
010908

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/s/  
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WEI CHEN  
02/22/2012

ANNE M PILARO  
02/22/2012

I concur with the reviewer's conclusion that this 505(b)(2) NDA is fileable. There are no comments to be included in the 74-day deficiency letter, and no additional action is indicated from the nonclinical discipline.

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

**NDA/BLA Number:**  
203,231

**Applicant:** Sagent

**Stamp Date:** August 30, 2011

**Drug Name:** (b) (4)  
(zoledronic acid)

**NDA/BLA Type:** commercial

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

	Content Parameter	Yes	No	Comment
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NDA/BLA or Supplement**

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

Wei Chen, Ph.D. 10/24/2011  
 \_\_\_\_\_  
 Reviewing Pharmacologist Date

Anne M. Pilaro, Ph.D. 10/24/2011  
 \_\_\_\_\_  
 Team Leader/Supervisor Date

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/s/  
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WEI CHEN  
10/25/2011

ANNE M PILARO  
10/26/2011

I concur with the reviewer's conclusion that this NDA is fileable.