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RESEARCH**

*APPLICATION NUMBER:*

**203231Orig1s000**

**SUMMARY REVIEW**

## Memo for Regulatory Action

<b>Date</b>	8/2/2013
<b>From</b>	Amna Ibrahim
<b>Subject</b>	Deputy Division Director Memo
<b>NDA/BLA #</b>	203231
<b>Applicant Name</b>	ACS Dobfar Info S.A.
<b>Date of Submission</b>	06/03/2013
<b>PDUFA Goal Date</b>	8/3/2013
<b>Proprietary Name / Established (USAN) Name</b>	Zoledronic Acid Injection
<b>Dosage Forms / Strength</b>	Intravenous formulation/ 4mg/100mL
<b>Proposed Indication(s)</b>	<ol style="list-style-type: none"> <li>1. Hypercalcemia of malignancy</li> <li>2. Patients with multiple myeloma and patients with documented bone metastases from solid tumors, in conjunction with standard antineoplastic therapy. Prostate cancer should have progressed after treatment with at least one hormonal therapy</li> </ol>
<b>Action:</b>	Approval

This is the 4<sup>th</sup> cycle of submission for NDA 203231 for zoledronic acid using the 505(b)(2) pathway, relying listed drug Zometa 4 mg/5 mL (NDA 21223). Please also see previous reviews. A brief history, including that of the current submission, is provided below.

- The NDA was initially submitted on 8/29/2011, and a ‘Refusal to File’ letter was issued because of insufficient stability data.
- This NDA was resubmitted on 1/9/2012. The single-use bag (b) (4) [redacted] After discussions with the sponsor, the label was modified to clarify that this drug product is intended for patients with a normal kidney function (for whom dose reduction of zoledronic acid is not required) and was finalized. In addition, based on the stability data, a 12-month expiration period was granted. However, due to patents issues, a Tentative Approval was granted on 11/9/2012.
- On 1/8/2013, there was a Class 1 resubmission which adequately addressed the patent issues. In this submission, method validation issues including an unknown peak were identified. See review by Joyce Crich PhD, dated 2/11/2013. As a result, a Complete Response letter was issued on 3/1/2013. A letter dated March 25, 2013 was written by FDA’s Division of Pharmaceutical Analysis identifying additional deficiencies. This letter was signed in DARRTS on 6/24/2013.

- In the current class 1 resubmission, all deficiencies have been resolved. Per CMC reviewer, Joyce Crich PhD, “Since the Complete Response (CR) Letter issued by the Agency dated 01-MAR-2013 based on the deficiencies found by the Methods Validation conducted by FDA’s Division of Pharmaceutical Analysis (DPA) in St. Louis, the applicant provided response in Amendment SN 0028 dated 04-MAR-2013. However, this amendment did not completely address the deficiencies refer to Dr. John Kauffman’s review titled “Re: NDA203231: Response to def-resp-0028” dated 25-MAR-2013, refer to DARRTS dated 24-JUN-2013 under the name of Consult Rev-Quality-02 (Methods Validation Review). Note: this review document was shared with the applicant via an email sent by the project manager Kim Robertson on 26-MAR-2013 There were follow up communications between FDA’s St. Louis Lab, applicant and the CMC review team via teleconferences for the purpose of resolving the CR deficiencies. In addition, there were follow up Method Validation Reviews written by St. Louis Lab based on their additional validation work. Those reviews can be found in DARRTS dated 17-APR- 2013 and 24-MAY-2013 respectively. On 03-JUN-2013, the applicant submitted Amendment SN0029 containing responses to address the remaining deficiencies.” Dr Crich reviewed these responses by the applicant and found the applicant responses acceptable.

All other disciplines have previously found the NDA acceptable from their perspective. CDTL Ali Al Hakim, PhD also recommends approval for this NDA as all deficiencies have been resolved.

**Risk Benefit Assessment:**

The risk/benefit assessment for this NDA is the same as that for the listed drug it relies on.

**Regulatory Action:**

This NDA will be approved.

Amna Ibrahim MD  
Deputy Director  
Division of Oncology Products 1  
OHOP, CDER

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**This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.**  
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/s/  
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AMNA IBRAHIM  
08/02/2013