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Application Number 21-386
21-223/s-003

ENVIRONMENTAL ASSESSMENT and/or FONSI

DRA / CMC Documentation

**Zoledronate 4 mg
Powder for solution for infusion**

**Drug product
Environmental assessment information**

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A claim for ~~categorical~~ exclusion from the Environmental Assessment requirements under 21 CFR 25.31(b) - Action on an NDA, abbreviated application, or a supplement to such applications, or action on an OTC monograph - if the action increases the use of the active moiety, but the estimated concentration of the substance at the point of entry into the aquatic environment will be below 1 ppb.

As set forth in 21 CFR Part 25.31(b), **action on an NDA** is categorically excluded from the requirement to prepare an Environmental Assessment or an Environmental Impact Statement if the action increases the use of the active moiety, but the estimated concentration of the substance at the point of entry into the aquatic environment will be less than 1 part per billion (ppb). "Increased use", as defined in 21 CFR Part 25.5(a), will occur if the drug is "administered at higher dosage levels, for longer duration or for different indications than were previously in effect, or if the drug is a new molecular entity."

Novartis Pharmaceuticals Corporation is filing a Type 6 NDA, NDA 21-386 for Zometa® which provides an additional therapeutic indication for treatment of Bone Metastases.

Novartis Pharmaceuticals Corporation certifies that this submission for **Zoledronate 4 mg, Powder for solution for injection** qualifies for a categorical exclusion in accordance with 21 CFR Part 25.31(b) as the concentration of the active moiety **Zoledronic acid** will be significantly less than 1 ppb.

Further, Novartis Pharmaceuticals Corporation states that, to the best of its knowledge, no extraordinary circumstances exist which may significantly affect the quality of the human environment and would thus require the preparation of at least an Environmental Assessment.

**APPEARS THIS WAY
ON ORIGINAL**

Chemistry Assessment

A. Labeling and Package Insert

The vial and carton labeling [NDA 21-386 (BL), dated 21-Nov-01] and package insert are acceptable from a CMC view point.

B. Claim of Categorical Exclusion

NDA 21-386 for Zometa is filed as a Type 6 NDA, providing an additional therapeutic indication for treatment of bone metastases. The applicant certifies that the this NDA application qualifies for a categorical exclusion in accordance with 21 CFR Part 25.31(b) as the concentration of the active moiety zoledronic acid at the point of entry into the aquatic environment will be significantly less than 1 ppb.

Adequate information has been presented to show that the requested approval of NDA 21-386 qualifies for a categorical exclusion from the requirement to prepare an Environmental Assessment. The Claim of Categorical Exclusion is acceptable.

**APPEARS THIS WAY
ON ORIGINAL**