DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Ave
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Silver Spring, MD 20993

DEC 4 2013

Scott M. Lassman, Esq.
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Re: Docket No. FDA-2013-P-0247

Dear Mr. Lassman:

This letter responds to your letter to Dr. Janet Woodcock received on August 23, 2013 (August 23 Letter),[1] and submitted on behalf of Novartis Pharmaceuticals Corporation (Novartis), in which you request that the Food and Drug Administration (FDA or the Agency) permit Novartis to supplement the record for the citizen petition assigned docket number FDA-2013-P-0247 (Petition).[2] The August 23 Letter follows the Agency's denial of the Petition, for which the reasons are explained in a response dated August 1, 2013 (Petition Response).[3] The August 23 Letter also asks that FDA reconsider certain aspects of the Agency's response to the Petition, based on new information sought to be added to the record. Specifically, you ask the Agency to strike or modify Section III of the Petition Response on the basis of the "supplemented record." For the reasons discussed below, your request to supplement the record and your petition for reconsideration are denied.

A petition for reconsideration must be based on information contained in the administrative record of the decision for which reconsideration is sought.[4] That requirement would be rendered meaningless if FDA allowed petitioners to expand the administrative record to include new information after the Agency has issued its decision. In this case, Section III of the Petition Response is fully supported by the record, and no modifications will be made.

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[1] See August 23, 2013 letter from Scott L. Lassman, to Janet Woodcock, Director, Center for Drug Evaluation and Research (CDER), Docket No. FDA-2013-P-0247.

[2] The Petition requested that FDA not approve any abbreviated new drug application (ANDA) referencing Novartis's new drug application (NDA) for Reclast (zoledronic acid) injection, 5 milligrams (mg)/100 milliliters (mL) (NDA 021817), which sought approval based on omitting protected information in Reclast labeling. The Petition further requested that FDA only approve an ANDA for a zoledronic acid product whose labeling included adequate safety information, including all protected information in Reclast labeling relating to the osteoporosis indications.

[3] See August 1, 2013, letter from Janet Woodcock, Director, Center for Drug Evaluation and Research, to Gretchen Trout, Docket No. FDA-2013-P-0247.

[4] 21 CFR 10.33 (b), (d)(1), and (e) (providing that no new information or views may be included in a petition for reconsideration).

In Section III of the Petition Response, the Agency articulated its conclusion that Novartis misused the citizen petition process in what appeared to be an effort to delay generic competition.[5] The basis of this conclusion, which is described in more detail in the Petition Response, is that Novartis could have filed its Petition early enough to enable the Agency to resolve the issues that Novartis raised, without delaying approval of generic applications, some of which had already received tentative approval.[6] Instead, Novartis filed its Petition on February 28, 2013 — just 2 days before the expiration of the applicable exclusivity period — and filed a corrected version of its Petition that complied with the statute on March 1, 2013 — only 1 day before expiration of the applicable exclusivity.

As early as August 2008, Novartis was aware that at least one generic applicant had filed an abbreviated new drug application (ANDA) referencing Reclast (zoledronic acid) injection, 5 milligrams (mg)/100 milliliters (mL) (NDA 021817),[7] which is approved for the treatment of Paget's disease in men and women and four osteoporosis-related indications. In the Petition, Novartis stated that the information on which the Petition was based became known to the company on November 8, 2011.[8] Novartis does not disavow that certification, and it appears to be accurate. The context is important here. As of November 8, 2011, the Reclast labeling included two types of indications -- Paget's disease and osteoporosis. On that date, the patent related to use in osteoporosis (U.S. Patent 8,052,987) issued. This patent would potentially prevent the marketing of a generic version of Reclast with labeling indicating use for osteoporosis until 2023. But this patent would not prevent the marketing of a generic version with labeling only for Paget's disease upon the expiration of pediatric exclusivity associated with other patents on March 2, 2013.

It is well established in FDA law, and understood by those familiar with the generic drug approval process, that a generic drug can be approved with labeling for less than all indications of the innovator reference listed drug (RLD) if there is a patent on one or more of those indications that prevents their inclusion in the labeling.[9] Thus, on November 8, 2011, it could have been expected that one or more generic applicants would seek approval of a generic version

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[5] See Petition Response at 12.

[6] The August 23 Letter asserts that FDA agreed with several parts of Petition and changed the generic label as a result. That, as the Petition Response notes, is not the point. As we stated on page 12 of the Petition Response : "We note that the 25-day delay in approval of the ANDAs was entirely the result of the timing of Novartis's Petition, rather than its merits. Had the Petition been filed, for example, even one month before the date on which pediatric exclusivity associated with the '130 patent expired, those issues would have been resolved in time for approval of the ANDAs on that date."

[7] See "Paragraph IV Patent Certifications" at http://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/AbbreviatedNewDrugApplicationANDAGenerics/UCM293268.pdf (list of dates of first paragraph IV certifications, showing first certification for a generic version of Reclast on August 29, 2008).

[8] See Petition at 7.

[9] This is commonly known as a "section viii statement," in which an applicant acknowledges that a given method of use patent has been listed, but states that the patent at issue does not claim a use for which the applicant seeks approval (see section 505(j)(2)(A)(viii) of the Federal Food, Drug, and Cosmetic Act). Such a statement requires the ANDA applicant to omit or "carve out" from its labeling information pertaining to the protected use (21 CFR 314.92(a)(1) and 314.94(a)(12)(iii)(A)).

of Reclast in 2013, with the "carve out" of information concerning osteoporosis from the generic labeling, rather than waiting until the expiration of the osteoporosis patent in 2023. Novartis is a sophisticated company with respect to the development and marketing of generic drugs and can reasonably be expected to have anticipated such carve outs. Indeed, in its 2012 Annual Report, Novartis informed its stockholders that "Reclast/Aclasta is expected to face generic challenges in 2013 when the patent on its active ingredient, zoledronic acid, will expire in the US and other major markets."[10]

In addition, Novartis concedes that one of its in-house attorneys knew in October 2012 that Wockhardt was pursuing a labeling carve out.[11] Nonetheless, Novartis chose to wait until February 20, 2013, to file a lawsuit against a large number of generic manufacturers stating "on information and belief" that some generic manufacturers would be seeking approval of generic versions of Reclast with the osteoporosis information carved out. In the August 23 Letter, Novartis asserts that it was not until February 26, 2013, in the context of a hearing in that lawsuit, that certain generic companies "publicly disclosed for the first time" that they were pursuing this strategy.[12] Novartis appears to be suggesting that until that time, Novartis anticipated that no generic applicant would be seeking approval for a generic version of Reclast prior to expiration of the osteoporosis patent in 2023. As noted, we do not find this position to be persuasive.[13]

You have stated Novartis's position that it has not misused the citizen petition process. We have considered your arguments, and we are not persuaded that until February 20, 2013, Novartis did not anticipate that a generic manufacturer might seek approval of a generic version of Reclast with the osteoporosis information carved out from the labeling. As noted above, pharmaceutical companies - such as Novartis - familiar with the generic drug approval process could have anticipated that at least some generic applicants would seek approval of generic versions of Reclast for its Paget's disease indication, with a carve out of osteoporosis information covered by the osteoporosis use patent, when the compound patent on the drug product and related pediatric exclusivity expired on March 2, 2013.

As you have acknowledged, a generic applicant is not obligated to inform the innovator that the applicant is seeking an approval of its generic product using a labeling carve out to avoid patent

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[10] Securities and Exchange Commission Form 20-F: Annual and transition report of foreign private issuers pursuant to sections 13 or 15(d); Filing Date: 2013-01-23 | Period of Report: 2012-12-31, at 36.

[11] See August 23 Letter at 4, note 2. Novartis asserts that the attorney was precluded from further disseminating that information by a Protective Order governing patent litigation. We do not find this persuasive. The petition need not have disclosed that any particular applicant was seeking approval, and the petition in fact did not do so. In any case, given its stated concern about the public health effects of the label carve out, Novartis and its counsel could have sought permission from the court with jurisdiction to address its concerns with FDA.

[12] See August 23 Letter at 5.

[13] We note that in the February 28, 2013 version of the Petition, which was corrected because it did not comply with the applicable requirements for certifications, the petitioner stated that "over the past 10 months, many of the developments that are significant to this Petition, and to the elaboration of the regulatory and clinical implications of omitting protected information from Reclast labeling, took place" (February 28, 2013 version of the Petition at 7). No explanation is provided of what developments those were and why none of those developments led Novartis to file its lawsuit and seek confirmation of carve out filings prior to February 20, 2013.

infringement.[14] Therefore, in light of the well-established generic drug approval practice that permits a carve out of patent-protected conditions of use, the holder of a reference listed drug need not wait until it has explicit acknowledgment that a generic applicant is pursuing a carve out strategy before raising concerns about the possibility of such a carve out with FDA. Certainly, we cannot countenance an innovator strategy of waiting until the last moment to try to obtain a formal acknowledgment and then filing the petition in the 11th hour, with the result of delaying generic competition.

For the reasons stated above, your petition for reconsideration and request to supplement the record are denied.

Sincerely,

Leslie Kux
Assistant Commissioner for Policy

[14] See August 23 Letter at 4.