U.S. FOOD & DRUG ADMINISTRATION

Kurt R. Karst
Director
Hyman, Phelps & McNamara, P.C.
700 13th Street, N.W., Suite 1200
Washington, D.C. 20005-5929

Re: Docket No. FDA-2019-P-4261 May 14, 2020

Dear Mr. Karst:

This letter responds to your citizen petition received on September 10, 2019 (Petition), requesting that the Food and Drug Administration (FDA or Agency) designate ultramicrosize griseofulvin tablets, 250 milligrams (mg), approved under abbreviated new drug application (ANDA) 204371 held by Mountain LLC as the new reference standard in the *Approved Drug Products With Therapeutic Equivalence Evaluations* (the Orange Book).[1]

We have carefully considered the Petition. For the reasons described below, your Petition is granted.

I. BACKGROUND

Section 505(j) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 355(j)) allows the submission of an ANDA to market a generic version of a previously approved drug product. To obtain approval, the ANDA applicant must show, among other things, that the generic drug product: (1) has the same active ingredient(s), dosage form, route of administration, strength, conditions of use, and, with certain exceptions, labeling as the listed drug; and (2) is bioequivalent to the listed drug.

A *listed drug* is a new drug product: (1) that has been approved under section 505(c) of the FD&C Act for safety and effectiveness or under section 505(j) of the FD&C Act; (2) whose approval has not been withdrawn or suspended under section 505(e)(1) through (e)(5) or (j)(6) of the FD&C Act; and (3) that has not been withdrawn from sale for what FDA has determined are reasons of safety or effectiveness.[2] Listed drug status is evidenced by the drug product's identification in the current edition of FDA's Orange Book as an approved drug.[3] A *reference listed drug* (RLD) is the listed drug identified by FDA as the drug product upon which an

[1] The Orange Book is available at http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm. Although your petition refers to the product as ultramicrocrystalline griseofulvin tablets, we refer to the product as ultramicrosize griseofulvin tablets in this response consistent with the drug product's description in the Orange Book.

[2] § 314.3(b) (21 CFR 314.3(b)).

[3] Id.

applicant relies in seeking approval of its ANDA.[4] Generally, an RLD is a drug product approved in a new drug application (NDA) under section 505(c) of the FD&C Act.

A *reference standard* is the drug product selected by FDA that an applicant seeking approval of an ANDA must use in conducting an in vivo bioequivalence study required for approval.[5] FDA generally selects a single reference standard that ANDA applicants must use in any in vivo bioequivalence testing required for approval. A single reference standard ensures the greatest level of consistency between a generic drug and its RLD and among generic drugs. Generally, the RLD will be the drug product selected by the Agency as the reference standard for conducting in vivo bioequivalence testing.[6] In certain circumstances, however, the Agency may select a generic drug product as the reference standard for bioequivalence testing. For instance, if the RLD has been discontinued from marketing, FDA may select a therapeutically equivalent[7] generic drug product as the reference standard.[8]

II. DISCUSSION

In the Petition, you request that FDA designate ultramicrosize griseofulvin tablets, 250 mg, approved under ANDA 204371 held by Mountain LLC, as the new reference standard (Petition at 1). You state that the current reference standard and RLD, which is Gris-PEG (ultramicrosize griseofulvin) tablets, 250 mg, held by Valeant Pharmaceuticals International, Inc. (Valeant) under NDA 050475, is not commercially available and appears to have been discontinued from marketing (Petition at 1-2).

We have reviewed the information in the docket, regulatory filings for the current reference standard, and third-party commercial data regarding ultramicrosize griseofulvin tablets, 250 mg. Based on this information, FDA concludes that the current reference standard, Valeant's Gris-PEG (ultramicrosize griseofulvin) tablets, 250 mg, drug product is unavailable in the market. Accordingly, FDA has determined it is appropriate for the Agency to select a new reference standard.[9]

In this instance, we have determined that it is appropriate to select ANDA 204371 held by Mountain LLC as the new reference standard for ultramicrosize griseofulvin tablets, 250 mg. It is therapeutically equivalent to the current reference standard, and it is the current market leader as determined by FDA based on commercial data.[10]

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[4] Id.

[5] Id.

[6] § 314.94(a)(3) (21 CFR 314.94(a)(3)).

[7] "Therapeutic equivalents are approved drug products that are pharmaceutical equivalents for which bioequivalence has been demonstrated, and that can be expected to have the same clinical effect and safety profile when administered to patients under the conditions specified in the labeling" (§ 314.3(b)).

[8] "Abbreviated New Drug Applications and 505(b)(2) Applications," 81 FR 69580 at 69619 (Oct. 6, 2016).

[9] See 81 FR at 69619.

[10] We note that FDA will not approve any ANDA that uses the reference standard to demonstrate bioequivalence until FDA determines that the RLD was not withdrawn from sale for safety or effectiveness reasons. See § 314.161 (21 CFR 314.161) and § 314.122 (21 CFR 314.122).

III. CONCLUSION

For the reasons described in this response, the Petition is granted, and FDA will identify ANDA 204371 for ultramicrosize griseofulvin tablets, 250 mg, held by Mountain LLC, as the new reference standard in the Orange Book.

Sincerely,

Douglas C. Throckmorton -S

Digitally signed by Douglas C. Throckmorton -S
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