FDA U.S. FOOD & DRUG ADMINISTRATION

FEB 0 5 2020

Amy Schutte
Senior Associate
Lachman Consultant Services, Inc.
1600 Stewart Avenue, Suite 604
Westbury, NY 11590

Re: Docket No. FDA-2019-P-3809

Dear Ms. Schutte:

This letter responds to your citizen petition received on August 12, 2019 (Petition), requesting that the Food and Drug Administration (FDA or Agency) designate either Permethrin Cream 5% approved under abbreviated new drug application (ANDA) 074806 held by Actavis Laboratories, Inc. or Permethrin Cream 5% approved under ANDA 076369 held by Perrigo Israel Pharmaceuticals, Ltd. 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 to the extent that it requests that FDA select Permethrin Cream 5% held by Perrigo Israel Pharmaceuticals, Ltd. as the reference standard.

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of the FD&C Act for safety and effectiveness or under section 505(j) of the FD&C Act; (2) whose approval has not been withdrawn or suspended under section 505(e)(1) through (e)(5) or (j)(6) of the FD&C Act; and (3) that has not been withdrawn from sale for what FDA has determined are reasons of safety or effectiveness.[2] Listed drug status is evidenced by the drug product's identification in the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.

[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 either Permethrin Cream 5%, approved under ANDA 074806 held by Actavis Laboratories, Inc. or Permethrin Cream 5%, approved under ANDA 076369 held by Perrigo Israel Pharmaceuticals, Ltd. as the new reference standard (Petition at 1). You state that the current reference standard and reference listed drug (RLD) is Elimite (permethrin) Cream 5% held by Mylan Pharmaceuticals, Inc. (Mylan) under new drug application (NDA) 019855, and based on information available in the marketplace, Mylan is not currently distributing its Elimite (permethrin) Cream 5% under NDA 019855 (Petition at 1-2).

As a preliminary matter, we note that an RLD generally is a drug product approved under section 505(c) of the FD&C Act based on full reports of investigations of safety and effectiveness. Accordingly, Mylan's NDA 019855 for Elimite (Permethrin) Cream 5% is the RLD and would be the basis for submission of an ANDA for Permethrin Cream 5%.

We have reviewed the information in the docket, regulatory filings for the current reference standard, and third-party commercial data regarding Permethrin Cream 5%. Based on this information, FDA concludes that the current reference standard, Mylan's Elimite (permethrin) Cream 5% drug product is unavailable in the market. Accordingly, FDA has determined it is appropriate for the Agency to identify a new reference standard.[9]

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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.

In this instance, we have determined that it is appropriate to select ANDA 076369 held by Perrigo Israel Pharmaceuticals, Ltd. as the new reference standard for Permethrin Cream 5% because it is the current market leader as determined by FDA based on commercial data.[10]

III. CONCLUSION

For the reasons described in this response, the Petition is granted to the extent that it requests that FDA select Permethrin Cream 5%, ANDA 076369, held by Perrigo Israel Pharmaceuticals, Ltd. as the reference standard.

Sincerely,

Janet Woodcock, M.D.
Director
Center for Drug Evaluation and Research

[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)."