HOWARD S. SUH
Direct No: 212.878.7914
Email: HSuh@FoxRothschild.com

February 11, 2020

Division of Dockets Management
Food and Drug Administration
Department of Health and Human Services
5630 Fishers Lane, Room 1061 (HFA-305)
Rockville, MD 20852

Electronic Submission

Citizen Petition

The undersigned ("Petitioner") submits this Citizen Petition pursuant to the Federal Food, Drug and Cosmetic Act ("FDC Act") and in accordance with 21 C.F.R. §§ 10.25(a) and 10.30 with regard to the Reference Standard ("RS") for Ketorolac Tromethamine Tablets, 10 mg designated by Food and Drug Administration ("FDA") and listed in the Approved Drug Products with Therapeutic Equivalence Evaluations ("Orange Book"). As per the current Orange Book, Abbreviated New Drug Application ("ANDA") 074761 held by Mylan Pharmaceuticals Inc., is designated as the RS for Ketorolac Tromethamine Tablets, 10 mg. However, it is commercially unavailable. For this reason, Petitioner requests that FDA designate ANDA 074754 held by Teva Pharmaceuticals USA Inc. as the new RS for Ketorolac Tromethamine Tablets, 10 mg to maintain a pathway for ANDA submissions.

I. ACTION REQUESTED

Petitioner requests that FDA designate ANDA 074754 (Ketorolac Tromethamine Tablets, 10 mg) held by Teva Pharmaceuticals USA Inc. as a RS for purposes of FDA evaluation of ANDAs for Ketorolac Tromethamine Tablets, 10 mg.

II. STATEMENT OF GROUNDS

Section 505(j) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) permits any person to submit to the FDA an ANDA to seek approval to market a generic drug. In general, to obtain approval of an ANDA for a generic drug, an ANDA applicant first must identify the previously approved drug product it seeks to duplicate, i.e., the Reference Listed Drug (“RLD”), and must show that its proposed generic drug is bioequivalent to the RLD and is the same with respect to active ingredient(s), dosage form, route of administration, strength, labeling, and conditions of use,

among other characteristics. Because an ANDA applicant is relying on FDA's finding that the RLD is safe and effective, the RLD is a drug product approved under section 505(c) of the FD&C Act for which FDA has made a finding of safety and effectiveness. FDA identifies in the Orange Book listed drugs that are eligible to be RLDs.

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 of the ANDA. To facilitate generic drug development, FDA generally selects a single reference standard that ANDA applicants must use in any in-vivo testing conducted to support a demonstration of bioequivalence. FDA selects a single reference standard to ensure the greatest level of consistency between a generic drug and its RLD and among generic drugs. Ordinarily, the reference standard selected by FDA will be the RLD.

Where FDA cannot select a drug product approved under section 505(c) of the FD&C Act as the reference standard (e.g., where the RLD has been withdrawn from sale for reasons other than safety and effectiveness), FDA generally will select a previously approved ANDA that referred to the RLD as the reference standard. If there are multiple approved generic products that referred to the RLD and have the same active ingredient, dosage form, route of administration, and strength, FDA usually will select the generic market leader, based on units sold, as the reference standard. FDA also will consider selecting a new reference standard when the Agency determines that the quantity of the current reference standard in distribution is so limited that a potential ANDA applicant is not able to obtain a sufficient quantity for in vivo bioequivalence testing (even if the current reference standard is not in the Discontinued Section of the Orange Book).

As per FDA's Draft Guidance for Industry, Referencing Approved Drug Products in ANDA Submissions (Jan. 2017), "*If there is a reference standard in the Active Section of the Orange Book but there are limited or no quantities of the reference standard in distribution, or a potential ANDA applicant believes a reference standard other than the one selected by FDA is appropriate, then the potential applicant may submit a citizen petition under 21 CFR 10.25(a) and 10.30 to request that FDA select that different listed drug also as a reference standard*".

Despite diligent efforts to obtain sufficient quantities of the present RS (Ketorolac Tromethamine Tablets, 10 mg, approved under ANDA 074761 held by Mylan Pharmaceuticals Inc.), the drug product is not commercially available and appears to have been discontinued from marketing at least since January 2019.

Based on the IMS Health data (Appendix 1), Ketorolac Tromethamine Tablets, 10 mg, approved under ANDA 074754 held by Teva Pharmaceuticals USA Inc. appears to lead the U.S. market in terms of the number of units sold and therefore, is appropriate for RS designation. Further, the IMS data also indicates that, currently, Ketorolac Tromethamine Tablets, 10 mg for the U.S. market is manufactured under only two ANDAs (ANDA 074754 held by Teva Pharmaceuticals USA Inc. and ANDA 210616 held by Cycle Pharmaceuticals Ltd.). Therefore, at this time, there is limited competition.

In order to maintain a pathway for ANDA submissions and promote competition, the Petitioner requests FDA to designate ANDA 074754, held by Teva Pharmaceuticals USA Inc., as the new RS for Ketorolac Tromethamine Tablets, 10 mg.

III. ENVIRONMENTAL IMPACT

An environmental assessment report on the action requested in this petition is not required under 21 C.F.R. § 25.31.

IV. ECONOMIC IMPACT

In accordance with 21 C.F.R. § 10.30(b), economic impact information will be promptly provided if requested by the Commissioner.

V. CERTIFICATION

Petitioner certifies that, to the best knowledge and belief of Petitioner, this petition includes all information and views on which the petition relies, and that it includes representative data and information known to the petitioner which are unfavorable to the petition.

Sincerely,

Howard S. Suh /s/

Howard Suh
Partner
Fox Rothschild LLP
101 Park Ave.
17th Floor
New York, NY 10178
(212) 878-7914 - direct
Email: HSuh@foxrothschild.com