Hyman, Phelps & McNamara, P.C.
700 Thirteenth Street, N.W., Suite 1200
Washington, DC 20005
Attn: Kurt Karst

Sent via email to: Kkarst@hpm.com

Docket No. FDA-2024-P-2779

Dear Kurt Karst:

This is in response to your petition received on June 10, 2024, by the U.S. Food and Drug Administration (FDA or Agency), requesting permission to submit an Abbreviated New Drug Application (ANDA) for the following drug product: Diclofenac Potassium Tablets, 12.5 mg. The listed drug product to which you refer in your petition is Cataflam (Diclofenac Potassium) Tablets, 25 mg and 50 mg, approved under new drug application (NDA) 020142 and held by Novartis Pharmaceuticals Corp.

Your request involves a change in strength from that of the listed drug product (i.e., from 25 mg and 50 mg to 12.5 mg). The change that you request is the type of change that is permissible under section 505(j)(2)(C) of the Federal Food, Drug, and Cosmetic Act (Act), subject to FDA approval of a petition submitted under that section of the Act. However, for the reasons explained below, the Agency denies your request.

We have reviewed your petition under section 505(j)(2)(C) of the Act and FDA's implementing regulations at 21 CFR 314.93. FDA will approve a petition properly submitted under § 314.93 unless FDA finds, among other grounds for denying such a petition, that investigations must be conducted to show the safety and effectiveness of the proposed drug product, or that any of the proposed changes from the RLD would jeopardize the safe or effective use of the product so as to necessitate significant labeling changes to address the newly introduced safety or effectiveness problem. See section 505(j)(2)(C) of the Act; 21 CFR 314.93(e)(1)(i), (iv).

The Agency has determined that your proposed change in strength raises questions of safety and effectiveness. The proposed changes from the RLD are not supported by the RLD labeling, and investigations must be conducted to show the safety and effectiveness of the proposed change in strength. Additionally, the proposed change in strength would also jeopardize the safe or effective use of the product so as to necessitate significant labeling changes to address the newly introduced safety or effectiveness problem.

You state that "the availability of a new 12.5 mg tablet strength will provide a prescribing physician with the ability to '[u]se the lowest effective dose for the shortest duration consistent with individual patient treatment goals.'" Petition at 3. The dosage described in the currently approved RLD labeling recommends a daily dosage of 100 mg/day to 200 mg/day in divided doses – 50 mg two to four times per day. There is no evidence in the RLD labeling that a single 12.5 mg tablet, or any other daily dosage that is not specified in the RLD labeling, is a safe and effective dose. Accordingly, investigations would be necessary to demonstrate safety and efficacy of the proposed strength if the petitioner intends for the labeling to describe the 12.5 mg strength, or another daily dosage that is not specified by the current labeling, as the "lowest effective dose." While the petitioner provided some evidence of safety and efficacy for the 12.5 mg strength available outside the US, the data provided in support of the petition (Attachments 3-6) are not permitted to be submitted in an ANDA.[1] Additionally, a 12.5 mg strength is not congruent with the RLD labeling, as the RLD labeling does not support 12.5 mg dose increments and only specifies 50 mg increments when increasing the dosage (e.g., from 50 mg twice daily to three times daily). As a result, investigations must be conducted to show the safety and effectiveness of the proposed change in strength.

In addition, the proposed change in strength from the RLD may result in misinterpretation by patients and prescribers that a single 12.5 mg tablet is an appropriate and acceptable dose. The proposed change in strength would also change the number of tablets administered to patients under the labeled dosing recommendations, and may result in miscalculations or errors in achieving the proper dose. Because of the increased risk of medication errors, the proposed labeling would need specific warning instructions that 12.5 mg is not an approved dose, that a 12.5 mg dose cannot be used as an increment for dose titration, and to use multiple 12.5 mg tablets to achieve the analgesic effect. As a result, the proposed change in strength would jeopardize the safe or effective use of the product so as to necessitate significant labeling changes to address the newly introduced safety or effectiveness problem.

Therefore, this petition is being denied because investigations must be conducted to show the safety and effectiveness of the proposed change in strength, and additionally because your proposed product, Diclofenac Potassium Tablets, 12.5 mg, would necessitate significant labeling changes to address the newly introduced safety or effectiveness problem posed by the proposed strength. Please contact Division of Anesthesiology, Addiction Medicine, and Pain Medicine in the Office of Neuroscience at (301) 796 - 2280 if you wish to pursue approval of your product under section 505(b) of the Act.

[1] See section 505(j)(2)(A) of the Act ("The Secretary may not require that an abbreviated application contain information in addition to that required by clauses (i) through (viii).").

If you disagree with our determination concerning the approvability of your petition as originally submitted, you may seek a reconsideration of the denial following the procedures set forth in 21 CFR 10.33. Requests for reconsideration must be based solely on the information contained in your original petition and must be submitted in accordance with 21 CFR 10.20, in the format outlined in § 10.33 and no later than 30 days after the date of the decision involved. Petitions for reconsideration should be filed with the Dockets Management Branch at the address listed below. If there is additional information, not included as part of your original submission that you would like the Agency to consider, you should submit a new petition including all the necessary information to the Dockets Management Branch.

A copy of this letter denying your petition will be placed on public display in the Dockets Management Branch, Room 1061, Mail Stop HFA-305, 5630 Fishers Lane, Rockville, MD 20852.

Sincerely,

William Chong, M.D.
Director
Office of Safety and Clinical Evaluation
for Ilun Murphy, M.D.
Director
Office of Generic Drugs
Center for Drug Evaluation and Research

William Chong

Digitally signed by William Chong
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