Aavis Pharmaceuticals
9488 Jackson Trail Road
Hoschton, GA 30548
Attention: Dhananjay Barot

Docket No. FDA-2019-P-5759

Dear Dhananjay Barot:

This is in response to your petition received on December 6, 2019, by the U.S. Food and Drug Administration (FDA or Agency) and your amendment dated May 3, 2021, requesting permission to submit an Abbreviated New Drug Application (ANDA) for the following drug product: Chlorzoxazone and Acetaminophen Tablets, 250 mg/300 mg. The listed drug product to which you refer in your petition is Butapap® (butalbital and acetaminophen, 50 mg/325 mg), approved under A089987 and held by Mikart LLC.[1]

Your request involves a change in one active ingredient for another active ingredient in a combination drug product (i.e., substituting chlorzoxazone for butalbital). 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 the petition does not contain information to show that the different active ingredient of the drug product is of the same pharmacological or therapeutic class as the ingredient of the reference listed drug that is to be changed and that the drug product can be expected to have the same therapeutic effect as the reference listed drug when administered to patients for each condition of use in the listed drug's labeling for which the applicant seeks approval. See section 505(j)(2)(C) of the Act; 21 CFR 314.93(e)(1)(iii)(B).

The Agency has determined that your proposed change in active ingredient raises questions of safety and effectiveness. The proposed change in this petition for the active ingredient is not within the same pharmacological or therapeutic class and cannot be expected to have the same therapeutic effect as the reference listed drug when administered to patients for the condition of use in the listed drug's labeling. Additionally, investigations must be conducted to show the safety and effectiveness of the drug product or any of its active ingredients, or strength, which differ from the reference listed drug. See 21 CFR 314.93(e)(1)(i).

[1] ANDA 089987 is identified in the *Approved Drug Products with Therapeutic Equivalence Evaluations* (Orange Book) as the reference standard for this drug product. If you resubmit this petition, we note that you are required to identify a reference listed drug (RLD). See 21 CFR 314.93; 21 CFR 314.3(b). The RLD generally is a drug product approved under section 505(c) of the Act based on full reports of investigations of safety and effectiveness.

In addition, the Pediatric Research Equity Act (PREA) provides that a person who submits an application or supplement under section 505 for a new active ingredient, new indication, new dosage form, new dosing regimen, or new route of administration shall submit assessments adequate to evaluate the safety and effectiveness of the drug for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration in each pediatric subpopulation for which the drug is safe and effective, unless this requirement is waived. Section 505B of the Act. If a change proposed in a suitability petition triggers the need for pediatric studies under PREA to assess safety and efficacy in a relevant pediatric subpopulation and FDA does not waive the requirement, the proposed product will not be eligible to be approved in an ANDA and the suitability petition must be denied. 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) [of Section 505(j)(2)(A)].").

Because you are seeking a change in active ingredient, this proposed product triggers PREA. This petition is being denied because the active ingredient (chlorzoxazone) of the proposed combination drug product is not of the same pharmacological or therapeutic class as those of the reference listed drug and the proposed drug combination is not expected to have the same therapeutic effect as the reference listed drug when administered to patients for each condition of use in the reference listed drug's labeling for which you seek approval. Additionally, investigations must be conducted to show the safety and effectiveness of the drug product or any of its active ingredients, or strength, which differ from the reference listed drug, as the drug product combination was previously found ineffective in the Drug Efficacy Study Implementation (DESI)[2] and there are safety concerns related to hepatotoxicity. Therefore, because your petition does not meet the applicable requirements under section 505(j)(2)(C) of the Act and 21 CFR 314.93, it is not necessary to address the question of whether pediatric studies are necessary under PREA. Please contact the Division of Anesthesiology, Addiction Medicine, and Pain Medicine (DAAP) at (301) 796-2280 if you wish to pursue approval of your product under section 505(b) of the Act.

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 H. Chong -S

Digitally signed by William H. Chong -S
Date: 2023.11.15 08:39:20 -05'00'

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

[2] 54 Fed. Reg. 18157 (Apr. 27, 1989).