

Food and Drug Administration
Rockville MD 20857

FEB 28 2003

Shotwell & Carr, Inc.
Attention: Paul W. Carr
3535 Firewheel Dr
Suite A
Flower Mound, TX 75028-2628

Docket No. 02P-0056/CPI

Dear Mr. Carr:

This is in response to your petition filed on January 31, 2002, requesting permission to file an Abbreviated New Drug Application (ANDA) for the following drug products: Butalbital and Acetaminophen Tablets, 25 mg/300 mg and 50 mg/600 mg. The listed drug product to which you refer in your petition is Phrenilin® (Butalbital and Acetaminophen) Tablets, 50 mg/325 mg, approved under ANDA 87-811 held by Amarin Pharmaceuticals Inc.

Your requests involve a change in strength of both the acetaminophen and the butalbital components from that of the listed drug product. (1) You request a change in strength of the acetaminophen component only (increase) from that of the listed drug (i.e., from Butalbital and Acetaminophen Tablets, 50 mg/325 mg, to Butalbital and Acetaminophen Tablets, 50 mg/600 mg). (2) You also request a change in strength (decrease) of both the butalbital and acetaminophen components from that of the listed drug (i.e., from Butalbital and Acetaminophen Tablets, 50 mg/325 mg, to Butalbital and Acetaminophen Tablets, 25 mg/300 mg). The changes you request are the type of changes that are authorized under Section 505(j)(2)(C) of the Federal Food, Drug, and Cosmetic Act (Act). Under Section 505(j)(2)(C)(i) of the Act, the FDA must approve a petition seeking a strength that differs from the strength of the listed drug product unless it finds that investigations must be conducted to show the safety and effectiveness of the differing strength.

We have reviewed your petition under Section 505(j)(2)(C) of the Act and have determined that it is **approved in part and denied in part**. This letter represents the Food and Drug Administration's (FDA) determination that (1) an ANDA may be submitted solely for the proposed product, Butalbital and Acetaminophen Tablets, 50 mg/600 mg, and (2) an ANDA may **not** be submitted for the proposed product, Butalbital and Acetaminophen Tablets, 25 mg/300mg. An explanation follows:

(1) Approved in Part:

With respect to your proposed product, Butalbital and Acetaminophen Tablets, 50 mg/600 mg,

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the FDA finds that the change in the strength of the acetaminophen component for the specific proposed drug product does not pose questions of safety or effectiveness because the proposed strength of the acetaminophen component falls within acceptable limits established by the Food and Drug Administration (FDA). In addition, the uses and route of administration of the proposed drug product are the same as that of the listed drug product.

The dosing instructions for the reference listed drug recommend one to two tablets every four hours not to exceed a total daily dose of six tablets. The proposed product approximately doubles the per tablet dose of acetaminophen. Since the recommended labeling indicates that one to two tablets may be administered at each dosing interval, the dose of acetaminophen that you propose is contemplated by the labeling. In addition, we note that Phrenilin® Forte (Butalbital and Acetaminophen) Capsules, 50 mg/650 mg, are an approved drug product. Therefore, the FDA concludes that there are no safety or effectiveness issues related to a dose of 600 mg of acetaminophen in combination with 50 mg of butalbital and that investigations are not necessary in this instance. In addition, if shown to meet bioavailability requirements, the proposed drug product can be expected to have the same therapeutic effect as the listed reference drug product.

When an ANDA is submitted for your proposed drug product, the proposed labeling should reflect the maximum number of doses per day that can be administered for your proposed drug product. For this specific product, the dosage and administration section of the labeling should specify one tablet every four hours and that the total daily dose should not exceed 6 tablets. Please note that it is recommended that the maximum single adult dose of acetaminophen may not exceed 1000 mg, and the total daily dose of the acetaminophen component should not exceed the maximum total daily dose for adults of 4000 mg established by the Agency for its safe and effective range. Please refer to the Tentative Final Monograph for Internal Analgesic, Antipyretic, and Antirheumatic Drug Products for Over-the-Counter Human Use (53 FR 46204, November 16, 1988). Please consult with the Labeling Review Branch at (301) 827-5846 if you have any questions regarding the proposed labeling for the specific drug product.

The partial approval of this petition to allow an ANDA to be submitted for the above-referenced drug product does not mean that the FDA has determined that an ANDA will be approved for the drug product. The determination of whether an ANDA will be approved is not made until the ANDA itself is submitted and reviewed by the FDA.

To permit review of your ANDA submission, you must submit all information required under Sections 505(j)(2)(A) and (B) of the Act. To be approved, the drug product will, among other things, be required to meet current bioavailability requirements under Section 505(j)(2)(A)(iv) of the Act. We suggest that you submit your protocol for this drug product to the Office of Generic Drugs, Division of Bioequivalence, prior to the submission of your ANDA. During the review of your application, the FDA may require the submission of additional information.

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The listed drug product to which you refer in your ANDA must be the one upon which you based this petition. In addition, you should refer in your ANDA to the appropriate petition docket number cited above, and include a copy of this letter in the ANDA submission.

(2) Denied in Part:

The Agency has determined that the proposed change in strength for your proposed drug product, Butalbital and Acetaminophen Tablets, 25 mg/300 mg, raises questions of effectiveness because the Agency has concluded that the effectiveness of a 25 mg dose of butalbital in the proposed product has not been established. There are no products currently listed in *Approved Drug Products with Therapeutic Equivalence Evaluations* (the Orange Book) that contain less than 50 mg of butalbital. Based on information submitted by the petitioner, it is not reasonable to assume that the proposed product would be efficacious for the proposed indication due to the subtherapeutic dose. **Therefore, FDA is denying this portion of the petition under Section 505(j)(2)(C)(i) because investigations are necessary to show the safety and effectiveness of the proposed drug product.**

If you disagree with our determination concerning the acceptability 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 Section 10.20, in the format outlined in Section 10.33 and no later than 30 days after the date of the decision involved. Petition 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 FDA to consider, you should submit a new petition including all the necessary information to the Dockets Management Branch.

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

Sincerely yours,



Gary J. Buehler
Director
Office of Generic Drugs
Center for Drug Evaluation and Research