

March 1, 2007

OVERNIGHT COURIER 3/01/07

Dockets Management Branch
Food and Drug Administration
Department of Health and Human Services, HFA-305
5630 Fishers Lane, Room 1061
Rockville, Maryland 20852

CITIZEN SUITABILITY PETITION

The undersigned, on behalf of a client, submits this petition in quadruplicate under Section 505(j)(2)(C) of the Federal Food, Drug, and Cosmetic Act ("the FDC Act"), 21 U.S.C. § 355(j)(2)(C), and 21 C.F.R. §§ 10.20, 10.30, and 314.93 to request that the Commissioner of Food and Drugs make a determination that an 505(j)(2)(C) application may be submitted for two strengths of Promethazine Hydrochloride and Hydrocodone Bitartrate Syrup, 6.25 mg/ 2.5 mg per 5 mL and 6.25 mg/ 1.67 mg per 5 mL.

A. Action Requested

The petitioner requests that the Commissioner of Food and Drugs make a determination that a promethazine hydrochloride in combination with hydrocodone bitartrate, in strengths consisting of 6.25 mg of promethazine hydrochloride and the variable strengths of 2.5 mg and 1.67 mg of hydrocodone bitartrate per 5 mL of the syrup dosage form, is suitable for submission as an 505(j)(2)(C) application. The reference listed drug upon which this petition is based is Prometh w/ Codeine, application #88-763, held by Actavis Mid Atlantic according to the Approved Drug Products with Therapeutic Equivalence Evaluations ("Orange Book"). This petition is submitted for a change in one of the active ingredients from the established reference listed drug as well as additional dosage strength. The proposed product would differ in the analgesic narcotic and antitussive component with hydrocodone bitartrate being substituted for codeine phosphate and two varying dosage strengths of the hydrocodone bitartrate.

B. Statement of Grounds

The Federal Food, Drug, and Cosmetic Act provides for the submission of an 505(j)(2)(C) application for a new drug that differs in one active ingredient from a listed combination drug provided that the FDA has approved a petition seeking permission to file such an application. This petition requests a change in one active ingredient and an addition in the strength for the proposed drug product from the of the reference listed drug.

2007P-0076

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The approved product labeling for Promethazine HCl and Codeine Phosphate Syrup is marketed under the brand name Prometh w/ Codeine. A copy of the labeling for the reference listed drug is provided as *Attachment A*.

According to the approved labeling of the reference listed drug product, Prometh w/ Codeine is administered to adults with the "average effective dose for adults (16 years of age and over) is: 1 teaspoonful (5 mL) every 4 to 6 hours, not to exceed 30 mL in 24 hours.

The combination of Prometh w/ Codeine is contraindicated in pediatric patients less than 16 years of age, because the combination may cause fatal respiratory depression in this age population.

The labeling also contains a boxed Warning attributable to the promethazine FDA Alert of 04/2006. This warning will be included in the labeling for the proposed product.

The listing of Prometh w/ Codeine can be found on the "Prescription Drug Products" list in the CDER's Electronic Orange Book Query and is included as *Attachment B*.

The dosage for the proposed product is consistent with the dosage approved in the reference-listed drug product's labeling with a change in the dosing of the hydrocodone bitartrate taking in account the potency difference of 5 to 1. Hydrocodone is a semi-synthetic opiate agonist and is similar to other phenanthrene derivatives such as codeine. It is commonly available as an analgesic and antitussive in combination with other agents.

The proposed labeling for Promethazine HCl and Hydrocodone Bitartrate Syrup in the varying strengths is included as *Attachment C*. Labeling for the proposed product will be consistent with the approved labeling for the reference listed drug, Prometh w/ Codeine, the products upon which this petition is based, taking into account any variances between the analgesic narcotics/ antitussives.

According to the "Orange Book" there is at least one other base antihistamine combined with either codeine or hydrocodone. This provides historical precedence of the compatible nature of the codeine base in exchange of the hydrocodone base. Tussionex® Pennkinetic® is chlorpheniramine polistirex with hydrocodone polistirex and Codeprex™ Pennkinetic® is the combination of chlorpheniramine polistirex with codeine polistirex. These products can be found on the "Prescription Drug Products" list in the CDER's Electronic Orange Book Query and is included as *Attachment D* for the convenience of the reviewer. The approved labeling is also provided for both products as *Attachment E*.

In summary, the reference-listed drug product differs from the proposed dosage form, primarily, with the change from codeine phosphate to hydrocodone bitartrate. This is consistent with the safety and efficacy of the new product. The indications remain unchanged and the dosing is consistent with that recommended in the labeling of the approved reference listed drug product. Moreover we believe that the additional dosing strength will provide convenience, benefit and choice for the adult population. Therefore, we are asking the Agency to conclude that clinical investigations are not necessary to demonstrate the proposed product's safety or effectiveness.

C. Pediatric Use Information

This petition requests a slight change for the new dosage form from that of the listed drug. Therefore, the petitioner also requests a full waiver from the pediatric study requirements of the Pediatric Research Equity Act of 2003, per 21 CFR § 314.55 (2)(i) *"The drug product does not represent a meaningful therapeutic benefit over existing treatments for pediatric patients"* The approved listed drug product's labeling current is contraindicated for the pediatric population and does not contain pediatric dosing due to the use of promethazine hydrochloride. The petitioner is committed to replicating a similar dosing schedule in its labeling.

D. Environmental Impact

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

E. Economic Impact

The petitioner does not believe that this is applicable in this case, but will agree to provide such analysis if requested by the Agency.

F. Certification

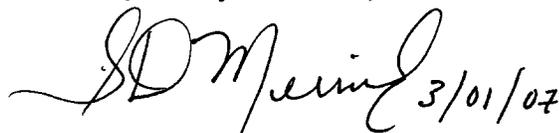
The undersigned certifies to the best of his knowledge that this petition includes all the information and views on which the petition relies and that all representative data or information, however unfavorable, known to the petitioner is included.

The petitioner also requests an in vivo bioavailability or bioequivalence waiver per 21 CFR 320.22(d)2 based the similarity of the active ingredients and the proportionality of the dosing strengths.

For the aforementioned reasons, the undersigned requests that the Commissioner approve this petition and find that an application for Promethazine Hydrochloride and Hydrocodone Bitartrate Syrup, 6.25 mg/ 2.5 mg per 5 mL and 6.25 mg/ 1.67 mg per 5 mL be suitable for submission as an ANDA.

If there are any questions or concerns, please do not hesitate to contact the undersigned at s.merrick@sovpharm.com via email or by phone at (817) 284-0429.

Respectfully submitted,



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