4160-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2008-P-0555[

Determination That HYCODAN (Hydrocodone Bitartrate and Homatropine Methylbromide) Tablets, 5 Milligrams/1.5 Milligrams, and HYCODAN (Hydrocodone Bitartrate and Homatropine Methylbromide) Oral Solution, 5 Milligrams/5 Milliliters and 1.5 Milligrams/ 5 Milliliters, Were Not Withdrawn From Sale for Reasons of Safety or Effectiveness

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) has determined that HYCODAN (hydrocodone bitartrate and homatropine methylbromide) tablets, 5 milligrams (mg)/1.5 mg, and HYCODAN (hydrocodone bitartrate and homatropine methylbromide) oral solution, 5 mg/ 5 milliliters (mL) and 1.5 mg/5 mL, were not withdrawn from sale for reasons of safety or effectiveness. This determination will allow FDA to approve abbreviated new drug applications (ANDAs) for hydrocodone bitartrate and homatropine methylbromide tablets, 5 mg/1.5 mg, and HYCODAN (hydrocodone bitartrate and homatropine methylbromide) oral solution, 5 mg/5 mL and 1.5 mg/5 mL, if all other legal and regulatory requirements are met.

FOR FURTHER INFORMATION CONTACT:

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SUPPLEMENTARY INFORMATION: In 1984, Congress enacted the Drug Price Competition and Patent Term Restoration Act of 1984 (Public Law 98-417) (the 1984 amendments), which authorized the approval of duplicate versions of drug products under an ANDA procedure. ANDA applicants must, with certain exceptions, show that the drug for which they are seeking approval contains the same active ingredient in the same strength and dosage form as the "listed drug," which is a version of the drug that was previously approved. ANDA applicants do not have to repeat the extensive clinical testing otherwise necessary to gain approval of a new drug application (NDA). The only clinical data required in an ANDA are data to show that the drug that is the subject of the ANDA is bioequivalent to the listed drug.

The 1984 amendments include what is now section 505(j)(7) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(j)(7)), which requires FDA to publish a list of all approved drugs. FDA publishes this list as part of the "Approved Drug Products With Therapeutic Equivalence Evaluations," which is known generally as the "Orange Book." Under FDA regulations, drugs are removed from the list if the Agency withdraws or suspends approval of the drug's NDA or ANDA for reasons of safety or effectiveness or if FDA determines that the listed drug was withdrawn from sale for reasons of safety or effectiveness (21 CFR 314.162).

A person may petition the Agency to determine, or the Agency may determine on its own initiative, whether a listed drug was withdrawn from sale for reasons of safety or effectiveness. This determination may be made at any time after the drug has been withdrawn from sale, but

must be made prior to approving an ANDA that refers to the listed drug (§ 314.161 (21 CFR 314.161)). FDA may not approve an ANDA that does not refer to a listed drug.

HYCODAN (hydrocodone bitartrate and homatropine methylbromide) tablets, 5 mg/ 1.5 mg, and HYCODAN (hydrocodone bitartrate and homatropine methylbromide) oral solution, 5 mg/5 mL and 1.5 mg/5 mL, are the subject of NDA 05-213, held by Endo Pharmaceuticals, and initially approved on March 23, 1943. In 1982, a Drug Efficacy Study Implementation review concluded that HYCODAN syrup, tablets, and powder were effective "for the symptomatic relief of cough." (47 FR 23809, June 1, 1982). Subsequently, the sponsor submitted an NDA for HYCODAN (hydrocodone bitartrate and homatropine methylbromide) tablets, 5 mg/1.5 mg, and HYCODAN (hydrocodone bitartrate and homatropine methylbromide) oral solution, 5 mg/5 mL and 1.5 mg/5 mL, which was approved on July 26, 1988. HYCODAN is indicated for the symptomatic relief of cough in adults and children 6 years of age and older.

In a letter dated January 4, 2008, Endo Pharmaceuticals notified FDA that HYCODAN (hydrocodone bitartrate and homatropine methylbromide) tablets, 5 mg/1.5 mg, were being discontinued, and FDA moved the drug product to the "Discontinued Drug Product List" section of the Orange Book. Vintage Pharmaceutical, Inc., submitted a citizen petition dated October 15, 2008 (Docket No. FDA-2008-P-0555), under 21 CFR 10.30, requesting that the Agency determine whether HYCODAN (hydrocodone bitartrate and homatropine methylbromide) tablets, 5 mg/1.5 mg, were withdrawn from sale for reasons of safety or effectiveness. Although the citizen petition did not request it, FDA has determined, on its own initiative, whether the oral solution dosage form was withdrawn for safety or effectiveness reasons.

After considering the citizen petition and reviewing Agency records and based on the information we have at this time, FDA has determined under § 314.161 that HYCODAN

(hydrocodone bitartrate and homatropine methylbromide) tablets, 5 mg/1.5 mg, and HYCODAN (hydrocodone bitartrate and homatropine methylbromide) oral solution, 5 mg/5 mL and 1.5 mg/ 5 mL, were not withdrawn for reasons of safety or effectiveness. The petitioner has identified no data or other information suggesting that HYCODAN (hydrocodone bitartrate and homatropine methylbromide) tablets, 5 mg/1.5 mg, or HYCODAN (hydrocodone bitartrate and homatropine methylbromide) oral solution, 5 mg/5 mL and 1.5 mg/5 mL, were withdrawn for reasons of safety or effectiveness. We have carefully reviewed our files for records concerning the withdrawal of HYCODAN (hydrocodone bitartrate and homatropine methylbromide) tablets, 5 mg/1.5 mg, and HYCODAN (hydrocodone bitartrate and homatropine methylbromide) oral solution, 5 mg/5 mL and 1.5 mg/5 mL, from sale. We have also independently evaluated relevant literature and data for possible postmarketing adverse events. We have found no information that would indicate that these products were withdrawn from sale for reasons of safety or effectiveness.

Accordingly, the Agency will continue to list HYCODAN (hydrocodone bitartrate and homatropine methylbromide) tablets, 5 mg/1.5 mg, and HYCODAN (hydrocodone bitartrate and homatropine methylbromide) oral solution, 5 mg/5 mL and 1.5 mg/5 mL, in the "Discontinued Drug Product List" section of the Orange Book. The "Discontinued Drug Product List" delineates, among other items, drug products that have been discontinued from marketing for reasons other than safety or effectiveness. ANDAs that refer to HYCODAN (hydrocodone bitartrate and homatropine methylbromide) tablets, 5 mg/1.5 mg, or HYCODAN (hydrocodone bitartrate and homatropine methylbromide) oral solution, 5 mg/5 mL and 1.5 mg/5 mL, may be approved by the Agency as long as they meet all other legal and regulatory requirements for the

approval of ANDAs. If FDA determines that labeling for this drug product should be revised to meet current standards, the Agency will advise ANDA applicants to submit such labeling.

Dated: December 22, 2011.

Leslie Kux,

Acting Assistant Commissioner for Policy.

[FR Doc. 2011-33549 Filed 12/29/2011 at 8:45 am; Publication Date: 12/30/2011]