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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 1978N-0224 (formerly Docket No. 78N-0224); DESI 11853]

Trimethobenzamide Hydrochloride Suppositories; Withdrawal of Approval

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the resolution of issues concerning trimethobenzamide hydrochloride suppositories. This notice announces the withdrawal of approval of the new drug application (NDA) for Tigan (trimethobenzamide hydrochloride) Suppositories. The notice also declares that the marketing of unapproved trimethobenzamide hydrochloride suppository products is unlawful and subject to FDA regulatory action. FDA is taking these actions because trimethobenzamide hydrochloride suppositories lack substantial evidence of effectiveness.

ADDRESSES: Requests for an opinion on the applicability of this notice to a specific trimethobenzamide hydrochloride suppository product should be identified with Docket No. 1978N-0224 and reference number DESI 11853 and directed to the Office of Compliance, Division of New Drugs and Labeling Compliance (HFD-310), New Drugs and Labeling Team, Center for Drug Evaluation and Research, Food and Drug Administration, 11919 Rockville Pike, Rockville, MD 20852.

DATE: Effective [insert date 30 days after date of publication in the FEDERAL REGISTER].

FOR FURTHER INFORMATION CONTACT:

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Brian L. Pendleton,

Center for Drug Evaluation and Research (HFD-7),

Food and Drug Administration,

5600 Fishers Lane,

Rockville, MD 20857,

301-594-2041.

SUPPLEMENTARY INFORMATION:

I. Background

As part of its Drug Efficacy Study Implementation (DESI) program, in a notice published in the FEDERAL REGISTER on February 24, 1971 (36 FR 3435) (the 1971 notice), FDA announced the following conclusions regarding certain drug products that contain trimethobenzamide hydrochloride: (1) The products were probably effective for nausea and vomiting due to radiation therapy or travel sickness and for emesis associated with operative procedures, labyrinthitis, or Meniere's syndrome; (2) they were lacking substantial evidence of effectiveness for the treatment of nausea and vomiting due to infections, underlying disease processes, or drug administration; and (3) they were possibly effective for all other labeled indications. The 1971 notice listed three trimethobenzamide hydrochloride products: Tigan Solution for Injection (NDA 11-853), Tigan Capsules (NDA 11-854), and Tigan Suppositories (NDA 11-855). Roche Laboratories held the NDAs for these three products.

On January 9, 1979, we published a notice in the FEDERAL REGISTER (44 FR 2021) (the 1979 suppository notice) announcing that we were reclassifying trimethobenzamide hydrochloride suppositories to lacking substantial evidence of

effectiveness and proposing to withdraw approval of the NDAs for trimethobenzamide hydrochloride suppositories. The 1979 suppository notice stated that NDA 17-529 for Tigan Suppositories, held by Beecham Laboratories (Beecham), had not been included in the 1971 notice, but was affected by the new notice. (In the same issue of the January 9, 1979, FEDERAL REGISTER (44 FR 2017) (the 1979 injection and capsule notice), we published a notice announcing that we were reclassifying trimethobenzamide hydrochloride injection and capsules to effective for certain indications and to lacking substantial evidence of effectiveness for their other (previously designated) less-than-effective indications. On December 24, 2002, we published the final evaluation for trimethobenzamide hydrochloride injection and capsules (67 FR 78476).)

In the 1979 suppository notice, we gave notice of an opportunity for a hearing to the holders of the NDAs for trimethobenzamide hydrochloride suppositories, and to all other interested persons, stating that we proposed to issue an order under section 505(e) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 355(e)) withdrawing approval of the NDAs and all amendments and supplements thereto (44 FR 2021 at 2021 to 2022). We stated that the notice of an opportunity for a hearing encompassed all issues relating to the legal status of the drug products subject to the notice, including identical, related, or similar drug products as defined in § 310.6 (21 CFR 310.6) of our regulations. In accordance with section 505 of the act and parts 310 and 314 (21 CFR parts 310 and 314), we gave the holders of the NDAs and all other persons who manufacture or distribute a drug product that is identical, related, or similar to a drug product named in the notice an opportunity for a hearing to show why approval of the NDAs involved should not be withdrawn, and an opportunity to raise, for administrative

determination, all issues relating to the legal status of a named drug product and all identical, related, or similar drug products (44 FR 2021 at 2022).

The 1979 suppository notice stated that the failure of an applicant or any other person subject to the notice to file a timely written appearance and request for a hearing, as required by § 314.200, constituted an election by the person not to make use of the opportunity for a hearing and a waiver of any contentions concerning the legal status of any drug product subject to the notice. The notice further stated that any such drug product could not thereafter lawfully be marketed, and we would initiate appropriate regulatory action to remove such drug products from the market (44 FR 2021 at 2022).

In a letter dated January 30, 1979, Beecham requested a hearing on the proposed withdrawal of NDA 17-529 for Tigan Suppositories. In a letter dated March 5, 1979, Beecham submitted data in support of its request for a hearing. Beecham was the only party to request a hearing. On April 13, 1979, we published a notice in the FEDERAL REGISTER announcing that we were withdrawing the approval of NDA 11-8550 (the only other NDA named in the 1979 suppository notice), effective April 23, 1979 (44 FR 22199).

On November 12, 1999, King Pharmaceuticals, Inc., 501 Fifth St., Bristol, TN 37620 (King), purchased from Roberts Pharmaceutical Corp. the NDAs for the Tigan products previously held by Beecham: NDA 17-529 (suppositories), NDA 17-530 (injection), and NDA 17-531 (capsules). We subsequently initiated discussions with King on bringing the Tigan products into compliance with the 1979 notices on trimethobenzamide hydrochloride drugs.

In an agreement that became effective on August 16, 2001 (the Agreement), FDA and King agreed to take several actions to resolve the matter of the compliance of Tigan products with the 1979 notices. Among other things, King agreed to withdraw the request for a hearing (originally submitted by Beecham) on matters related to NDAs 17-529 (Tigan Suppositories), 17-530 (Tigan Injection), and 17-531 (Tigan Capsules), and all amendments and supplements thereto, within 10 days of the effective date of the Agreement. In a letter dated August 24, 2001, King withdrew its request for a hearing on these matters in accordance with the Agreement. The issues relating to Tigan Capsules and Injection were resolved in 2001 and 2002, and on December 24, 2002, we published a notice in the FEDERAL REGISTER announcing our final evaluation of these products (67 FR 78476).

II. Resolution of Issues Concerning Tigan Suppositories

King notified us in a letter dated March 21, 2005, that it had decided not to pursue additional studies for Tigan Suppositories. In a letter dated August 19, 2005, we asked King, in accordance with the Agreement, to request the withdrawal of NDA 17-529 for Tigan Suppositories. In a letter dated September 6, 2005, King requested that we withdraw NDA 17-529.

As stated in section I of this document, King has withdrawn its request for a hearing on matters related to NDA 17-529. No party other than Beecham (a previous holder of NDA 17-529) submitted a request for a hearing in response to the 1979 suppository notice. Therefore, all other parties waived any possible contentions regarding the legal status of their trimethobenzamide hydrochloride suppository products.

III. Withdrawal of Approval of NDA 17-529 for Tigan Suppositories

As a result of the events described in section II of this document, we have concluded that Tigan Suppositories have not been shown to be effective. Therefore, we are withdrawing approval of the NDA for this product.

Under § 310.6, this notice applies to any drug product that is identical, related, or similar to Tigan Suppositories and is not the subject of an approved NDA. Any person who wishes to determine whether a specific product is covered by this notice should write to the Division of New Drugs and Labeling Compliance (see ADDRESSES).

The Director of the Center for Drug Evaluation and Research, under section 505(e) of the act and under the authority delegated to him, finds that, on the basis of the information in this docket on Tigan Suppositories (NDA 17-529), evaluated together with the evidence available to FDA when the application for this product was approved, there is a lack of substantial evidence that this product has the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in its labeling.

Therefore, based on the foregoing finding, the approval of NDA 17-529, including all amendments and supplements thereto, is withdrawn effective [insert date 30 days after date of publication in the FEDERAL REGISTER]. Shipment in interstate commerce of Tigan Suppositories or any identical, related, or similar trimethobenzamide hydrochloride suppository product that is not the subject of an approved NDA will then be unlawful.

We note that under enforcement policies regarding drugs marketed without required applications described in the agency's guidance entitled Marketed Unapproved Drugs—Compliance Policy Guide, it is a high priority for the agency to take enforcement

action against those unapproved drug products that lack evidence of effectiveness. Firms should be aware that we intend to take enforcement action without further notice against any firm that manufactures or ships in interstate commerce any unapproved product covered by this notice after [insert date 30 days after date of publication in the FEDERAL REGISTER]. Firms that discontinue or have already discontinued manufacturing products covered by this notice may want to notify us that they are no longer manufacturing those products. A firm that wishes to notify us of product discontinuation should send a letter, signed by the firm's chief executive officer, fully identifying the discontinued product, including its National Drug Code (NDC) number. The firm should send the letter to the Division of New Drugs and Labeling Compliance, New Drugs and Labeling Team (see ADDRESSES). Firms should also update the listing of their products under section 510(j) of the act (21 U.S.C. 360(j)) to reflect discontinuation of unapproved or otherwise discontinued products. We plan to rely on our existing records, the results of a subsequent inspection, or other available information when we evaluate whether to take enforcement action.

Dated: 3/14/07

March 14, 2007.
Douglas C. Throckmorton,
Deputy Director,
Center for Drug Evaluation and Research.

J. Ahmy 3/30/07

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