DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2001–N–0274 (formerly 01N–0196)]

Phenylpropanolamine; Withdrawal of Approval of 13 New Drug Applications and 7 Abbreviated New Drug Applications

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is withdrawing approval of 13 new drug applications (NDAs) and 7 abbreviated new drug applications (ANDAs) for products containing phenylpropanolamine. The basis for the withdrawals is that the products are no longer considered safe due to the association of phenylpropanolamine use with increased risk of hemorrhagic stroke. The holders of these NDAs and ANDAs have waived their opportunity for a hearing.

DATES: Effective February 20, 2014.

FOR FURTHER INFORMATION CONTACT: Emily Helms Williams, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, Rm. 6280, Silver Spring, MD 20993–0002, 301–796–3381.

SUPPLEMENTARY INFORMATION: On November 3, 2000, the Director of FDA's Center for Drug Evaluation and Research (the Director) sent a letter to holders of NDAs and ANDAs for drug products containing phenylpropanolamine requesting that they voluntarily discontinue marketing any such products due to developments indicating an association between phenylpropanolamine use and increased risk of hemorrhagic stroke. Subsequently, in a notice published in the **Federal Register** on August 14, 2001 (66 FR 42665), the Director offered an opportunity for a hearing on a proposal to issue an order, under section 505(e) of the Federal Food, Drug, and Cosmetic Act (the FD&C Act) (21 U.S.C. 355(e)) and 21 CFR 314.150(a)(2), withdrawing approval of 13 NDAs and 8 ANDAs for products containing phenylpropanolamine. (Although the August 14, 2001, notice stated that FDA proposed to withdraw approval of 16 NDAs and 8 ANDAs, the notice listed only 13 NDAs and 8 ANDAs.) The following products, all of which have been discontinued, were listed in the notice:

TABLE 1—NDAS AND ANDAS FOR WHICH FDA HAS PROPOSED TO WITHDRAW APPROVAL OF THE APPLICATIONS

Application No.	Drug	Applicant
NDA 11–694	Dimetane-DC Syrup	A.H. Robins Co., P.O. Box 8299, Philadelphia, PA 19101.
NDA 12–152	Ornade Extended-Release Tablet	SmithKline-Beecham, 1250 South Collegeville Rd., P.O. Box 5089, Collegeville, PA 19426.
NDA 12–436	Dimetapp Extended-Release Tablet	Whitehall-Robins, 5 Giralda Farms, Madison, NJ 07940.
NDA 13–087	Dimetapp Elixir	Do.
NDA 18–050	Corsym Extended-Release Suspension	Medeva Americas, Inc., 755 Jefferson Rd., P.O. Box 1710, Rochester, NY 14603.
NDA 18–099	Contac Extended-Release Capsule	SmithKline Beecham Consumer Health, L.P., 1500 Littleton Rd., Parsippany, NJ 07054.
NDA 18–298	Tavist-D Extended-Release Tablet	Novartis Consumer Health, Inc., 560 Morris Ave., Summit, NJ 07901.
NDA 18–556	Demazin Extended-Release Tablet	Schering-Plough HealthCare Products, Three Oak Way, P.O. Box 603, Berkeley Heights, NJ 07922.
NDA 18–809	Phenylpropanolamine Hydrochloride (HCl) Chlorpheniramine Maleate Extended-Release Capsule.	Schwarz Pharma, 6140 West Executive Dr., Mequon, WI 53092.
NDA 19–410	Hycomine Syrup	Endo Pharmaceuticals, Inc., 500 Endo Blvd., Garden City, NY 11530.
NDA 19–411	Hycomine Pediatric Syrup	Do.
NDA 19–613	Contac Extended-Release Tablet	Novartis Consumer Health, Inc.
NDA 20–640	Tavist-D Extended-Release Tablet	Do.
ANDA 71–099	Bromatapp Extended-Release Tablet	Teva Pharmaceuticals, USA, 1090 Horsham Rd., P.O. Box 1090, North Wales, PA 19454.
ANDA 88–359	Drize Extended-Release Capsule	B. F. Ascher & Co., Inc., 15501 West 109th St., Lenexa, KS 66219.
ANDA 88–681	Chlorpheniramine Maleate and Phenylpropanolamine HCl Extended-Release Capsule.	Chelsea Laboratories, 896 Orlando Ave., West Hempstead, NY 11552.
ANDA 88–687	Biphetap Elixir	Morton Grove Pharmaceuticals, Inc., 6451 Main St., Morton Grove, IL 60053.
ANDA 88–688	Bromanate Elixir	Alpharma, U.S. Pharmaceuticals Division, 333 Cassell Dr., suite 3500, Baltimore, MD 21224.
ANDA 88–723	Bromanate DC Syrup	Do.
ANDA 88–904	Myphetane DC Syrup	Morton Grove Pharmaceuticals, Inc.
ANDA 88–940	Chlorpheniramine Maleate and Phenylpropanolamine HCl Extended-Release Capsule.	Geneva Pharmaceuticals, Inc., 2555 West Midway Blvd., P.O. Box 446, Broomfield, CO 80038.

FDA issued the notice after an epidemiologic case-control study conducted by investigators at Yale University School of Medicine (Yale Hemorrhagic Stroke Project) demonstrated an association between phenylpropanolamine (an ingredient used in prescription and over-the-counter (OTC) drug products as a nasal decongestant to relieve stuffy nose or nasal congestion and in OTC weight control drug products to control appetite) and increased risk of hemorrhagic stroke. The notice included FDA's belief that the data from the Yale Hemorrhagic Stroke Project, taken together with spontaneous reports of hemorrhagic stroke and reports in the published medical literature, provided evidence that nasal decongestant and weight control drug products containing phenylpropanolamine are no longer safe. The Director proposed to withdraw approval of the NDA and ANDA products containing phenylpropanolamine based on her conclusion that they were no longer

shown to be safe for use under the conditions that formed the basis upon which the applications were approved.

In the August 14, 2001, notice, FDA provided the NDA and ANDA holders an opportunity to request a hearing to show why approval of the NDAs or ANDAs should not be withdrawn. One company, KV Pharmaceutical, requested a hearing by letter dated September 13, 2001, but that request was subsequently withdrawn by letter dated October 15, 2001. No other party requested a hearing on this matter following publication of the notice in the **Federal Register**. As stated above, all products listed in the notice were subsequently discontinued.

Subsequent to the August 14, 2001, notice, one of the ANDAs listed in that notice was withdrawn. In a notice published in the **Federal Register** of February 20, 2002 (67 FR 7702), FDA withdrew approval of ANDA 71–099 for BROMATAPP Extended-Release Tablets after the application holder informed FDA that the product was no longer being marketed and requested withdrawal.

In a letter to FDA dated February 25, 2013, Pfizer requested on behalf of its subsidiaries, Wyeth Pharmaceuticals, Inc. and A.H. Robins, that FDA withdraw approval of NDA 11–694 for DIMETANE–DC under § 314.150(d), noting that the product has been discontinued and is no longer marketed. In that letter, Pfizer and its named subsidiaries waived any opportunity for a hearing provided under the August 14, 2001, notice. In a response letter of March 28, 2013, the Agency acknowledged A.H. Robins' agreement to permit FDA to withdraw approval of DIMETANE–DC under § 314.150(d) and to waive its opportunity for a hearing.

For the reasons discussed in the August 14, 2001 notice, the Director, under section 505(e)(2) of the FD&C Act and under authority delegated to her by the Commissioner, finds that new evidence of clinical experience, not contained in the applications listed in table 1 and not available at the time the applications were approved, shows that phenylpropanolamine is not shown to be safe for use under the conditions of use that formed the basis upon which the applications were approved (21 U.S.C. 355(e)(2)). Therefore, approval of the NDAs listed in table 1 is hereby withdrawn. Furthermore, the Director finds that the ANDAs listed in table 1 refer to the drugs that are the subject of the NDAs listed above. Therefore, as required under section 505(j)(6) of the FD&C Act, approval of the ANDAs listed in table 1 is also withdrawn.

Under 21 CFR 314.161 and 314.162(a)(1), FDA will remove the products containing phenylpropanolamine named in table 1 from the list of drug products with effective approvals published in FDA's ''Approved Drug Products With Therapeutic Equivalence Evaluations.'' FDA will not approve or accept ANDAs that refer to these drug products.

Dated: February 14, 2014.

Leslie Kux,

Assistant Commissioner for Policy.

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2014–N–0200]

Standards for the Interoperable Exchange of Information for Tracing of Human, Finished, Prescription Drugs, in Paper or Electronic Format; Establishment of a Public Docket

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice; establishment of docket; request for comments.

SUMMARY: The Food and Drug Administration (FDA) is establishing a public docket to receive information and comments on standards for the interoperable exchange of information associated with transactions involving human prescription drugs in a finished dosage form (prescription drugs) to comply with new requirements in the Drug Supply Chain Security Act (DSCSA). We are seeking information from drug manufacturers, repackagers, wholesale distributors, dispensers (primarily pharmacies) and other drug supply chain stakeholders and interested parties, including standards organizations, State and Federal Agencies, and solution providers. In particular, stakeholders and other interested parties are requested to comment about the interoperable exchange of transaction information, transaction history, and transaction statements, in paper or electronic format, for each transfer of product in which a change of ownership occurs. This action is related to FDA's implementation of the DSCSA.

DATES: Submit either electronic or written comments by April 21, 2014.

ADDRESSES: Submit electronic comments to *http://www.regulations.gov.* Submit written comments to the Division of Dockets Management (HFA–305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number found in brackets in the heading of this document.

FOR FURTHER INFORMATION CONTACT: Connie T. Jung, Office of Compliance, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Silver Spring, MD 20933, 301–796–3130.

SUPPLEMENTARY INFORMATION:

I. Background

On November 27, 2013, the DSCSA (Title II, Pub. L. 113–54) was signed into law. The DSCSA outlines critical steps to build an electronic, interoperable system to identify and trace certain prescription drugs as they are distributed within the United States. Section 202 of the DSCSA, which adds section 582 to the Federal Food, Drug, and Cosmetic Act (FD&C Act), directs the Secretary of Health and Human Services (the Secretary) to establish standards for the interoperable exchange of transaction information, transaction history, and transaction statements, in paper or electronic format, in consultation with other appropriate Federal officials, manufacturers, repackagers, wholesale drug distributors, dispensers, and other pharmaceutical distribution supply chain stakeholders.

FDA has been engaged in efforts to improve the security of the drug supply chain for many years to protect U.S. patients from unsafe, ineffective, and poor quality drugs. Since the formation of the first FDA Counterfeit Drug Task Force in 2003, FDA has strongly advocated for a multilayered approach to securing the supply chain and protecting consumers from the threats posed by counterfeit and diverted drugs. The ability to track and trace finished prescription drugs plays a significant role in providing transparency and accountability in the drug supply chain. Under section 505D of the FD&C Act (21 U.S.C. 355e), FDA has been evaluating existing and emerging standards, system attributes and needs, and adoption of track and trace and authentication systems and technology. The system that will be established under DSCSA will enhance FDA's ability to help protect U.S. consumers from exposure to drugs that may be counterfeit, stolen, contaminated, or otherwise harmful by improving detection and removal of potentially dangerous drugs from the drug supply chain.

FDA is announcing the establishment of a public docket to provide an opportunity for interested persons to