



DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

AUG 05 2013

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David L. Rosen, B.S. Pharm., J.D.
Foley & Lardner LLP
3000 K Street, NW, 6th Floor
Washington, DC 20007-5143

Re: Docket No. FDA-2013-P-0241

Dear Mr. Rosen:

This letter responds to your citizen petition received on February 27, 2013, requesting that the Food and Drug Administration (FDA) determine whether CYTOXAN (cyclophosphamide) for Injection, new drug application (NDA) 12-142, originally approved as a lyophilized powder, was voluntarily withdrawn or withheld from sale for reasons of safety or effectiveness. In particular, we determined whether CYTOXAN (cyclophosphamide) for Injection (lyophilized formulations), 100 milligrams (mg)/vial, 200 mg/vial, 500 mg/vial, 1 gram (g)/vial, and 2 g/vial, were withdrawn for safety or effectiveness reasons. Although your petition did not address the non-lyophilized formulations of CYTOXAN (cyclophosphamide) for Injection, in 100 mg/vial and 200 mg/vial strengths, NDA 12-142, those strengths have also been discontinued. Therefore, on our own initiative, we have also determined whether those strengths were withdrawn for safety or effectiveness reasons.

FDA has reviewed its records and determined that CYTOXAN (cyclophosphamide) for Injection (lyophilized formulations), 100 mg/vial, 200 mg/vial, 500 mg/vial, 1 g/vial, and 2 g/vial, and CYTOXAN (cyclophosphamide) for Injection, 100 mg/vial and 200 mg/vial, were not withdrawn for safety or effectiveness reasons. Thus, FDA will maintain CYTOXAN (cyclophosphamide) for Injection (lyophilized formulations), 100 mg/vial, 200 mg/vial, 500 mg/vial, 1 g/vial, and 2 g/vial, and CYTOXAN (cyclophosphamide) for Injection, 100 mg/vial and 200 mg/vial, in the "Discontinued Drug Product List" section of *Approved Drug Products With Therapeutic Equivalence Evaluations* (the Orange Book).

Enclosed is a copy of the *Federal Register* notice that announces the FDA determination.
If you require any further information, please feel free to call me at (301) 796-2465.

Sincerely yours,

A handwritten signature in black ink, appearing to read 'C. Kirk', with a stylized, cursive flourish.

Christine E. Kirk
Office of Regulatory Policy
Center for Drug Evaluation and Research

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2013-P-0241]

Determination That CYTOXAN (Cyclophosphamide) for Injection Was 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 CYTOXAN (cyclophosphamide) for Injection (lyophilized formulations), 100 milligrams (mg)/vial, 200 mg/vial, 500 mg/vial, 1 gram (g)/vial, and 2 g/vial, and CYTOXAN (cyclophosphamide) for Injection (non-lyophilized formulations), 100 mg/vial and 200 mg/vial, were not withdrawn from sale for reasons of safety or effectiveness. This determination will allow FDA to approve abbreviated new drug applications (ANDAs) for these products, if all other legal and regulatory requirements are met.

FOR FURTHER INFORMATION CONTACT: Christine Kirk, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, Rm. 6280, Silver Spring, MD 20993-0002, 301-796-2465.

SUPPLEMENTARY INFORMATION: In 1984, Congress enacted the Drug Price Competition and Patent Term Restoration Act of 1984 (Pub. L. 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 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.

CYTOXAN (cyclophosphamide) for Injection (lyophilized formulations), 100 mg/vial, 200 mg/vial, 500 mg/vial, 1 g/vial, and 2 g/vial, and CYTOXAN (cyclophosphamide) for Injection, 100 mg/vial and 200 mg/vial, are the subject of NDA 012142, held by Baxter Healthcare, and initially approved on November 16, 1959. CYTOXAN for Injection is an alkylating drug product indicated for treatment of malignant lymphomas, Hodgkin's disease, lymphocytic lymphoma, mixed-cell type lymphoma, histiocytic lymphoma, Burkitt's lymphoma, multiple myeloma, leukemias, mycosis fungoides, neuroblastoma, adenocarcinoma of ovary, retinoblastoma, breast carcinoma, and minimal change nephrotic syndrome in pediatric patients.

CYTOXAN (cyclophosphamide) for Injection (lyophilized formulations), 100 mg/vial, 200 mg/vial, 500 mg/vial, 1 g/vial, and 2 g/vial, and CYTOXAN (cyclophosphamide) for Injection, 100 mg/vial and 200 mg/vial, are currently listed in the "Discontinued Drug Product List" section of the Orange Book.

Foley & Lardner LLP submitted a citizen petition dated February 26, 2013 (Docket No. FDA-2013-P-0241), under 21 CFR 10.30, requesting that the Agency determine whether CYTOXAN (cyclophosphamide) for Injection (lyophilized formulations), 100 mg/vial, 200 mg/vial, 500 mg/vial, 1 g/vial, and 2 g/vial, were voluntarily withdrawn or withheld from sale for reasons of safety or effectiveness. Although the citizen petition did not address the non-lyophilized 100 mg/vial and 200 mg/vial formulations, those strengths have also been discontinued. On our own initiative, we have also determined whether those strengths were 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 CYTOXAN (cyclophosphamide) for Injection (lyophilized formulations), 100mg/vial, 200mg/vial, 500 mg/vial, 1 g/vial, and 2 g/vial, and CYTOXAN (cyclophosphamide) for Injection, 100 mg/vial and 200 mg/vial, were not withdrawn for reasons of safety or effectiveness. The petitioner has identified no data or other information suggesting that CYTOXAN (cyclophosphamide) for Injection (lyophilized formulations), 100 mg/vial, 200 mg/vial, 500 mg/vial, 1 g/vial, and 2 g/vial, or CYTOXAN (cyclophosphamide) for Injection, 100 mg/vial and 200 mg/vial, were withdrawn for reasons of safety or effectiveness. We have carefully reviewed our files for records concerning the withdrawal of CYTOXAN (cyclophosphamide) for Injection (lyophilized formulations), 100 mg/vial, 200 mg/vial, 500 mg/vial, 1 g/vial, and 2 g/vial, and CYTOXAN (cyclophosphamide) for Injection, 100 mg/vial and 200 mg/vial, 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 CYTOXAN (cyclophosphamide) for Injection (lyophilized formulations), 100 mg/vial, 200 mg/vial, 500 mg/vial, 1 g/vial, and 2 g/vial, and CYTOXAN (cyclophosphamide) for Injection, 100 mg/vial and 200 mg/vial, 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 CYTOXAN (cyclophosphamide) for Injection (lyophilized formulations), 100 mg/vial, 200 mg/vial, 500 mg/vial, 1 g/vial, and 2 g/vial, or CYTOXAN (cyclophosphamide) for Injection, 100 mg/vial and 200 mg/vial, 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 these drug products should be revised to meet current standards, the Agency will advise ANDA applicants to submit such labeling.

Dated: July 30, 2013.

Leslie Kux,

Assistant Commissioner for Policy.

[FR Doc. 2013-18731 Filed 8-2-13; 8:45 am]

BILLING CODE 4160-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Health Resources and Services Administration

Privacy Act of 1974; Report of an Altered System of Records

AGENCY: Health Resources and Services Administration, Department of Health and Human Services (HHS).

ACTION: Notice of an altered system of records and deletion of a related system.

SUMMARY: In accordance with the requirements of the Privacy Act of 1974 (5 U.S.C. 552a), the Health Resources and Services Administration (HRSA) is publishing notice of a proposal to alter the system of records entitled and numbered National Practitioner Data Bank for Adverse Information on Physicians and other Health Care Practitioners (NPDB), #09-15-0054, to include information covered under a related system of records, the Healthcare Integrity and Protection Data Bank (HIPDB), SORN 09-90-0103, which is being deleted. The NPDB SORN was last published March 30, 2012 (77 FR 19295). The proposed alterations to the NPDB SORN include revising the Purpose section, expanding the Categories of Individuals, Categories of Records, and Record Sources Categories sections, revising two existing routine uses and adding one new routine use, deleting three unnecessary routine uses, and updating the Authority and Policies and Practices sections.

DATES: HRSA filed an altered system report with the Chair of the House Committee on Government Reform and Oversight, the Chair of the Senate Committee on Homeland Security and Governmental Affairs, and the Administrator, Office of Information and Regulatory Affairs, Office of Management and Budget (OMB) on July 17, 2013. To ensure all parties have adequate time in which to comment, the system alterations proposed in this notice will become effective 30 days from the publication of this notice in the **Federal Register** or 40 days from the date the altered system report was submitted to OMB and Congress, whichever is later, unless HRSA receives comments that require alterations to this notice. The HIPDB SORN will be considered deleted when

the system alterations proposed in this notice are effective.

ADDRESSES: Please address comments to Associate Administrator, Bureau of Health Professions, Health Resources and Services Administration, 5600 Fishers Lane, Room 9-05 Rockville, Maryland 20857. Comments received will be available for inspection at this same address from 9:00 a.m. to 3:00 p.m. (Eastern Standard Time Zone), Monday through Friday.

FOR FURTHER INFORMATION CONTACT: Director, Division of Practitioner Data Banks, Bureau of Health Professions, Health Resources and Services Administration, 5600 Fishers Lane, Room 8-103, Rockville, Maryland 20857; Telephone: (301) 443-2300. This is not a toll-free number.

SUPPLEMENTARY INFORMATION:

I. Merger of HIPDB Into NPDB

The NPDB and the HIPDB were authorized by separate laws to improve the quality of health care and to combat fraud and abuse, respectively. Title IV of the Health Care Quality Improvement Act (Title IV) and Section 1921 of the Social Security Act (Section 1921) govern the NPDB. Section 1128E of the Social Security Act (Section 1128E) governs the HIPDB. There was overlap between the two data banks following implementation of Section 1921 legislation in March 2010. Section 1921 expanded the scope of the NPDB, requiring each state to adopt a system of reporting to the Secretary certain adverse licensure actions taken against health care practitioners and health care entities by any authority of the state responsible for the licensing of such practitioners or entities. It also required each state to report any negative action or finding that a state licensing authority, a peer review organization, or a private accreditation entity has finalized against a health care practitioner or entity. Practically speaking, Section 1921 resulted in, among other consequences, including in the NPDB the vast majority of information contained in the HIPDB. On March 23, 2010, the Affordable Care Act was signed into law. Section 6403 of the law called for the elimination of duplication between the NPDB and the HIPDB. Section 1921 and Section 1128E statutory authorities were altered to eliminate duplicative reporting requirements.

The NPDB and HIPDB will merge to form one data bank. The HIPDB will cease operations following the merge, but the underlying statutory authority will remain intact and actions reported under that authority will now be moved

to the NPDB. HRSA published a Final Rule merging the two databank systems on April 5, 2013 (78 FR 20473) that went into effect on May 6, 2013.

II. Proposed Alterations to NPDB

The revised NPDB SORN that follows includes these system alterations:

- revises the Purpose section to reflect the addition of information previously collected under the HIPDB related to fraud and abuse, specifically the inclusion of health care providers and suppliers and collection of health care related criminal convictions, civil judgments, and other adjudicated actions
- expands the Categories of Individuals section to include health care providers and health care suppliers
- expands the Categories of Records section to include records of federal licensure or certification actions, health care related criminal convictions, health care related civil judgments, and other adjudicated actions or decisions. These additional records resulted in one revised and eleven new personally identifiable information data elements numbered 4 and 21-31, respectively.
- expands the "Records Sources Categories" section to include federal licensing and certification agencies, federal and state prosecutors and attorneys, health plans, federal government agencies, and state law and fraud enforcement agencies
- revises two routine uses (numbered 8 and 15) to reflect inclusion of health care providers and suppliers and to remove outdated references to only Section 1921 information;
- adds one new routine use (numbered 14) to allow disclosure of certain information to health plans
- deletes three unnecessary routine uses, pertaining to the Comptroller General, the U.S. Attorney General, and statistical information (numbered 7, 8 and 12 in the current version of the SORN, published March 30, 2012)
- updates the Authority section to cite Section 1128E of the Social Security Act as amended by the Patient Protection and Affordable Care Act of 2010
- updates the Policies and Procedures section related to Safeguards, specifically removing reference to only Title IV reporting

III. Background on the Privacy Act

The Privacy Act (5 U.S.C. 552a) governs the means by which the U.S. Government collects, maintains, and uses information about individuals in a system of records. A "system of records" is a group of any records under the control of a federal agency from