DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket Nos. FDA–2020–P–1344 and FDA–2023–P–2655]

Determination That CYTOXAN (Cyclophosphamide) for Injection (Sterile Dry Powder Excipient-Free Formulation), 500 Milligrams/Vial, 1 Gram/Vial, and 2 Grams/Vial, and CYTOXAN (Cyclophosphamide) for Injection (Sterile Dry Powder With Sodium Chloride Formulation), 500 Milligrams/Vial, 1 Gram/Vial, and 2 Grams/Vial, Were Not Withdrawn From Sale for Reasons of Safety or Effectiveness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 or the Agency) has determined that the sterile dry powder excipient-free formulation of CYTOXAN (cyclophosphamide) for Injection, 500 milligrams (mg)/vial, 1 gram (g)/vial, and 2 g/vial, and the sterile dry powder with sodium chloride formulation of CYTOXAN (cyclophosphamide) for Injection, 500 mg/vial, 1 g/vial, and 2 g/vial, were not withdrawn from sale for reasons of safety or effectiveness. This determination means that FDA will not begin procedures to withdraw approval of abbreviated new drug applications (ANDAs) that refer to the sterile dry powder excipient-free formulation or the sterile dry powder with sodium chloride formulation of these drug products, and it will allow FDA to continue to approve ANDAs that refer to these formulations of CYTOXAN as long as they meet relevant legal and regulatory requirements.

FOR FURTHER INFORMATION CONTACT: Tereza Hess, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, Rm. 6221, Silver Spring, MD 20993–0002, 202–768–5659, *Tereza.Hess@fda.hhs.gov.*

SUPPLEMENTARY INFORMATION: Section 505(j) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 355(j)) allows the submission of an ANDA to market a generic version of a previously approved drug product. To obtain approval, the ANDA applicant must show, among other things, that the generic drug product: (1) has the same active ingredient(s), dosage form, route of administration, strength, conditions of use, and (with certain exceptions) labeling as the listed drug, which is a version of the drug that was previously approved, and (2) is bioequivalent to the listed drug. ANDA applicants do not have to repeat the extensive clinical testing otherwise necessary to gain approval of a new drug application (NDA).

Section 505(j)(7) of the FD&C Act 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: (1) whenever a listed drug is voluntarily withdrawn from sale and ANDAs that referred to the listed drug have been approved and (2) 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 (sterile dry powder with sodium chloride formulation), with the 500 mg/vial, initially approved on May 4, 1964, the 1 g/vial, initially approved on August 30, 1982, and the 2 g/vial, initially approved on August 30, 1982, are the subjects of NDA 012142, held by Baxter Pharmaceuticals. Subsequently, CYTOXAN (cyclophosphamide) for Injection (lyophilized powder with mannitol) was also approved under NDA 012142, with the 500 mg/vial approved on January 4, 1984; the 1 g/vial approved on September 24, 1985; and the 2 g/vial approved on December 10, 1985. On November 7, 2003, the lyophilized powder with mannitol formulation in 500 mg/vial, 1 g/vial, and 2 g/vial strengths was reformulated and approved as a sterile dry powder excipient-free formulation under Supplement 107 to NDA 012142. On March 31, 2012, the CYTOXAN (cyclophosphamide) for Injection, sterile dry powder with sodium chloride formulation in 500 mg/vial, 1 g/vial, and 2 g/vial strengths was reformulated and approved as a lyophilized powder with mannitol formulation under Supplement 113. CYTOXAN is 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 the ovary, retinoblastoma, breast carcinoma, and minimal change nephrotic syndrome in pediatric patients.

FDA previously determined that certain CYTOXAN (cyclophosphamide) for Injection formulations and strengths were not discontinued from sale for reasons of safety or effectiveness, but these determinations did not address all previously approved formulations and strengths. In the **Federal Register** of March 1, 2004 (69 FR 9630), FDA issued a determination that CYTOXAN (cyclophosphamide) for Injection (non-lyophilized formulation), 2 g/vial, was not withdrawn from sale for reasons of safety or effectiveness. In the **Federal Register** of August 5, 2013 (78 FR 47321), FDA issued a determination 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 (non-lyophilized formulations), 100 mg/vial and 200 mg/vial, were not withdrawn from sale for reasons of safety or effectiveness. Neither of the previous **Federal Register** notices expressly indicate that the determinations were made for the sterile dry powder excipient-free formulation of CYTOXAN (cyclophosphamide) for Injection in the 500 mg/vial, 1 g/vial, and 2 g/vial strengths or the sterile dry powder with sodium chloride formulation of CYTOXAN (cyclophosphamide) for Injection, 500 mg/vial, 1 g/vial, and 2 g/vial.

The sterile dry powder excipient-free formulation of CYTOXAN (cyclophosphamide) for Injection, 500 mg/vial, 1 g/vial, and 2 g/vial, and the sterile dry powder with sodium chloride formulation of CYTOXAN (cyclophosphamide) for Injection, 500 mg/vial, 1 g/vial, and 2 g/vial, are discontinued.

Lachman Consultant Services, Inc., submitted a citizen petition dated May 5, 2020 (Docket No. FDA–2020–P–1344), under 21 CFR 10.30, requesting that the Agency determine whether discontinued formulations of all strengths of CYTOXAN (cyclophosphamide) for Injection approved under NDA 012142, including the sterile dry powder excipient-free formulation of CYTOXAN (cyclophosphamide) for Injection, 500 mg/vial, 1 g/vial, and 2 g/vial, were withdrawn from sale for reasons of safety or effectiveness. Epic Pharma,

LLC submitted a citizen petition dated June 27, 2023 (Docket No. FDA–2023–P–2655), also requesting that the Agency determine whether the sterile dry powder excipient-free formulation of CYTOXAN (cyclophosphamide) for Injection, 500 mg/vial, 1 g/vial, and 2 g/vial, were withdrawn from sale for reasons of safety or effectiveness. Although the citizen petitions did not specifically address the sterile dry powder with sodium chloride formulation of CYTOXAN (cyclophosphamide) for Injection, 500 mg/vial, 1 g/vial, and 2 g/vial, this formulation also has been discontinued. We have also determined whether the sterile dry powder with sodium chloride formulation of CYTOXAN (cyclophosphamide) for Injection, 500 mg/vial, 1 g/vial, and 2 g/vial, was withdrawn for safety or effectiveness.

After considering the citizen petitions 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 (sterile dry powder excipient-free formulation), 500 mg/vial, 1 g/vial, and 2 g/vial, and CYTOXAN (cyclophosphamide) for Injection (sterile dry powder with sodium chloride formulation), 500 mg/vial, 1 g/vial, and 2 g/vial, were not withdrawn for reasons of safety or effectiveness. The petitioners have identified no data or other information suggesting that the sterile dry powder excipient-free formulation of CYTOXAN (cyclophosphamide) for Injection, 500 mg/vial, 1 g/vial, and 2 g/vial, or the sterile dry powder with sodium chloride formulation of CYTOXAN (cyclophosphamide) for Injection, 500 mg/vial, 1 g/vial, and 2 g/vial, were withdrawn for reasons of safety or effectiveness. We have carefully reviewed our files for records concerning the withdrawal of the sterile dry powder excipient-free formulation of CYTOXAN (cyclophosphamide) for Injection, 500 mg/vial, 1 g/vial, and 2 g/vial, and the sterile dry powder with sodium chloride formulation of CYTOXAN (cyclophosphamide) for Injection, 500 mg/vial, 1 g/vial, and 2 g/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 drug products were withdrawn from sale for reasons of safety or effectiveness.

Accordingly, the Agency has determined that the sterile dry powder excipient-free formulation of CYTOXAN (cyclophosphamide) for Injection, 500 mg/vial, 1 g/vial, and 2 g/vial, and the sterile dry powder with sodium chloride formulation of CYTOXAN (cyclophosphamide) for Injection, 500 mg/vial, 1 g/vial, and 2 g/vial, drug products have been discontinued from marketing for reasons other than safety or effectiveness. FDA will not begin procedures to withdraw approval of approved ANDAs that have the sterile dry powder excipient-free formulation or the sterile dry powder with sodium chloride formulation. ANDAs that refer to CYTOXAN (cyclophosphamide) for Injection, 500 mg/vial, 1 g/vial, and 2 g/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: October 5, 2023.

Lauren K. Roth,

Associate Commissioner for Policy.

[FR Doc. 2023–22494 Filed 10–11–23; 8:45 am]

BILLING CODE 4164–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2023–N–2030]

Agency Information Collection Activities; Submission for Office of Management and Budget Review; Comment Request; Allegations of Regulatory Misconduct Voluntarily Submitted to the Center for Devices and Radiological Health

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA or we) is announcing that a proposed collection of information has been submitted to the Office of Management and Budget (OMB) for review and clearance under the Paperwork Reduction Act of 1995.

DATES: Submit written comments (including recommendations) on the collection of information by November 13, 2023.

ADDRESSES: To ensure that comments on the information collection are received, OMB recommends that written comments be submitted to *https://www.reginfo.gov/public/do/PRAMain.* Find this particular information collection by selecting ''Currently under Review—Open for Public Comments'' or by using the search function. The OMB control number for this information collection is 0910–0769. Also include the FDA docket number found in brackets in the heading of this document.

FOR FURTHER INFORMATION CONTACT: Domini Bean, Office of Operations, Food and Drug Administration, Three White Flint North, 10A–12M, 11601 Landsdown St., North Bethesda, MD 20852, 301–796–5733, *PRAStaff@fda.hhs.gov.*

SUPPLEMENTARY INFORMATION: In compliance with 44 U.S.C. 3507, FDA has submitted the following proposed collection of information to OMB for review and clearance.

Allegations of Regulatory Misconduct Voluntarily Submitted to the Center for Devices and Radiological Health

OMB Control Number 0910–0769—Extension

This information collection supports the voluntary submission of allegations of regulatory misconduct to FDA's Center for Devices and Radiological Health (CDRH). An allegation of regulatory misconduct is a claim that a medical device manufacturer or individuals marketing medical devices or electronic products regulated by CDRH may be doing so in a manner that violates the law. Reporting these allegations can help make FDA aware of regulatory concerns it may not learn of otherwise. This information can help FDA identify the potential risks to patients and determine whether further investigation is warranted, as well as any steps needed to address or correct a potential violation. Anyone may file a complaint reporting an allegation of regulatory misconduct. FDA encourages people submitting allegations to include supporting information and contact information in case additional information is needed for FDA to understand the allegation and act on the report; however, you can choose to submit a report anonymously. FDA will not share your identity or contact information with anyone outside FDA unless required to do so by law, regulation, or court order.

Allegations of regulatory misconduct may include failure to register and list a medical device, marketing uncleared or unapproved products, failure to follow quality system requirements, or misleading promotion.

You can submit an allegation through the Allegations of Regulatory Misconduct Form (*https://www.fda.gov/medical-devices/reporting-allegations-regulatory-misconduct/allegations-regulatory-misconduct-form*), by email, or by regular mail.