U.S. FOOD & DRUG ADMINISTRATION

CERTIFIED MAIL-RETURN RECEIPT REQUESTED

Bristol Myers Squibb Company
Attention: Annie Sturgess, Ph.D.
Vice President, Global Regulatory Sciences-CMC
86 Morris Avenue
Summit, NJ 07901
USA

February 2, 2022

Dear Sir/Madam:

This letter is being sent under Section 506C(f) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) for the reasons set forth below.

Section 506C of the FD&C Act requires a manufacturer of a drug product that is "life-supporting, life-sustaining, or intended for use in the prevention or treatment of a debilitating disease or condition" to notify the Food and Drug Administration (FDA or the Agency) of: (1) a permanent discontinuance in the manufacture of the drug; or (2) an interruption of the manufacture of the drug that is likely to lead to a meaningful disruption[1] in the supply of that drug in the United States; and (3) the reason(s) for such discontinuance or interruption of manufacturing (section 506C(a) of the FD&C Act). The notification must be submitted at least 6 months prior to the date of the discontinuance or interruption of manufacturing, or as soon as practicable thereafter, but in no case later than 5 business days after the permanent discontinuance or interruption in manufacturing occurs (section 506C(b) of the FD&C Act; 21 CFR 314.81(b)(3)(iii)(b)(2)). Compliance with this notification requirement is essential to facilitating the mitigation and/or prevention of a shortage or potential shortage, and ultimately may ensure availability of critical drugs for patients.

If a person fails to submit this required notification within the required timeframe, FDA must issue a letter to that person informing the person of the failure to comply with the FD&C Act (section 506C(f) of the FD&C Act).

Paclitaxel protein-bound particles for injectable suspension (albumin-bound), 100 mg/vial (marketed under the tradename Abraxane), is a product that is "life-supporting, life-sustaining, or intended for use in the prevention or treatment of a debilitating disease or condition." This product has approved indications for: 1) the treatment of breast cancer after failure of combination chemotherapy for metastatic disease or relapse within 6 months of adjuvant chemotherapy. Prior therapy should have included an anthracycline unless clinically contraindicated, 2) the first-line treatment of locally advanced or metastatic non-small cell lung cancer, in combination with carboplatin, in patients who are not candidates for curative surgery or radiation therapy, and 3) the first-line treatment of patients with metastatic adenocarcinoma of the pancreas, in combination with gemcitabine.

[1] Section 506C(h)(3) of the FD&C Act defines "meaningful disruption" to mean "a change in production that is reasonably likely to lead to a reduction in the supply of a drug by a manufacturer that is more than negligible and affects the ability of the manufacturer to fill orders or meet expected demand for its product," and "does not include interruptions in manufacturing due to matters such as routine maintenance or insignificant changes in manufacturing so long as the manufacturer expects to resume operations in a short period of time." Section 506C(h)(3).

It is our understanding that sometime during April 2021, there was an interruption in the manufacture of paclitaxel protein-bound particles for injectable suspension (albumin-bound). This interruption was likely to lead to a meaningful disruption in the supply of this drug product in the United States. The Agency learned of the interruption on June 18, 2021, after FDA contacted Bristol Myers Squibb Company (BMS) about the supply of their paclitaxel product. Since that time, BMS communicated their mitigation efforts and assurances of continued supply to FDA. However, the Agency learned of insufficient supply from outside stakeholders in late September 2021, and paclitaxel protein-bound particles for injectable suspension (albumin-bound) was determined to be in shortage soon thereafter, on October 5, 2021. Our records indicate that BMS did not notify FDA of the interruption in manufacture of this product prior to FDA's outreach. Accordingly, we are issuing you this letter to notify you of your noncompliance with the FD&C Act.

No later than thirty calendar days after the issuance of this letter, you must submit to the Agency a written response setting forth the basis for noncompliance with section 506C of the FD&C Act and providing the required notification, including the reason(s) for the interruption in manufacturing that led to a disruption in the supply of paclitaxel protein-bound particles for injectable suspension (albumin-bound) in April 2021 (section 506C(f)(2) of the FD&C Act).

No later than forty-five calendar days after the issuance of this letter, FDA will make this letter and your response to the letter available to the public on FDA's Drug Shortage website, unless the Agency determines that this letter was issued in error, or, after review of your response, determines that there was a reasonable basis for noncompliance (section 506C(f)(3) of the FD&C Act). In posting the letter and your response on the Drug Shortage website, FDA would protect confidential commercial information and trade secrets, if any, as required by applicable law.

If you have further questions, please contact the Drug Shortage Staff at (240) 402-7770.

Please submit all communications regarding this drug product to the following address. Please also send electronic copies to: drugshortages@fda.hhs.gov.

Drug Shortage Staff
Food and Drug Administration
WO 22, Room 6204
10903 New Hampshire Avenue
Silver Spring, MD 20993

Sincerely,

CAPT Valerie Jensen, R.Ph., USPHS (Ret.)
Associate Director
Drug Shortage Staff
Center for Drug Evaluation and Research