CERTIFIED MAIL-RETURN RECEIPT REQUESTED

Padagis US LLC December 6, 2023
Attention: Katie Jirik
Regulatory Affairs Manager, Regulatory Affairs
3940 Quebec Avenue North, Minneapolis, MN 55427

Dear 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).

Cyclosporine Injection, USP, 250 mg/5 mL (50 mg/mL), 5 mL Ampule, 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 is indicated for the prophylaxis of organ rejection in kidney, liver, and heart allogeneic transplants. The drug may also be used in the treatment of chronic rejection in patients previously treated with other immunosuppressive agents.

It is our understanding that in July 2023, Padagis US LLC (Padagis) permanently discontinued the manufacture of

[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."

Cyclosporine Injection. The Agency learned of concerns about availability from outside stakeholders in September 2023. Subsequently, FDA contacted Padagis about its supply of Cyclosporine Injection, and on September 21, 2023, Padagis informed FDA that the product had been permanently discontinued. Our records indicate that Padagis did not notify FDA of the permanent discontinuance 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 permanent discontinuance in manufacture of Cyclosporine Injection in July 2023 (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,

Valerie Jensen

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