04 January 2024

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

Subject: Response to FDA Letter of Non-Compliance
ANDA 065151; Cyclosporine Injection, USP 50 mg/mL

Dear Sir or Madam:

Padagis US LLC (Padagis) is hereby providing this letter in response to the FDA letter dated 06 December 2023, which FDA sent under 506C(f) of the Federal Food, Drug, and Cosmetic Act concerning the discontinuance of Cyclosporine Injection USP, 250 mg/mL; ANDA 065151, NDC 00574-0866-10.

Specifically, the FDA letter stated, "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 Cyclosporine Injection. The Agency learned of concerns about availability from outside stakeholders in September 2023. Subsequently, FDA contracted 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."

Chronology of Events

Padagis acquired ANDA 065151 from American Regent, the previous ANDA owner, in 2020. The approved manufacturing site at the time of purchase was Jubilant HollisterStier General Partnership (JHS). All testing required for release of the product was performed by JHS with the exception of testing of related substances, which at the time of purchase was performed by American Regent. Following purchase of the ANDA and a transition period, American Regent's support for the product ceased. Consequently, Padagis submitted a supplement on August 8, 2022 to request approval of testing of related substances by JHS. Absent approval of a supplement adding a new, qualified related substances testing facility, Padagis is unable to release product to the market. During the pendency of review of the submitted supplement, Padagis formally sent out product discontinuation announcements to customers on July 20, 2023 to put them on notice of the

potential supply disruption. In an oversight, Padagis failed to notify FDA of the product discontinuation. Ultimately, the supplement was not approved and was withdrawn on September 20, 2023. Padagis is yet to identify a suitable facility for related substances testing.

To ensure future compliance to notify the FDA of discontinuation of any product under 506C of the FD&C Act, Padagis is comprehensively reviewing our procedures to identify supply interruptions/discontinuations and communicate such interruptions/discontinuations for drug products determined to be medically necessary, as defined within Section 506C of the FD&C Act.

If you have any questions or need additional information regarding this response, please contact me via phone at 763-732-0402 or via email at regulatoryaffairs.usa@padagis.com.

Sincerely,

Padagis US LLC
Briana Hedtke
Senior Manager Regulatory Affairs