PAR
PHARMACEUTICAL
an endo international company

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May 19, 2016

VIA EMAIL AND FED EX

Captain Valerie Jensen
Associate Director
Drug Shortage Staff
Food and Drug Administration
WO 22, Room 6204
10903 New Hampshire Avenue
Silver Spring, MD 20993

Re: Response to FDA Letter dated April 19, 2016, Regarding Noncompliance with Section 506C of the Federal Food, Drug and Cosmetic Act

Dear Captain Jensen:

This letter is in response to FDA's letter dated April 19, 2016, regarding noncompliance with Section 506C of the Federal Food, Drug and Cosmetic Act. Par Pharmaceutical ("Par") recognizes its obligations as a pharmaceutical manufacturer and is committed to being in full compliance with all applicable regulatory requirements, including Section 506C of the Food Drug and Cosmetic Act.

We acknowledge that Par Pharmaceutical was not aware that the interruption in the manufacture of Tretinoin Capsules by [redacted] (b) (4) on November 13, 2015 would lead to a potential product shortage. As a result of the subsequent ambiguity in the availability of product from [redacted] (b) (4) and the expected availability of product from the other approved manufacturer, Teva Pharmaceuticals, Par did not notify FDA of the interruption in [redacted] (b) (4) s manufacturing within FDA's required timeframe.

There are a number of factors that contributed to the ambiguity regarding product supply and to the delay in Par Pharmaceutical informing FDA of this manufacturing interruption within the required timeframe. Par has subsequently identified and is correcting the elements within our current system to prevent recurrence of any future delay in reporting manufacturing interruptions for medically necessary products.

Based on the November 13, 2015 action by the French regulatory authority, l'Agencie National de Securite du Medicament et des produits de sante ("ANSM"), to suspend [redacted] (b) (4) s manufacturing operations at their [redacted] (b) (4) facility, Par took the following actions:

- Upon notification of the potential for foreign capsule intermingling in [redacted] (b) (4) capsule products, Par reviewed all lots of Tretinoin Capsules in distribution and determined that the product currently in the market was not impacted.
- There was one lot of Tretinoin Capsules in process at the time of the manufacturing interruption notification. Par instructed [redacted] (b) (4) that the product would remain in quarantine until remedial actions were taken.
- Par was aware that [redacted] (b) (4) was responding to their Regulatory issues. Remediation by [redacted] (b) (4) included the addition of cameras and multiple procedural changes to prevent and detect any malicious acts of contamination.
- Par Pharmaceutical did not know the time frame required for [redacted] (b) (4) to investigate and resolve the open issues nor, at the time, did Par fully appreciate the potential impact on the market of the manufacturing interruption.

Other factors also contributed to the ambiguity regarding Tretinoin product supply, including:

- Teva is another active company in the Tretinoin Capsules market. Par did not know, and had no means of knowing, that Teva had an issue with their API supplier.
- Based on Par's distribution data filed with FDA in Annual Reports, the sale of Tretinoin Capsules is very small. Par has distributed approximately [redacted] (b) (4) bottles of 100 capsules in 2014 and [redacted] (b) (4) bottles of 100 capsules in 2015. As of Q4 2015, Par and Teva had [redacted] (b) (4) % and [redacted] (b) (4) % market share, respectively. In light of Par's situation with the CMO, it was reasonable to expect that Teva would be able to fully supply market demand for the product.
- On February 17, 2016, the Drug Shortage Staff contacted Par inquiring about a drug shortage for Tretinoin Capsules.
- Over the course of February and March 2016, Par worked with Drug Shortage Staff to release the lot that was on hold (in quarantine) to relieve the reported drug shortage, as it was uncertain when a new supply would come from [redacted] (b) (4) Lot 49816M13 was released to the market on March 10, 2016 with a Dear Healthcare Provider letter to alert the Healthcare Providers that the content of all Par's Tretinoin Capsules bottles must be verified prior to dispensing. Teva's drug shortage notification was posted on the FDA's website on March 11, 2016, one day after Par's. Proposals were made to ANSM to manufacture medically necessary drugs under protocol by [redacted] (b) (4) and the application holders. Par signed a protocol requesting manufacture of Tretinoin Capsules for medically necessary products in the US that was submitted to the ANSM on March 11, 2016.

- On March 30, 2016 (b) (4) notified Par that ANSM granted approval on March 29, 2016 for manufacturing of Tretinoin Capsules to restart at the (b) (4) site under protocol.

As a result of Par's increased awareness of the potential frailty of the supply chain for medically necessary products, Par commits to implementing a formal mechanism to identify and communicate future supply interruptions for drug products determined to be medically necessary, as defined within Section 506C of the FD&C Act.

Par believes we have acted diligently with FDA and our external manufacturer to remedy the immediate drug shortage scenario with respect to Tretinoin Capsules. Par commits to take the necessary corrective and preventative actions to assure against future recurrence.

If you have any questions or need any additional information, please do not hesitate to contact me at (845) 364-4800 or William.McIntyre@parpharm.com. I will also contact you by telephone to assure that this submission complies with your expectations.

Sincerely,

William R. McIntyre, Ph.D.
Senior Vice President of Regulatory Affairs
Par Pharmaceutical

cc: Kevin Charrier
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