December 18, 2018

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

FDA DRUG SHORTAGE RESPONSE

ANDA # 074529
Toposar® (Etoposide Injection USP 20mg/mL)

Dear FDA Drug Shortage Staff:

Teva Pharmaceuticals USA, Inc. is hereby providing this letter in response to the Food and Drug Administration (FDA) letter received on October 31, 2018, dated September 18, 2018 sent under Section 506C (f) of the Federal Food, Drug, and Cosmetic Act concerning the failure to notify FDA of interruption in manufacturing of Etoposide Inection (b)(4)mg (ANDA 074529).

Teva would like to provide the Agency with a chronology of events concerning the reason for the interruption in manufacturing of this product along with the communication shared with the Agency.

On October 27, 2017, Teva inventory was below safety stock levels for Toposar® Injection on two out of the three presentations; Toposar® Injection 20mg/mL 1x25mL and Toposar® Injection 20mg/mL 1x50mL while maintaining sufficient quantities of Toposar® Injection 20mg/mL 1x5mL. New production was being planned when the active pharmaceutical ingredient (API) manufacturer experienced problems supplying their material. The API manufacturer subsequently commenced the allocation of open orders. This issue resulted in delays in our scheduled production which in turn caused a backorder by November of 2017 for the 20mg/mL 1x25mL and 20mg/mL 1x50mL presentations. Throughout the process Teva worked closely with the API manufacturer who committed to delivering additional supply of the API. By December 27, 2017 the inventory of Toposar® 20mg/mL 1x5mL presentation had also dropped below safety stock and on January 2, 2018 Teva notified FDA Drug Shortage via NextGen. On the same day FDA contacted Teva and we confirmed the drug shortage was expected to last until the first quarter of 2018.

The expectation was that the API manufacturer would deliver the API and it was not expected that our temporary backorder would create a market drug shortage. Upon realizing that we would not have sufficient product to supply the demand Teva notified FDA within 3 business days. It is our understanding that this drug shortage was also attributed and further exasperated by other approved manufacturers who also were experiencing difficulty in manufacturing and supplying the commercial market.

On February 26, 2018, FDA contacted Teva to inquire about supply. Teva informed the Agency that product was back in inventory and as long as the API supplier continues to supply without interruption there should be no impact to the Teva product supply to the market. On April 4, 2018 Teva notified FDA of limited quantities and product being allocated due to API shortage. Periodic backorders of Toposar were anticipated until the API requirements could be fully obtained. On October 26, 2018 Teva informed FDA that as of October 25, 2018 all of the presentations of the product were available.

Teva is committed to the needs of our patients and we are committed to working diligently to assure supplying the commercial market with Toposar and all medically necessary products.

We hope this written response appropriately satisfies the Agency 's request of noncompliance for the interruption in manufacturing that led to an unforeseeable disruption in the supply of Toposar® Injectable in 2017.

This letter may contain trade secrets and confidential commercial information (collectively, the "Protected Information"). We request that the Protected Information not be disclosed outside of the Government pursuant to FOIA Exemption 4 (5 U.S .C. section 552(b)(4)) and 18 U.S.C. section 1905.

D R. Bonilla 18 Dec 2018

David R. Bonilla
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Teva Pharmaceuticals