April 30, 2019

Division of Dockets Management
Food and Drug Administration
Department of Health and Human Services
5630 Fishers Lane, Room 1061 (HFA-305)
Rockville, MD 20852

Citizen Petition

Dear Sir/ Madam,

The undersigned, Encube Ethicals Private Limited (Encube), respectfully submits this petition pursuant to the Federal Food, Drug and Cosmetic Act ("FDC Act") and in accordance with 21 C.F.R. §§ 10.25(a) and 10.30 to request the commissioner of Food and Drugs to take action with respect to Reference Standard designation for Fluorouracil Topical Solution, 5%.

The Reference Listed Drug (RLD) and Reference Standard (RS) for Fluorouracil Topical Solution, 5% designated in the Approved Drug Product with Therapeutic Equivalence Evaluations (the Orange Book) is EFUDEX (Fluorouracil Solution) 5%, approved by the FDA under NDA # N016831. For the purposes of development of the generic version of this product, Encube Ethicals Private Limited (Encube) has attempted to source samples of EFUDEX (Fluorouracil Solution) 5%, manufactured by Valeant Pharmaceuticals International and has been informed that the no multiple batches and sufficient quantities can be obtained for in vivo bioequivalence clinical endpoint study. Further, the product had been on a long-term manufacturer's backorder with no anticipated availability.

A. Action Requested

In order to proceed with its generic development, the undersigned respectfully requests that FDA to designate Fluorouracil Topical Solution, 5% manufactured by Taro Pharmaceutical Industries Ltd. and approved by the FDA under ANDA # A076526, as the Reference Standard for this product.

B. Statement of Grounds

The FD&C Act and FDA's regulations require an ANDA applicant to refer in its ANDA to the specific listed drug on which the applicant relies in seeking approval of its ANDA. This drug is Reference Listed Drug (RLD). FDA identifies products designated as RLDs in the Orange Book. FDA also selects a drug product, which should be used for demonstration of in vivo bioequivalence by an applicant seeking ANDA approval. These products are identified in the Orange Book as Reference Standards (RS). In the case of EFUDEX (Fluorouracil Solution) 5%, manufactured by Valeant Pharmaceuticals International and approved under NDA # N016831, has been designated as both the RLD and RS (relevant section of the Orange Book is attached). For the purposes of

development of the generic version of this product, Encube Ethicals Private Limited (Encube) has attempted to procure samples of EFUDEX (Fluorouracil Solution) 5% from multiple sources in the U.S.A, and has been informed that the product had no multiple batches and sufficient quantities can be obtained for in vivo bioequivalence clinical end point study and product had been on a long-term manufacturer's backorder with no anticipated availability. In order to proceed with its generic development, Encube respectfully requests that another new Reference Standard, available on the U.S. market, be selected by the FDA i.e. Fluorouracil Topical Solution, 5% manufactured by Taro Pharmaceutical Industries Ltd. and approved by the FDA under ANDA # A076526.

C. Environmental Impact

An environmental assessment report on the action requested in this petition is not required under 21 C.F.R. § 25.31.

D. Economic Impact

In accordance with 21 C.F.R. § 10.30(b), economic impact information is to be submitted only when requested by the Commissioner following review of the petition. The Petitioner hereby commits to promptly provide this information, if so requested.

E. Certification

The undersigned certifies that, to the best knowledge and belief of the undersigned, this petition includes all information and views on which the petition relies, and that it includes representative data and information known to the petitioner which is unfavorable to the petition.

Sincerely,

Jayant Muley
Digitally signed by Jayant Muley
Date: 2019.04.30 14:35:58 +05'30'

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