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By Electronic Delivery

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

Citizen Petition

Dear Sir/ Madam,

The undersigned hereby submits this Citizen Petition under Section 505(j) of the Federal Food, Drug, and Cosmetic Act and in accordance with 21 CFR 10.25(a), 10.30, to request that the Food and Drug Administration (FDA) **designate a suitable alternative reference standard (RS)** for Ropinirole Hydrochloride Extended Release Tablets in response to the unavailability of the existing RS in the market.

A. Action Requested

The undersigned requests that FDA designate a suitable alternative RS from the listed drugs in the *Approved Drug Products with Therapeutic Equivalence Evaluations* (The Orange Book) for Ropinirole Hydrochloride Extended-Release Tablets, for purpose of conducting bioequivalence studies to support a post-approval Supplement for ANDA 091395 (Ropinirole Hydrochloride Extended Release Tablets, 2 mg, 4 mg, 6 mg, 8 mg and 12 mg).

B. Statement of Grounds

In order to obtain ANDA approval, an applicant must first identify reference listed drug (RLD) and/or RS which he/she seeks to duplicate and must demonstrate, among others, that the proposed generic drug product is bioequivalent to the RLD/RS.

Ropinirole Hydrochloride Extended-Release Tablets listed in the Orange Book are shown in Appendix 1. The Orange Book currently lists GlaxoSmithKline LLC's Requip XL (NDA 022008) as a RLD and Requip XL 2 mg as a RS.

However, though not marked as discontinued on the list, the RS seems to be no longer available for sale, based on the following observations:

i. Three different US-based pharmacies confirmed 2 mg strength cannot be supplied due to unavailability. (Appendix 2)
ii. Requip XL labeling on DailyMed states that Marketing End Date of 2 mg strength is September 30, 2019. (Appendix 3)
iii. When searched for NDA number (i.e., 022008), National Drug Code (NDC) for 2 mg strength is not available on NDC Directory, while NDC of the other four strengths are shown. (Appendix 4)
iv. IQVIA data reveals that the RS was not marketed in the US in 4Q 2019 (Appendix 5).

Such shortage of RS prevents the ANDA holder from performing *in vivo* bioequivalence studies which is required for a post-approval Supplement for certain level 3 changes as per the guidance for industry on *SUPAC-MR: Modified Release Solid Oral Dosage Forms Scale-Up and Postapproval Changes: Chemistry, Manufacturing, and Controls; In Vitro Dissolution Testing and In Vivo Bioequivalence Documentation* (September 1997).

Hence, Citizen Petition is hereby filed as per Section III.C.2 and III.C.3 of draft guidance for industry on *Referencing Approved Drug Products in ANDA Submissions* (January 2017) which states that:

"FDA also will consider selecting a new reference standard when the Agency determines that the quantity of the current reference standard in distribution is so limited that a potential ANDA applicant is not able to obtain a sufficient quantity for in vivo bioequivalence testing (even if the current reference standard is not in the Discontinued Section of the Orange Book)."

"If there is a reference standard in the Active Section of the Orange Book but there are limited or no quantities of the reference standard in distribution, or a potential ANDA applicant believes a reference standard other than the one selected by FDA is appropriate, then the potential applicant may submit a citizen petition under 21 CFR 10.25(a) and 10.30 to request that FDA select that different listed drug also as a reference standard."

Section III.C.2 of the aforementioned draft guidance for industry also states that:

"When selecting a new reference standard, FDA generally selects a drug product that is therapeutically equivalent to the discontinued RLD and is the market leader based on units sold."

Please be advised that according to the IQVIA database (provided in Appendix 5), Dr. Reddy's Laboratories Ltd's generic drug product (ANDA 201576) appears to be the market leader in terms of units sold in the year of 2019, hence an eligible RS candidate.

In consideration of the above, the petitioner respectfully requests that FDA designate "Ropinirole Hydrochloride Extended Release Tablets, 2 mg, ANDA 201576 held by Dr. Reddy's Laboratories Ltd" as a RS, as FDC Act § 505(j) allows the marketing of generic versions of previously approved drug products when the generic drug product is the subject of an ANDA.

C. Environmental Impact

A claim for categorical exclusion of the requirements for an environmental assessment is made pursuant to 21 CFR 25.31(a) and 25.15(d).

D. Economic Impact Statement

Pursuant to 21 CFR 10.30(b), an economic impact analysis will be provided upon request.

E. Certification

The undersigned certifies that, to the best of 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 this petition.

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Sincerely,

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