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BY ELECTRONIC SUBMISSION

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

The undersigned ("Petitioner") submits this Citizen 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 with regard to the FDA-designated Reference Standard ("RS") for Carbidopa and Levodopa Tablets, 25 mg/250 mg. The current RS, approved under New Drug Application ("NDA") 017555, is commercially unavailable. For this reason, Petitioner requests that the Food and Drug Administration ("FDA") take action to maintain a pathway for ANDA submissions for Carbidopa and Levodopa Tablets, 25 mg/250 mg, 25 mg/100 mg, and 10 mg/100 mg. Specifically, Petitioner requests that FDA designate an additional (or new) RS for Carbidopa and Levodopa Tablets and amend the *Approved Drug Products with Therapeutic Equivalence Evaluations* ("Orange Book") to reflect ANDA 074260 (and specifically the 25 mg/250 mg strength) as a RS for the drug.

I. ACTION REQUESTED

Petitioner requests that FDA designate ANDA 074260 (Carbidopa and Levodopa Tablets, 25 mg/250 mg) held by Actavis Elizabeth LLC ("Actavis") (or another appropriate ANDA) as a RS for purposes of FDA evaluation of ANDAs for Carbidopa and Levodopa Tablets, 25 mg/250 mg, 25 mg/100 mg, and 10 mg/100 mg.

II. STATEMENT OF GROUNDS

FDC Act § 505(j) allows the marketing of generic versions of previously approved drug products based on FDA approval of an ANDA. To obtain ANDA approval, the applicant must show, among other things, that with respect to a listed drug (i.e., a previously approved drug product), the generic drug product has the same active ingredient(s) in the

same strength, dosage form and route of administration, has essentially identical labeling, and is bioequivalent.

A "listed drug" includes a new drug product that has an effective approval under FDC Act § 505(j), that has not been withdrawn or suspended under FDC Act §§ 505(e)(1) through (5) or (j)(5), and that has not been withdrawn from sale for reasons of safety or effectiveness. See 21 C.F.R. § 314.3. Listed drugs are identified in FDA's Orange Book. An RLD is the listed drug identified by FDA as the drug product on which an ANDA applicant should rely in seeking approval of an application. The product designated by FDA as the "reference standard," in the Orange Book, must be used to conduct the in vivo bioequivalence testing required for FDA approval. However, where there is a "limited or no quantities of the reference standard in distribution" a potential ANDA applicant may request designation of a new RS through the submission of a citizen petition. FDA, *Draft Guidance for Industry, Referencing Approved Drug Products in ANDA Submissions*, at 9 (Jan. 2017).

Despite diligent efforts to obtain sufficient quantities of the current RS—Sinemet (carbidopa and levodopa tablets, 25 mg/250 mg) approved under NDA 017555—the drug product is not commercially available. Sinemet appears to be on back order and cannot be obtained to conduct studies to establish bioequivalence. As such, Sinemet is shielded from additional generic competition.

There is a sound basis for selecting one of the ANDAs—and preferably ANDA 074260—listed in the Orange Book (below) as a new RS: Carbidopa and Levodopa Tablets 25 mg/250 mg, held by Actavis, appears to lead the U.S. market in terms of number of tablets sold (as per IMS data), and should therefore be more readily accessible and more appropriate for RS designation.

TABLET;ORAL						
CARBIDOPA AND LEVODOPA						
AB		ACTAVIS ELIZABETH	10MG;100MG	A074260	001	Sep 03, 1993
AB			25MG;100MG	A074260	002	Sep 03, 1993
AB			25MG;250MG	A074260	003	Sep 03, 1993
AB		APOTEX INC	10MG;100MG	A077120	001	Jun 02, 2008
AB			25MG;100MG	A077120	002	Jun 02, 2008
AB			25MG;250MG	A077120	003	Jun 02, 2008
AB		MAYNE PHARMA	10MG;100MG	A073618	001	Aug 28, 1992
AB			25MG;100MG	A073589	001	Aug 28, 1992
AB			25MG;250MG	A073607	001	Aug 28, 1992
AB		MYLAN	10MG;100MG	A090324	001	Sep 28, 2009
AB			25MG;100MG	A090324	002	Sep 28, 2009
AB			25MG;250MG	A090324	003	Sep 28, 2009
AB		SUN PHARM INDS	10MG;100MG	A078536	001	Oct 28, 2008
AB			25MG;100MG	A078536	002	Oct 28, 2008
AB			25MG;250MG	A078536	003	Oct 28, 2008
SINEMET						
AB	+	MERCK SHARP DOHME	10MG;100MG	N017555	001	
AB	+		25MG;100MG	N017555	003	
AB	+!		25MG;250MG	N017555	002	

Accordingly, the undersigned requests that FDA designate in the Orange Book Carbidopa and Levodopa Tablets, 25 mg/250 mg, approved under one of the above-cited ANDAs (and, in particular, ANDA 074260) as a new RS.

III. ENVIRONMENTAL IMPACT

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

IV. 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. Petitioner hereby commits to promptly provide this information, if so requested.

V. CERTIFICATION

Petitioner certifies that, to the best knowledge and belief of Petitioner, 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,

Kurt R. Karst

KRK/eam