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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 Guanfacine Hydrochloride Tablets, Eq 1mg base and Eq 2mg base. The current RS, approved under Abbreviated New Drug Application ("ANDA") 074796, is commercially unavailable. For this reason, Petitioner requests that the Food and Drug Administration ("FDA") take action to maintain a pathway for ANDA submissions. Petitioner requests that FDA designate an additional (or new) RS for Guanfacine Hydrochloride Tablets, Eq 1mg base and Eq 2mg base, and amend the *Approved Drug Products with Therapeutic Equivalence Evaluations* ("Orange Book") to reflect ANDA 075109 as a RS for the drug.

## I. ACTION REQUESTED

Petitioner requests that FDA designate ANDA 075109 (Guanfacine Hydrochloride Tablets, Eq 1mg base and Eq 2mg base) as a RS for purposes of FDA evaluation of ANDAs for Guanfacine Hydrochloride Tablets, Eq 1mg base and Eq 2mg base.

## 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A "listed drug" includes a new drug product that has an effective approval under FDC Act § 505(j), that has not been withdrawn or suspended under FDC Act §§ 505(e)(1) through (5) or (j)(5), and that has not been withdrawn from sale for reasons of safety or effectiveness.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 present RS—Guanfacine Hydrochloride Tablets, Eq 1mg base and Eq 2mg base (ANDA 074796)—which was designated as such in June 2018 after the brand-name RLD was discontinued from marketing, the drug product is not commercially available and appears to have been discontinued from marketing. As such, Guanfacine Hydrochloride Tablets, Eq 1mg base and Eq 2mg base, is shielded from additional generic competition.

There is a sound basis for selecting an ANDA other than ANDA 074796—and preferably ANDA 075109—as a new RS. Guanfacine Hydrochloride Tablets, Eq 1mg base and Eq 2mg base, held by Amneal Pharmaceuticals Inc. (ANDA 075109), appears to lead the U.S. market in terms of the number of tablets sold (as per IMS data), and should therefore be more readily accessible and more appropriate for RS designation.

In an effort to introduce further competition, FDA should designate one of the following ANDAs (other than ANDA 074796) listed in the Orange Book as the new (or an additional) RS for Guanfacine Hydrochloride Tablets, Eq 1mg base and Eq 2mg base, and preferably ANDA 075109.

| Mkt.Status | Active Ingredient | Proprietary Name | Appl No | Dosage Form | Route | Strength | TE Code | RLD | RS | Applicant Holder |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | |
| RX | GUANFACINE HYDROCHLORIDE | GUANFACINE HYDROCHLORIDE | A075109 | TABLET | ORAL | EQ 1MG BASE | AB | | | AMNEAL PHARMACEUTICAL |
| RX | GUANFACINE HYDROCHLORIDE | GUANFACINE HYDROCHLORIDE | A074673 | TABLET | ORAL | EQ 1MG BASE | AB | | | EPIC PHARMA LLC |
| RX | GUANFACINE HYDROCHLORIDE | GUANFACINE HYDROCHLORIDE | A074796 | TABLET | ORAL | EQ 1MG BASE | AB | | RS | MYLAN PHARMACEUTICALS INC |
| RX | GUANFACINE HYDROCHLORIDE | GUANFACINE HYDROCHLORIDE | A074145 | TABLET | ORAL | EQ 1MG BASE | AB | | | WATSON LABORATORIES INC |
| RX | GUANFACINE HYDROCHLORIDE | GUANFACINE HYDROCHLORIDE | A075109 | TABLET | ORAL | EQ 2MG BASE | AB | | | AMNEAL PHARMACEUTICAL |
| RX | GUANFACINE HYDROCHLORIDE | GUANFACINE HYDROCHLORIDE | A074673 | TABLET | ORAL | EQ 2MG BASE | AB | | | EPIC PHARMA LLC |
| RX | GUANFACINE HYDROCHLORIDE | GUANFACINE HYDROCHLORIDE | A074796 | TABLET | ORAL | EQ 2MG BASE | AB | | RS | MYLAN PHARMACEUTICALS INC |
| RX | GUANFACINE HYDROCHLORIDE | GUANFACINE HYDROCHLORIDE | A074145 | TABLET | ORAL | EQ 2MG BASE | AB | | | WATSON LABORATORIES INC |

Accordingly, the undersigned requests that FDA designate in the Orange Book Guanfacine Hydrochloride Tablets, Eq 1mg base and Eq 2mg base, approved under one of the above-cited ANDAs (and, in particular, ANDA 075109) 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