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24 October 2019

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

CITIZEN PETITION

Dear Sir/Madam:

The undersigned submits this petition pursuant to the Federal Food, Drug, and Cosmetic Act and 21 CFR 10.30 requesting the Commissioner of the Food and Drug Administration to designate Fresenius Kabi USA, LLC's (FK USA) Glucagon for Injection approved under 505(b)(2) NDA 201849 as therapeutically equivalent with an 'AP' rating to the reference listed drug (RLD) GlucaGen®, NDA 020918, by Novo Nordisk.

A. Action Requested

The petitioner requests that the Commissioner of the Food and Drug Administration designate Glucagon for Injection, 1 mg per vial, manufactured by FK USA (NDA 201849), as a therapeutic equivalent, with an 'AP' rating, to the reference listed drug (RLD) GlucaGen®, NDA 020918, by Novo Nordisk.

B. Statement of Grounds

FK USA's Glucagon for Injection drug product (NDA 201849) is therapeutically and pharmaceutically equivalent to the Reference Listed Drug (RLD), GlucaGen®, NDA 020918, by Novo Nordisk, and is expected to have the same clinical effect and safety profile as the RLD. A side-by-side pharmaceutical comparison of FK USA's NDA 201849 and the RLD NDA 020918 is provided in **Table 1** for the reviewer's convenience.

Table 1 Side-by-Side Pharmaceutical Equivalence Comparison of FK USA NDA 201849 and the RLD NDA 020918

Attributes	FK USA NDA 201849	RLD NDA 020918	Comparison
Strength	1 mg per vial	1 mg per vial	same
Product presentation	Diagnostic Aid: single-dose vial of Glucagon for Injection	Diagnostic Aid: single dose vial of GlucaGen for injection	same
	Diagnostic Kit: 1 single-dose vial of Glucagon for Injection with 1 single-dose vial of Sterile Water for Injection, USP	Diagnostic Kit: 1 single-dose vial of GlucaGen for injection with 1 vial of Sterile Water for Reconstitution	same
	Glucagon Emergency Kit for Low Blood Sugar: 1 single-dose vial of Glucagon for Injection with 1 single-dose syringe of Sterile Water for Injection, USP for reconstitution	GlucaGen HypoKit: 1 single-dose vial of GlucaGen for injection with 1 disposable syringe of Sterile Water for Reconstitution	same
Route of Administration	Subcutaneous, intramuscular or intravenous	Subcutaneous, intramuscular or intravenous	same
Dosage Form	Lyophilized powder	Lyophilized powder	same
Active Ingredient (drug product)	Glucagon	Glucagon	same
Active Ingredient (diluent)	Sterile Water for Injection, USP	Sterile Water for Injection, USP	same
Excipients	Lactose Monohydrate Hydrochloric Acid Sodium Hydroxide	Lactose Monohydrate Hydrochloric Acid Sodium Hydroxide	same
Labeling Indications	Glucagon for Injection is indicated for • the treatment of severe hypoglycemia • use as a diagnostic aid for use during radiologic examinations to temporarily inhibit movement of the gastrointestinal tract.	GlucaGen is indicated for: • the treatment of severe hypoglycemia • use as a diagnostic aid for use during radiologic examinations to temporarily inhibit movement of the gastrointestinal tract.	same

The "Approved Drug Products with Therapeutic Equivalence Evaluations", ("The Orange Book"), defines pharmaceutically equivalent drug products as follows:

- as identical dosage forms and route(s) of administration that contain identical amounts of the identical active drug ingredient
- meet the identical compendial or other applicable standards of identity, strength, quality, and purity

The "Approved Drug Products with Therapeutic Equivalence Evaluations", ("The Orange Book"), defines therapeutically equivalent drug products as follows:

- are approved as safe and effective.
- contain identical amounts of the identical active drug ingredient in the identical dosage form and route of administration
- meet compendial or other applicable standards of strength, quality, purity and identity
- are bioequivalent
- are adequately labeled
- manufactured in compliance with cGMP

According to the Orange Book Preface to the 39th Edition, therapeutically equivalent drug products can differ in certain other characteristics, such as shape, scoring configuration, release mechanisms, packaging, excipients, expiration date/time, minor aspects of labeling and storage conditions.

Table 1 demonstrates that the FK USA and RLD drug products are the same. The FK USA drug product has the same active ingredients, conditions of use, dosage form, route of administration, strength and labeling as the RLD. Reference is also made to *Draft Guidance for Industry-ANDAs for Certain Highly Purified Synthetic Peptide Drug Products That Refer to Listed Drugs of rDNA Origin*. FK USA has successfully established the nonclinical bridge comparing the impurity levels of FK USA's synthetic Glucagon for Injection and the RLD's recombinant GlucaGen®. With the issuance of the guidance in October 2017, Fresenius Kabi would have pursued the ANDA filing pathway, which therefore would have automatically granted an "AP" therapeutic equivalency rating.

FK USA's Glucagon for Injection, 505(b)(2) NDA 201849, also relied, in part, on the RLD data and previously published literature for safety and efficacy.

Based on all the above-mentioned reasons, FK USA kindly requests the Agency to grant a therapeutic equivalence rating 'AP' for NDA 201849 Glucagon for Injection.

C. Environmental Impact

In accordance with the requirements set forth in 21 CFR 25.31, FK USA hereby requests a Categorical Exclusion from the requirements to prepare an Environmental Impact Assessment.

D. Economic Impact

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

E. Certification

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

Sincerely,

Nicole Chutipisalkul

Digitally signed by Nicole Chutipisalkul
DN: c=US, st=Illinois, l=Lake Zurich, o=Fresenius Netcare, ou=IT, cn=Nicole Chutipisalkul, email=Nicole.Chutipisalkul@fresenius-kabi.com
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