Fresenius Kabi USA, LLC

Three Corporate Drive
Lake Zurich, Illinois 60047
T 847-550-2300
T 888-391-6300
www.fresenius-kabi.us

CITIZEN PETITION
VIA ELECTRONIC SUBMISSION

03 March 2022

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

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) Neostigmine Methylsulfate Injection approved under 505(b)(2) NDA 203629 as therapeutically equivalent with an 'AB' rating to the reference listed drug (RLD) Bloxiverz®, NDA 204078, by Avadel Legacy Pharmaceuticals LLC.

A. Action Requested

The petitioner requests that the Commissioner of the Food and Drug Administration designate Neostigmine Injection, 0.5 and 1.0 mg/mL, manufactured by FK USA (NDA 203692), as a therapeutic equivalent, with an 'AB' rating, to the reference listed drug (RLD) Bloxiverz®, NDA 204078, by Avadel Legacy Pharmaceuticals LLC.

B. Statement of Grounds

FK USA's Neostigmine Methylsuflate Injection drug product (NDA 210326) is therapeutically and pharmaceutically equivalent to the Reference Listed Drug (RLD), Bloxiverz®, NDA 204078, by Avadel Legacy Pharmaceuticals LLC. , 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 203692 and the RLD NDA 204078 is provided in Table 1 for the reviewer's convenience.

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Table 1 Side-By-Side Pharmaceutical Equivalence Comparison of FK USA NDA 203629 and RLD (NDA 204078)

Attributes	**FK USA NDA 203629**	**RLD NDA 204078**	**Comparison**
Strengths	0.5 mg/mL and 1.0 mg/mL	0.5 mg/mL and 1.0 mg/mL	same
Route of administration	Intravenous	Intravenous	same
Dosage Form	Sterile liquid	Sterile liquid	same
Active Ingredient	Neostigmine Methylsulfate	Neostigmine Methylsulfate	same
Excipients present per mL of solution	phenol 4.5 mg (preservative) and sodium acetate trihydrate 0.2 mg, in water for injection. The pH is adjusted, when necessary, with acetic acid/sodium hydroxide to a value of 5.5.	phenol 4.5 mg (preservative) and sodium acetate trihydrate 0.2 mg, in water for injection. The pH is adjusted, when necessary, with acetic acid/sodium hydroxide to a value of 5.5.	equivalent
Labeling Indications	Neostigmine Methylsulfate Injection, a cholinesterase inhibitor, is indicated for reversal of the effects of nondepolarizing neuromuscular blocking agents (NMBA) after surgery.	BLOXIVERZ is a cholinesterase inhibitor indicated for the reversal of the effects of nondepolarizing neuromuscular blocking agents (NBMA) after surgery.	same

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

1. Contain identical amounts of the same active drug ingredient in the same dosage form and route of administration
2. Meet compendial or other applicable standards of strength, quality, purity and identity

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

1. Are approved as safe and effective.
2. Contain identical amounts of the same active drug ingredient in the same dosage form and route of administration
3. Meet compendial or other applicable standards of strength, quality, purity and identity
4. Are bioequivalent
5. Are adequately labeled
6. Were manufactured under 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 RLD and FK drug products are identical. They are identical in active ingredient, formulation, dosage form, route of administration and indication. Because these products are injectable, bioequivalency is self evident under 21 CFR 314.94. Additionally, both products are approved by FDA, hence meeting the requirements for applicable standards, adequate labeling and manufacturing under GMP.

Based on all the above mentioned reasons, FK USA kindly requests the Agency to grant a therapeutic equivalence rating 'AP' for NDA 203629, Neostigmine Methylsulfate 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

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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.

Respectfully submitted,

Molly Ventrelli

Digitally signed by Molly Ventrelli
DN: c=US, st=Illinois, l=Lake Zurich, o=Fresenius Netcare, ou=IT, cn=Molly Ventrelli, email=molly.ventrelli@fresenius-kabi.com
Date: 2022.03.03 11:12:32 -06'00'

Molly Ventrelli
Sr. VP Regulatory Affairs
Phone: 847-550-2014 ‖ Fax: 847-550-7121
E-mail: Molly.Ventrelli@fresenius-kabi.com