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Division of Dockets Management
U.S. Food and Drug Administration
Department of Health and Human Services
5630 Fishers Lane, Room 1061
Rockville, MD 20852

SUITABILITY PETITION

Dear Sir/Madam:

The undersigned, on behalf of a client and in response to a directive from the Office of Generic Drugs, submits this Suitability Petition pursuant to Section 505(j)(2)(C) of the Federal Food, Drug, and Cosmetic Act ("FDC Act") and in accordance with 21 C.F.R. § 314.93 and 21 C.F.R. §§ 10.20 and 10.30 to request that the Commissioner of the U.S. Food and Drug Administration ("FDA") declare that the following drug product is suitable for consideration in an Abbreviated New Drug Application ("ANDA") as a pharmacy bulk package (100 mL, 500 mL, 1L and 2L):

Ropivacaine Hydrochloride Injection, USP, 0.2% (2 mg/mL)
Ropivacaine Hydrochloride Injection, USP, 0.5% (5 mg/mL)
Ropivacaine Hydrochloride Injection, USP, 1% (10 mg/mL)

A. Action Requested

The Petitioner requests that FDA declare that a pharmacy bulk package (100 mL, 500 mL, 1L and 2L) Ropivacaine Hydrochloride Injection, USP, is suitable for submission as an ANDA. As designated in FDA's *Approved Drug Products with Therapeutic Equivalence Evaluations* ("Orange Book"), the Reference Listed Drug ("RLD") upon which this Petition is based is Naropin® (ropivacaine hydrochloride injection) 0.2% (2 mg/mL), 0.5% (5 mg/mL), 0.75% (7.5 mg/mL) and 1% (10 mg/mL), submitted under NDA 020533 by Fresenius Kabi USA LLC ("Fresenius Kabi"). The RLD is available in varying single dose vial presentations including 10 mL, 20 mL and 30 mL vials. Additionally, the RLD offers the 0.2% (2 mg/mL) strength in 100 mL (200 mg/100 mL)

and 200 mL in 250 mL (400 mg/200 mL) flexible containers. The Petitioner seeks to introduce 0.2% (2. mg/mL), 0.5% (5 mg/mL), and 1% (10 mg/mL) strengths in a pharmacy bulk package (100 mL, 500 mL, 1L and 2L):

0.2%	200 mg per 100 mL (2 mg/mL)	100 mL PBP
0.2%	1000 mg per 500 mL (2 mg/mL)	500 mL PBP
0.2%	2000 mg per 1L (2 mg/mL)	1 L PBP
0.2%	4000 mg per 2L (2 mg/mL)	2 L PBP
0.5%	500 mg per 100 mL (5 mg/mL)	100 mL PBP
0.5%	2,500 mg per 500 mL (5 mg/mL)	500 mL PBP
0.5%	5,000 mg per 1L (5 mg/mL),	1 L PBP
0.5%	10,000 mg per 2L (5 mg/mL)	2 L PBP
1%	1,000 mg per 100 mL (10 mg/mL)	100 mL PBP
1%	5,000 mg per 500 mL (10 mg/mL),	500 mL PBP
1%	10,000 mg per 1L (10 mg/mL)	1 L PBP
1%	20,000 mg per 2L (10 mg/mL)	2 L PBP

B. Statement of Grounds

FDC Act § 505(j)(2)(A)(iii) provides for the submission of an ANDA for a drug product that differs in strength from that of the listed drug provided FDA has first approved a petition permitting the submission of such an application. Here, by nature of the bulk packaging, the proposed drug product will have a different total fill volume/total drug content than the RLD, which constitutes a change in strength under FDA regulations. *See* 21 C.F.R. § 314.3 (defining "strength" to include total quantity and concentration of drug in a container closure system).

Fresenius Kabi's Naropin® (ropivacaine hydrochloride injection), approved under NDA 020533, contains 0.2% (2 mg/mL), 0.5% (5 mg/mL), 0.75% (7.5 mg/mL) or 1% (10 mg/mL) of Ropivacaine Hydrochloride in an injectable dosage form. A copy of the current Orange Book entry for the Fresenius Kabi product, NDA 020533, is included in ***Attachment 1***. The proposed drug product also contains Ropivacaine Hydrochloride in an injectable dosage form in the intended strengths of 0.2% (2 mg/mL), 0.5% (5 mg/mL) or 1% (10 mg/mL); however, the total fill volume/total drug content differs.

While the Petitioner is seeking a change in total fill volume/total drug content, the concentration and intended delivered dose in the proposed drug product are consistent with the dosing recommendations of the RLD's approved labeling. Approved labeling for Fresenius Kabi's product is included as ***Attachment 2***. The proposed product is to be used as anticipated in the labeling but simply supplied in a pharmacy bulk package.

The availability of a larger size pharmacy bulk package would permit hospitals, non-acute ambulatory infusion centers and outsourcing facilities the option to use a more convenient packaging configuration that would reduce waste, permit the stocking of fewer vials, and help pharmacies achieve operational efficiencies that could result in an overall reduced cost of care. Further, the addition of a new Ropivacaine Hydrochloride product would help alleviate the ongoing shortage arising from increased demand of the drug. *See* FDA, Drug Shortage List, Ropivacaine Hydrochloride Injection (last visited June 3, 2024). A pharmacy bulk package of Ropivacaine Hydrochloride would increase supply of product and thereby mitigate the shortage.

The proposed labeling will include instructions for proper use. To ensure the safe use of the pharmacy bulk packaged Ropivacaine Hydrochloride, the labeling will reference the total dispensing time is to occur in a laminar flow work area and that the user adhere to USP <797>, "*Pharmaceutical Compounding – Sterile Preparation*", for aseptic handling requirements during pharmacy compounding. Other than these instructions, the change in fill volume/total drug content sought in this Petition, and the replacement of references to the Naropin® brand name with "ropivacaine hydrochloride", the labeling for the proposed product will be the same as the RLD. Proposed labeling is attached as ***Attachment 3***. The active ingredient, uses, indications, warnings, and directions for use will remain the same as that of the RLD, with the addition of instructions associated with the pharmacy bulk package presentation. The product is expected to have the same therapeutic effect as the RLD for each condition of use. Thus, the proposed change in fill volume/total drug content from that of the RLD does not raise questions of safety or efficacy for the proposed drug product. Therefore, FDA should conclude that clinical investigations are not necessary to demonstrate safety or effectiveness of the proposed drug product.

FDA has approved similar petitions for a change in total drug content/fill volume from a single dose vial to a pharmacy bulk package. For example, FDA approved Fresenius Kabi's Petition in 2021 requesting that FDA determine that Sodium Chloride 23.4% Injection USP, 100 mL fill in 100 mL and 200 mL fill in 200 mL plastic pharmacy bulk package vials are suitable for submission in an ANDA even though the RLD was approved as a 30 mL fill in 30 mL plastic vial. There, while the concentration remained unchanged at 234 mg/mL, the total drug content was changed from 7,020 mg/30 mL to 23,400 mg/100 mL and 46,800 mg/200 mL. Nevertheless, because the uses, dose, dosage form, and route of administration of the proposed product were the same as the listed drug product, FDA concluded that the change in total drug content would not jeopardize the safe or effective use of the product. ***Attachment 4***, Petition Response, Docket No. FDA-2018-P-4281 (May 27, 2021). The request in this Petition is comparable: This Petition also requests a change in total drug content/fill volume without change to the uses, dose, dosage form, and route of administration as compared to the listed drug product. Thus, FDA should grant this Petition.

The Pediatric Research Equity Act ("PREA"), enacted in December 2003, amended the FDC Act by requiring certain applications for a drug submitted under FDC Act § 505 to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is deferred or waived. *See* FDC Act § 505B(a)(1)(A)(i). Specifically, PREA applies to all applications for a new active ingredient, dosage form, indication, route of administration, or dosing regimen. ANDAs submitted under an approved suitability petition for a change in strength resulting from a difference in fill volume/total drug content are not subject to PREA requirements. *See* FDA, Pediatric Drug Development: Regulatory Considerations — Complying With the Pediatric Research Equity Act and Qualifying for Pediatric Exclusivity Under the Best Pharmaceuticals for Children Act Guidance for Industry, 8 (May 2023). Petitioner asserts that PREA is not applicable to the proposed Ropivacaine Hydrochloride Injection drug product because the proposed change concerns only a difference in fill volume/total drug content. As such, PREA should not serve as an impediment to the Agency granting this Petition.

C. Environmental Impact

A claim for categorical exclusion of the requirements for an environmental assessment is made pursuant to 21 C.F.R. § 25.31.

D. Economic Impact

Pursuant to 21 C.F.R. § 10.30(b), economic impact information is submitted only when requested by the Commissioner. This information will be promptly provided, if so requested.

E. Certification

The undersigned certifies that, to the best 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 are unfavorable to the Petition.

Sincerely,

Sara W. Koblitz

SWK/rh

Attachments