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SUBMITTED VIA REGULATIONS.GOV

Division of Dockets Management
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, 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 drug products Loperamide HCl Capsules, 1 mg and 4 mg, are suitable for consideration in an Abbreviated New Drug Application ("ANDA").

A. Action Requested

The petitioner requests that FDA declare that Loperamide HCl Capsules, 1 mg and 4 mg, are 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 Johnson & Johnson Consumer Inc.'s IMODIUM (loperamide HCl) Capsules, 2 mg, which is approved for prescription use under New Drug Application ("NDA") 017694.[1] The petitioner seeks to introduce new 1 mg and 4 mg loperamide HCl capsule strengths for prescription use.

[1] IMODIUM (loperamide HCl) Capsules, 2 mg (NDA 017694), is listed in the Discontinued Drug Product List section of the Orange Book and is not currently marketed. FDA has already determined that the drug product was not discontinued for reasons of safety or effectiveness, as it is listed in the Orange Book with the following

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.

IMODIUM approved under NDA 017694 contains 2 mg of loperamide HCl in a capsule dosage form. A copy of the current Orange Book entry for IMODIUM Capsules (NDA 017694) is included in ***Attachment 1***. The proposed drug product also contains loperamide HCl in a capsule dosage form, but in 1 mg and 4 mg strengths. The petition is thus seeking a change in capsule strengths to 1 mg and 4 mg of loperamide HCl from that of the RLD (2 mg).

The proposed change in strengths is consistent with the dosing recommendations of the RLD's approved labeling. For example, the prescribing information for the only marketed generic version of IMODIUM Capsules, and the FDA-assigned Reference Standard, approved under ANDA 072741, provides the following dosing information:

Acute Diarrhea

Adults and Pediatric Patients 13 Years and Older

The recommended initial dose is 4 mg (two capsules) followed by 2 mg (one capsule) after each unformed stool. The maximum daily dose is 16 mg (eight capsules). Clinical improvement is usually observed within 48 hours.

Pediatric Patients 2 to 12 Years of Age

In pediatric patients 2 to 5 years of age (20 kg or less), the non-prescription liquid formulation of loperamide (1 mg/5 mL) should be used; for ages 6 to 12, either loperamide hydrochloride capsules or the non-prescription liquid formulation of loperamide may be used. For pediatric patients 2 to 12 years of age, the following schedule for capsules or liquid will usually fulfill initial dosage requirements:

Recommended First Day Dosage Schedule

Two to five years (13 kg to 20 kg): 1 mg three times daily (3 mg total daily dosage)

Six to eight years (20 kg to 30 kg): 2 mg twice daily (4 mg total daily dosage)

Eight to twelve years (greater than 30 kg): 2 mg three times daily (6 mg total daily dosage)

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note: "Federal Register determination that product was not discontinued or withdrawn for safety or efficacy reasons."

Recommended Subsequent Daily Dosage

Following the first treatment day, it is recommended that subsequent loperamide hydrochloride capsules doses (1 mg/10 kg body weight) be administered only after a loose stool. Total daily dosage should not exceed recommended dosages for the first day.

Chronic Diarrhea

Adults

The recommended initial dose is 4 mg (two capsules) followed by 2 mg (one capsule) after each unformed stool until diarrhea is controlled, after which the dosage of loperamide hydrochloride capsules should be reduced to meet individual requirements. When the optimal daily dosage has been established, this amount may then be administered as a single dose or in divided doses.

The average daily maintenance dosage in clinical trials was 4 mg to 8 mg (two to four capsules per day). The maximum daily dosage is 16 mg (eight capsules per day). If clinical improvement is not observed after treatment with 16 mg per day for at least 10 days, symptoms are unlikely to be controlled by further administration. Loperamide hydrochloride capsules administration may be continued if diarrhea cannot be adequately controlled with diet or specific treatment.

Prescribing Information, Loperamide HCl Capsules, 2 mg, ANDA 072741 (Nov. 2016), available at https://dailymed.nlm.nih.gov/dailymed/getFile.cfm?setid=72a7ae47-cdf3-4949-b9f8-f29b153f787f&type=pdf.

The availability of new 1 mg and 4 mg strengths is consistent with the dosing instructions for the RLD (NDA 017694) and its approved generic equivalent (ANDA 072741) and could aid patient compliance in easily attaining the most effective dose (e.g., a 1 mg dose for pediatric dosing), and, in the case of the proposed 4 mg strength, by reducing pill burden (e.g., by allowing for administration of a single capsule instead of two 2 mg capsules). The proposed changes in strength from that of the RLD do not raise questions of safety or efficacy for the proposed drug products. Therefore, FDA should conclude that clinical investigations are not necessary to demonstrate safety or effectiveness of the proposed drug products.

There are no proposed changes in labeling with the exception of changes in strength sought in this petition. The uses, indications, warnings, and directions for use will remain the same as that of the RLD. Approved labeling for IMODIUM Capsules (NDA 017694), updated in October 2016, is included as ***Attachment 2***. Draft labeling for the proposed drug products is included as ***Attachment 3***. Therefore, the Petitioner requests that FDA find that changes in capsule strength from 2 mg to 1 mg and 4 mg of loperamide HCl raise no questions of safety or effectiveness.

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. See id. ANDAs submitted under an approved suitability petition for a change in strength are not subject to PREA requirements. See FDA, Draft Guidance for Industry, How to Comply with the Pediatric Research Equity Act, 4 (Sep. 2005). Petitioner asserts that PREA is not applicable to the proposed Loperamide HCl Capsules, 1 mg and 4 mg, drug products because the proposed changes concerns only new strengths. 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.

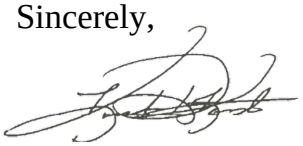
D. Economic Impact

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,



Kurt R. Karst