DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

NDA 19487/S-034

SUPPLEMENT APPROVAL

Johnson & Johnson Consumer, Inc.
McNeil Consumer Healthcare Division
Attention: Elizabeth Finn, PharmD
Director, Regulatory Affairs
7050 Camp Hill Road
Fort Washington, PA 19034-2210

Dear Dr. Finn:

Please refer to your Supplemental New Drug Application (sNDA) dated and received March 1, 2019, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Imodium® A-D (loperamide hydrochloride) oral solution, 1 mg /7.5 mL.

This "Changes Being Effected" supplemental new drug application provides for the following:

- After "**Ask a doctor before use if you have**" the bullet "a history of abnormal heart rhythm" has been added to the end of the list

- After "**Ask a doctor or pharmacist before use if you are taking**", the statement "a prescription drug. Loperamide may interact with certain prescription drugs" follows, and "antibiotics" has been removed

We have completed our review of this application. It is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text and package configurations (i.e., packaging configurations with immediate containers (bottles) containing no more than 32 mg in 8 fluid ounces of loperamide hydrochloride).

Taking higher-than-recommended doses of loperamide can cause serious cardiac events, including torsades de pointes, cardiac arrest, ventricular tachycardia, syncope, and death.[1] [2] Evidence suggests that package limitations and use of unit-dose packaging or flow-restrictors

[1] Rose BJ. High doses of loperamide can cause serious cardiac events. Pharm Today (2016); 22:34.
[2] FDA Drug Safety Communication: *FDA warns about serious heart problems with high doses of the antidiarrheal medicine loperamide (Imodium), including from abuse and misuse* is available at https://www.fda.gov/Drugs/DrugSafety/ucm504617.htm.

may reduce medication overdose and death.[3] [4] [5] We acknowledge your commitment on March 6, 2019 to market loperamide hydrochloride product configurations that are limited to total immediate container amounts of 16 mg in 4 fluid ounces and 32 mg in 8 fluid ounces. Contact the Division of Nonprescription Drug Products if you intend to market or distribute packages containing more than 32 mg of loperamide hydrochloride solution.

LABELING

Submit final printed labeling, with the revisions listed above, as soon as they are available, but no more than 30 days after they are printed. The final printed labeling must be identical to the 4 fluid ounce immediate container (bottle) and 8 fluid ounce immediate container (bottle) labeling submitted on March 1, 2019, and must be in the "Drug Facts" format (21 CFR 201.66), where applicable.

The final printed labeling should be submitted electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (April 2017, Revision 4)*. For administrative purposes, designate this submission "**Final Printed Labeling for approved NDA 19487/S-034**." Approval of this submission by FDA is not required before the labeling is used.

We remind you to remove the "See New Warning and Directions" flag on the principal display panel 6 months after marketing. The option of removing the word "New" from the flag and continue to display it on the principal display panel after 6 months is acceptable.

In addition, replace copyright placeholder "20XX" with appropriate year prior to marketing.

DRUG REGISTRATION AND LISTING

All drug establishment registration and drug listing information is to be submitted to FDA electronically, via the FDA automated system for processing structured product labeling (SPL) files (eLIST). At the time that you submit your final printed labeling (FPL), the content of labeling (Drug Facts) should be submitted in SPL format as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Information on submitting SPL files using eLIST may be found in the guidance for industry titled "SPL Standard for Content of Labeling Technical Qs and As" at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf. In addition, representative container or carton labeling, whichever includes Drug Facts, (where differences exist only in the quantity of contents statement) should be submitted as a JPG file.

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[3] Turvill JL, et al. Change in occurrence of paracetamol overdose in UK after introduction of blister packs. The Lancet (2000); 355:2048-2049.
[4] Hawton K, et al. Long term effect of reduced pack sizes of paracetamol on poisoning deaths and liver transplant activity in England and Wales: Interrupted time series analysis (2013); 346:f403.
[5] Chan TYK. Improvements in the packaging of drugs and chemicals may reduce the likelihood of severe intentional poisonings in adults. Human & Experimental Toxicology (2000); 19:387-391.

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Janice Adams-King, Safety Regulatory Project Manager, at 301-796-3713.

Sincerely,

{See appended electronic signature page}

Valerie Pratt, MD
Deputy Director for Safety
Division of Nonprescription Drug Products
Office of Drug Evaluation IV
Center for Drug Evaluation and Research

ENCLOSURES:
Carton and Container Labeling

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

VALERIE S PRATT
08/07/2019 09:53:00 AM