



NDA 19860/S-033

SUPPLEMENT APPROVAL

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

Dear Ms. Abraham:

Please refer to your Supplemental New Drug Application (sNDA) dated and received December 14, 2018, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Imodium[®] A-D (loperamide hydrochloride) tablet, 2 mg.

This “Changes Being Effected” supplemental new drug application provides for:

- Cartons containing no greater than 24-count size and limited to blister packaging only
- After “**Ask a doctor before use if you have**” the bulleted statement “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**”, the bulleted statement “taking a prescription drug. Loperamide may interact with certain prescription drugs.” has been added, and “antibiotics” has been removed

We have completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text and package configuration.

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 may reduce medication overdose and death.^{3 4 5} To support ongoing efforts to encourage the safe use of

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>.

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.

loperamide hydrochloride, we are approving packages that contain a maximum of 48 mg loperamide hydrochloride in unit-dose packaging. If you intend to market or distribute packages containing more than 48 mg loperamide hydrochloride or tablets that are not in unit-dose packaging, submit a prior approval supplement that includes data showing the proposed changes will not adversely impact the safety of the product.

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 24-count carton (blister) labeling submitted on December 14, 2018, 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 19860/S-033.**” Approval of this submission by FDA is not required before the labeling is used.

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.

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

ENCLOSURE:
Carton 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
03/07/2019 03:33:17 PM