DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 12462/S-045

SUPPLEMENT APPROVAL

G.D. Searle LLC, a subsidiary of Pfizer Inc.
Attention: Karen C. Baker, MD
Director, Pfizer Essential Health Global Regulatory Affairs Brands
235 East 42nd Street
New York, NY 10017

Dear Ms. Baker:

Please refer to your Supplemental New Drug Application (sNDA) dated and received October 15, 2015, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Lomotil® (diphenoxylate hydrochloride and atropine sulfate tablets, USP), 2.5 mg diphenoxylate hydrochloride/0.025 mg atropine sulfate tablets.

This Prior Approval supplemental new drug application provides for the following changes to the prescribing information:

- remove reference to the Lomotil oral solution
- remove larger sized packaging (bottles of 500, 1000, and 2500 tablets, and a carton of 100 unit dose tablets) from the How Supplied section
- add "hallucination" in the Adverse Reactions section
- expand the age in Contraindications for pediatric patients from 2 years of age to less than 6 years of age secondary to the risk of respiratory and central nervous system (CNS) depression
- add *Clostridium difficile* as the organism associated with pseudomembranous enterocolitis in the Contraindications section
- add a description of the anticholinergic and opioid toxicities to the Warnings section
- add the ages (i.e., patients 13 years of age and older) for which Lomotil is indicated in the Indications and Usage; Precautions, Pediatric use, and Dosage and Administration sections
- include opioid and anticholinergic effects to describe overdose symtpoms and update current management of toxicity in the Overdosage section

APPROVAL & LABELING

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

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Content of labeling must be identical to the enclosed labeling, with the addition of any labeling changes in pending "Changes Being Effected" (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.

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/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that include labeling changes for this NDA, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in MS Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes and annotate each change. To facilitate review of your submission, provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

All promotional materials that include representations about your drug product must be promptly revised to be consistent with the labeling changes approved in this supplement, including any new safety information [21 CFR 314.70(a)(4)]. The revisions in your promotional materials should include prominent disclosure of the important new safety information that appears in the revised package labeling. Within 7 days of receipt of this letter, submit your statement of intent to comply with 21 CFR 314.70(a)(4) to the address above, by fax to 301-847-8444, or electronically in eCTD format. For more information about submitting promotional materials in eCTD format, see the draft guidance for industry (available at: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM443702.pdf).

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 Heather Buck, Regulatory Project Manager, at (301) 796-1413.
Sincerely,

{See appended electronic signature page}

Joyce Korvick, M.D., M.P.H.
Deputy Director for Safety
Division of Gastroenterology and Inborn Errors Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

ENCLOSURE: Content of Labeling

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

JOYCE A KORVICK
10/05/2017