



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 8306/S-032

SUPPLEMENT APPROVAL

ANI Pharmaceuticals, Inc.
210 Main Street West
Baudette, MN 56623

Attention: Ellen Camos
Vice President, Regulatory Affairs

Dear Ms. Camos:

Please refer to your Supplemental New Drug Application (sNDA) dated September 21, 2016, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Promethazine Hydrochloride and Codeine Phosphate and Promethazine Hydrochloride, Phenylephrine Hydrochloride and Codeine Phosphate Oral Solutions.

We also refer to our letter dated August 31, 2016, notifying you, under Section 505(o)(4) of the FDCA, of new safety information that we believe should be included in the labeling for Promethazine Hydrochloride and Codeine Phosphate and Promethazine Hydrochloride, Phenylephrine Hydrochloride and Codeine Phosphate Oral Solutions. This information pertains to the serious risks of profound sedation, respiratory depression, coma, and death associated with the concomitant use of opioids and benzodiazepines or other central nervous system depressants, including alcohol.

This supplemental new drug application provides for revisions to the labeling for Promethazine Hydrochloride and Codeine Phosphate and Promethazine Hydrochloride, Phenylephrine Hydrochloride and Codeine Phosphate Oral Solutions, consistent with our August 31, 2016 correspondence.

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 text for the package insert and text for the Medication Guide, 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).

IMMEDIATE CONTAINER LABELS

Submit final printed carton and immediate container labels that are identical to the enclosed immediate container labels, as soon as they are available, but no more than 30 days after they are printed. Please submit these labels electronically according to the guidance for industry *Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (June 2008)*. For administrative purposes, designate this submission “**Final Printed Carton and Container Labels for approved NDA 8306/S-032.**” Approval of this submission by FDA is not required before the labeling is used.

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

Because none of these criteria apply to your application, you are exempt from this requirement.

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 Carol F. Hill, Senior Regulatory Health Project Manager for Safety, at (301) 301-796-1226.

Sincerely,

{See appended electronic signature page}

Sally Seymour, MD
Deputy Director for Safety
Division of Pulmonary, Allergy, and Rheumatology
Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

ENCLOSURE(S):

Content of Labeling
Container Labeling

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

/s/

SALLY M SEYMOUR
01/13/2017