DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 19111/S-022

SUPPLEMENT APPROVAL

UCB Inc.
8010 Arco Corporate Drive
Suite 100
Raleigh, NC 27617

Attention: Queen Arukwe, MS, RAC
Regulatory Strategic Partnership Lead

Dear Ms. Arukwe:

Please refer to your Supplemental New Drug Application (sNDA) dated February 9, 2018, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Tussionex Pennkinetic (hydrocodone polistirex and chlorpheniramine plistirex) Extended Release Oral Suspension.

We also refer to our letter dated January 11, 2018, notifying you, under Section 505(o)(4) of the FDCA, of new safety information that we believe should be included in the labeling for prescription codeine and hydrocodone opioid antitussives. This information pertains to the change in the benefit risk assessment for prescription codeine and hydrocodone containing opioid antitussives, particularly regarding the risk associated with use in children and adolescents. The following risks were described in our January 11, 2018 Notification Letter:

- respiratory depression and death, particularly in children;
- risk of respiratory depression and death with concomitant use of benzodiazepines;
- misuse, abuse, addiction, overdose, death;
- neonatal opioid withdrawal syndrome (NOWS);
- serotonin syndrome following the initiation of an opioid in patients who had previously been taking one or more serotonergic drugs;
- adrenal insufficiency in patients following the initiation of an opioid, more often following opioid use of greater than one month;
- androgen deficiency in patients with long-term exposure to opioids.

We also noted a September 11, 2017, FDA Pediatric Advisory Committee which concluded that the benefit-risk for use of prescription codeine and hydrocodone antitussives was not favorable for treatment of cough in children younger than 18 years of age.

This supplemental new drug application provides for revisions to the labeling for Tussionex Pennkinetic Extended Release, consistent with our January 11, 2018 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.

WAIVER OF HIGHLIGHTS SECTION

We are waiving the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of prescribing information. This waiver applies to all future supplements containing revised labeling unless we notify you otherwise.

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).

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients (which includes new salts and new fixed combinations), 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 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
Acting Director
Division of Pulmonary, Allergy, and Rheumatology Products
Office of Drug Evaluation II
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/

SALLY M SEYMOUR
06/28/2018