DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville, MD 20857

ANDA 203136

Amneal Pharmaceuticals
Attention: Candice Edwards
Senior Vice President, Regulatory & Clinical Affairs
85 Adams Avenue
Hauppauge, NY 11788

Dear Madam:

This is in reference to your abbreviated new drug application (ANDA) dated May 12, 2011, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (the Act), for Buprenorphine HCl and Naloxone HCl Dihydrate Sublingual Tablets, 2 mg (base)/0.5 mg (base) and 8 mg (base)/2 mg (base).

Reference is also made to your amendments dated May 27, June 6, September 28, October 21, November 30, December 15, 2011; May 17, June 4, August 17, September 18, October 3, October 9, December 21, 2012 and February 12, 2013 and to our letter dated January 6, 2012.

We have completed the review of this ANDA and have concluded that adequate information has been presented to demonstrate that the criteria for approval in section 505(j) of the Act have been met. Accordingly the ANDA is approved, effective on the date of this letter. The Division of Bioequivalence has determined your Buprenorphine HCl and Naloxone HCl Dihydrate Sublingual Tablets, 2 mg (base)/0.5 mg (base) and 8 mg (base)/2 mg (base) to be bioequivalent and, therefore, therapeutically equivalent to the reference listed drug product (RLD), Suboxone® (buprenorphine HCl and naloxone HCl dihydrate) Sublingual Tablets, 2 mg (base)/0.5 mg (base) and 8 mg (base)/2 mg (base) of Reckitt Benckiser. Your dissolution testing should be incorporated into the stability and quality control program using the same method proposed in your application.

Under section 506A of the Act, certain changes in the conditions described in this ANDA require an approved supplemental application before the change may be made.

RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS

Section 505-1 of the Act authorizes FDA to require the submission of a risk evaluation and mitigation strategy (REMS), if FDA becomes aware of new safety information and makes a determination that such a strategy is necessary to ensure that the benefits of the drug outweigh the risks [section 505-1(a)]. The details of the REMS requirements were outlined in our REMS notification letter dated January 6, 2012.

Your proposed REMS, submitted May 17 and August 17, 2012, and amended on February 12, 2013, and attached to this letter, is approved.

Your REMS must be fully operational before you introduce Buprenorphine Hydrochloride and Naloxone Hydrochloride Sublingual Tablets into interstate commerce.

The REMS consists of a Medication Guide, elements to assure safe use, and an implementation system.

This REMS will use a waiver-granted shared system for the elements to assure safe use. This waiver-granted shared REMS is known as the Buprenorphine-containing Transmucosal products for Opioid Dependence (BTOD) REMS Program, includes the following products:

ANDA 078633	Buprenorphine Hydrochloride Sublingual Tablets
ANDA 090360	Buprenorphine Hydrochloride Sublingual Tablets
ANDA 090622	Buprenorphine Hydrochloride Sublingual Tablets
ANDA 091422	Buprenorphine Hydrochloride and Naloxone Hydrochloride Sublingual Tablets
ANDA 203136	Buprenorphine Hydrochloride and Naloxone Hydrochloride Sublingual Tablets

Other products may be added in the future if additional Buprenorphine Hydrochloride Sublingual Tablets or Buprenorphine Hydrochloride and Naloxone Hydrochloride Sublingual Tablets are approved.

Under section 505-1(g)(2)(C) and (D), FDA can require the submission of a REMS assessment if FDA determines that new safety or effectiveness information indicates that a REMS element should be modified or included in the strategy, or if FDA determines that there may be a cause for action by FDA under section 505(e). Additionally, the details for what should be included in your joint REMS assessments and the dates of the REMS assessments are listed in Appendix 1.

We remind you that section 505-1(f)(8) of FDCA prohibits holders of an approved covered application with elements to assure safe use from using any element to block or delay approval of an application under section 505(b)(2) or (j). A violation of this provision in 505-1(f) could result in enforcement action.

Prominently identify the submission containing a proposed modification of the REMS or any REMS assessments with the following wording in bold capital letters at the top of the first page of the submission:

NEW SUPPLEMENT FOR ANDA 203136
PROPOSED REMS MODIFICATION
REMS ASSESSMENT

REPORTING REQUIREMENTS

Postmarketing reporting requirements for this ANDA are set forth in 21 CFR 314.80-81 and 314.98. The Office of Generic Drugs should be advised of any change in the marketing status of this drug.

Promotional materials may be submitted to FDA for comment prior to publication or dissemination. Please note that these submissions are voluntary. If you desire comments on proposed launch promotional materials with respect to compliance with applicable regulatory requirements, we recommend you submit, in draft or mock-up form, two copies of both the promotional materials and package insert directly to:

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion
5901-B Ammendale Road
Beltsville, MD 20705

We call your attention to 21 CFR 314.81(b)(3) which requires that all promotional materials be submitted to the Office of Prescription Drug Promotion with a completed Form FDA 2253 at the time of their initial use.

As soon as possible, but no later than 14 days from the date of this letter, submit, using the FDA automated drug registration and listing system (eLIST), the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format, as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm, that is identical in content to the approved labeling (including the package insert, and any patient package insert and/or Medication Guide that may be required). 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 via publicly available labeling repositories.

Sincerely yours,

{See appended electronic signature page}

Gregory P. Geba, M.D., M.P.H.
Director
Office of Generic Drugs
Center for Drug Evaluation and Research

Attachment: Appendix 1
REMS

Appendix 1

Dates for submission of waiver-granted shared REMS assessments

REMS assessments will be submitted to the FDA at each year, on August 30th. To facilitate inclusion of as much information as possible, while allowing reasonable time to prepare the submission, the reporting interval covered by each assessment will conclude no earlier than 60 days before the submission date for that assessment. WG Sponsors will each submit the same assessment so it will be received by the FDA on or before the due date.

REMS Assessment Plan

The REMS assessment plan should include, but is not limited, to the following:

1. An evaluation of patients' awareness and understanding of the serious risks associated with buprenorphine-containing products
2. A report on periodic assessments of the distribution and dispensing of the Medication Guide in accordance with 21 CFR 208.24
3. A report on failures to adhere to distribution and dispensing requirements, and corrective actions taken to address noncompliance
4. An evaluation of prescribers' awareness and understanding of the serious risks associated with buprenorphine-containing products
5. An evaluation of pharmacists' awareness and understanding of the serious risks associated with buprenorphine-containing products
6. An analysis to evaluate utilization patterns of buprenorphine-containing products including frequency of office visits, amount dispensed in prescriptions to new patients, and other indicators of adherence to practices important to safe use.
7. An analysis and summary of surveillance and monitoring activities for abuse, misuse, overdose and addiction and any intervention taken resulting from signals of abuse, misuse, overdose and addiction. Surveillance will include, among other sources, reports of pediatric exposures
8. Monitoring and evaluation of the implementation of the ETASU
9. An assessment of the extent to which the REMS is meeting its goals. Specific measures that will be proposed to increase awareness if surveys of patients, prescribers, and pharmacists indicate that awareness is not adequate.

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

/s/

ROBERT L WEST

02/22/2013

Deputy Director, Office of Generic Drugs, for
Gregory P. Geba, M.D., M.P.H.