DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

ANDA 090819

Actavis Elizabeth LLC
200 Elmora Avenue
Elizabeth, NJ 07207

Attention: Janak Jadeja, RPh
Director, Regulatory Affairs

Dear Madam:

This is in reference to your abbreviated new drug application (ANDA) dated October 1, 2008, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (FDCA), for Buprenorphine Hydrochloride Sublingual Tablets, 2 mg and 8 mg.

Reference is also made to the Complete Response letter issued by this office dated November 10, 2010, and to your amendments dated May 20, and November 15, 2011; June 12, August 6, August 20, October 4, December 5 and December 27, 2012; February 12, February 26, March 11, and September 10, 2013; March 25, and May 15, 2014; and January 23, 2015.

We note that the reference listed drug product (RLD) upon which you have based this ANDA, Subutex® (buprenorphine hydrochloride) Sublingual Tablets, 2 mg and 8 mg, of Reckitt Benckiser (Reckitt), is no longer being marketed in the U.S. and has been moved to the "Discontinued Drug Product List" section of the Agency's publication titled Approved Drug Products with Therapeutic Equivalence Evaluations, known generally as the "Orange Book." We note that the Agency published a Federal Register notice on February 13, 2015, Vol. 80, No. 30, in which it announced its determination that Reckitt's Subutex® Sublingual Tablets, 2 mg and 8 mg, were not withdrawn from sale for reasons of safety or effectiveness. This determination allows the agency to continue to approve applications that refer to Subutex®.

We have completed the review of this ANDA and have concluded that adequate information has been presented to demonstrate that the drug is safe and effective for use as recommended in the submitted labeling. Accordingly the ANDA is approved, effective on the date of this letter. The Division of Bioequivalence has determined your Buprenorphine Hydrochloride Sublingual Tablets, 2 mg and 8 mg to be bioequivalent and, therefore, therapeutically equivalent to the RLD, Subutex® Sublingual Tablets, 2 mg and 8 mg, 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 FDCA, 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 FDCA authorizes FDA to require the submission of a risk evaluation and mitigation strategy (REMS) if FDA determines 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. In that letter, you were also notified that pursuant to section 505-1(i) of the FDCA, a drug that is the subject of an ANDA and the listed drug it references must use a single, shared system for elements to assure safe use unless FDA waives that requirement.
The ANDAs for buprenorphine-containing transmucosal products
were granted a waiver from the single, shared system requirement in 505-1(i) of the FDCA, and the waiver-granted shared system REMS, known as the Buprenorphine-containing Transmucosal products for Opioid Dependence (BTOD) REMS, was approved on February 22, 2013. The most recent REMS modification was approved on February 12, 2015.

Your proposed REMS, that incorporates your product into the BTOD REMS, submitted on January 23, 2015 and appended to this letter is approved. The REMS consists of a medication guide, elements to assure safe use (ETASU), and an implementation system.

As discussed above, the BTOD REMS uses a waiver-granted shared system for the elements to assure safe use and the REMS assessments. This waiver-granted shared REMS currently includes the products listed on the FDA REMS website available at http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm111350.htm#Shared.

Other products may be added in the future if additional buprenorphine-containing transmucosal products for opioid dependence are approved.

Under section 505-1(g)(2)(C), FDA can require the submission of a REMS assessment if FDA determines that an assessment is needed to evaluate whether the approved strategy should be modified to ensure the benefits outweigh the risks of the drug or to minimize burden on the healthcare system of complying with the REMS.

We remind you that section 505-1(f)(8) of the 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:

ANDA 090819
REMS ASSESSMENT

NEW SUPPLEMENT FOR ANDA 090819
PROPOSED REMS MODIFICATION

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(s) 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.

The Generic Drug User Fee Amendments of 2012 (GDUFA) (Public Law 112-144, Title III) established certain provisions with respect to self-identification of facilities and payment of annual facility fees. Your ANDA identifies at least one facility that is subject to the self identification requirement and payment of an annual facility fee. Self-identification must occur by June 1 of each year for the next fiscal year. Facility fees must be paid each year by the date specified in the Federal Register notice announcing facility fee amounts. All finished dosage forms (FDFs) or active pharmaceutical ingredients (APIs) manufactured in a facility that has not met its obligations to self-identify or to pay fees when they are due will be deemed misbranded. This means that it will be a violation of federal law to ship these products in interstate commerce or to import them into the United States. Such violations can result in prosecution of those responsible, injunctions, or seizures of misbranded products. Products misbranded because of failure to self-identify or pay facility fees are subject to being denied entry into the United States.

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,

William P. Rickman -S

Digitally signed by William P. Rickman -S
DN: c=US, o=U.S. Government, ou=HHS, ou=FDA, ou=People, 0.9.2342.19200300.100.1.1=1300043242, cn=William P. Rickman -S
Date: 2015.02.19 15:53:54 -05'00'

Carol A. Holquist, RPh
Acting Deputy Director
Office of Regulatory Operations
Office of Generic Drugs
Center for Drug Evaluation and Research

Attachments: MedGuide
REMS