

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2012-P-1034]

Determination That SUBOXONE (Buprenorphine Hydrochloride and Naloxone Hydrochloride) Sublingual Tablets, 2 Milligrams/0.5 Milligrams and 8 Milligrams/2 Milligrams, Were Not Withdrawn From Sale for Reasons of Safety or Effectiveness

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) has determined that SUBOXONE (buprenorphine hydrochloride (HCl) and naloxone HCl) sublingual tablets, 2 milligrams (mg)/0.5 mg and 8 mg/2 mg, were not withdrawn from sale for reasons of safety or effectiveness. This determination will allow FDA to approve abbreviated new drug applications (ANDAs) for buprenorphine HCl and naloxone HCl sublingual tablets, 2 mg/0.5 mg and 8 mg/2 mg, if all other legal and regulatory requirements are met.

FOR FURTHER INFORMATION CONTACT: David E. Markert, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, Rm. 6248, Silver Spring, MD 20993-0002, 301-796-3602.

SUPPLEMENTARY INFORMATION:

I. Background

In 1984, Congress enacted the Drug Price Competition and Patent Term Restoration Act of 1984 (Pub. L. 98-417) (the 1984 amendments), which authorized the approval of duplicate versions of drug products under an ANDA procedure. ANDA applicants must, with certain exceptions, show that the drug for which they are seeking approval contains the same active ingredient in the same strength and dosage form as the "listed drug," which is a version of the drug that was previously approved. ANDA applicants do not have to repeat the extensive clinical testing otherwise necessary to gain approval of a new drug application (NDA).

The 1984 amendments include what is now section 505(j)(7) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(j)(7)), which requires FDA to publish a list of all approved drugs. FDA publishes this list as part of the "Approved Drug Products With Therapeutic Equivalence Evaluations," which is known generally as the

"Orange Book." Under FDA regulations, drugs are removed from the list if the Agency withdraws or suspends approval of the drug's NDA or ANDA for reasons of safety or effectiveness or if FDA determines that the listed drug was withdrawn from sale for reasons of safety or effectiveness (21 CFR 314.162).

A person may petition the Agency to determine, or the Agency may determine on its own initiative, whether a listed drug was withdrawn from sale for reasons of safety or effectiveness. This determination may be made at any time after the drug has been withdrawn from sale, but must be made prior to approving an ANDA that refers to the listed drug (§ 314.161 (21 CFR 314.161)). FDA may not approve an ANDA that does not refer to a listed drug.

SUBOXONE (buprenorphine HCl and naloxone HCl) sublingual tablets, 2 mg/0.5 mg and 8 mg/2 mg, are the subject of NDA 20-733, held by Reckitt Benckiser Pharmaceuticals, Inc. (Reckitt), and initially approved on October 8, 2002. SUBOXONE is indicated for maintenance treatment of opioid dependence.

In a letter dated September 18, 2012, Reckitt notified FDA that SUBOXONE (buprenorphine HCl and naloxone HCl) sublingual tablets, 2 mg/0.5 mg and 8 mg/2 mg, were being discontinued. Shortly thereafter, Reckitt publicly announced that it was discontinuing this product for safety reasons and that it had submitted a citizen petition requesting that FDA require all manufacturers of buprenorphine-containing products for the treatment of opioid dependence to implement certain public health safeguards (Ref. 1).¹ Reckitt later informed the Agency that it ceased distributing SUBOXONE sublingual tablets in March 2013, at which time FDA moved the product to the "Discontinued Drug Product List" section of the Orange Book.

Lachman Consultant Services, Inc. (Lachman), submitted a citizen petition dated September 27, 2012 (Docket No. FDA-2012-P-1034), under 21 CFR 10.30, requesting that the Agency

¹ The citizen petition (Docket No. FDA-2012-P-1028), which was submitted on September 25, 2012, also requested that FDA refuse to approve any ANDAs for buprenorphine HCl and naloxone HCl products for opioid dependence until the Agency determined whether SUBOXONE sublingual tablets were discontinued for safety reasons. In its February 22, 2013, response to the citizen petition, FDA concluded that this request was premature because Reckitt had not yet withdrawn SUBOXONE sublingual tablets from sale. Nonetheless, the Agency conducted a full review and analysis of the safety issues raised in Reckitt's citizen petition and determined, on the basis of the data available at that time, that withdrawal of SUBOXONE sublingual tablets from sale was not necessary for reasons of safety.

determine whether SUBOXONE (buprenorphine HCl and naloxone HCl) sublingual tablets, 2 mg/0.5 mg and 8 mg/2 mg, were withdrawn from sale for reasons of safety or effectiveness. The petitioner noted that Reckitt had publicly announced that it was discontinuing this product.

After considering Lachman's citizen petition and reviewing our records, including the safety analysis that the Agency prepared in connection with Reckitt's citizen petition, FDA has determined under § 314.161 that SUBOXONE (buprenorphine HCl and naloxone HCl) sublingual tablets, 2 mg/0.5 mg and 8 mg/2 mg, were not withdrawn for reasons of safety. We described the basis for this determination in our letter response to Reckitt's citizen petition (available at <http://www.regulations.gov> under Docket No. FDA-2012-P-1028). Since the issuance of that response, we have updated our reviews of relevant literature and data on this product. We found no additional information during this process that would indicate that SUBOXONE (buprenorphine HCl and naloxone HCl) sublingual tablets, 2 mg/0.5 mg and 8 mg/2 mg, were, or should have been, withdrawn from sale for reasons of safety.

FDA has also determined under § 314.161 that SUBOXONE (buprenorphine HCl and naloxone HCl) sublingual tablets, 2 mg/0.5 mg and 8 mg/2 mg, were not withdrawn for reasons of effectiveness. We have reviewed our records and other relevant data sources, and have found no information that would indicate that this product was ineffective as a maintenance treatment of opioid dependence.

Accordingly, the Agency will continue to list SUBOXONE (buprenorphine HCl and naloxone HCl) sublingual tablets, 2 mg/0.5 mg and 8 mg/2 mg, in the "Discontinued Drug Product List" section of the Orange Book. The "Discontinued Drug Product List" delineates, among other items, drug products that have been discontinued from marketing for reasons other than safety or effectiveness. ANDAs that refer to SUBOXONE (buprenorphine HCl and naloxone HCl) sublingual tablets, 2 mg/0.5 mg and 8 mg/2 mg, may be approved by the Agency as long as they meet all other legal and regulatory requirements for the approval of ANDAs. If FDA determines that labeling for this drug product should be revised to meet current standards, the Agency will advise ANDA applicants to submit such labeling.

II. References

The following reference has been placed on display in the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852, and may be seen by interested persons between 9 a.m. and 4 p.m., Monday through Friday, and is available electronically at <http://www.regulations.gov>. (FDA has verified the Web site address in this reference section, but FDA is not responsible for any subsequent changes to the Web site after this document publishes in the **Federal Register**.)

1. "Further US RB Pharmaceuticals Announcement," <http://www.rb.com/site/rkbr/templates/mediainvestors/general2.aspx?pageid=1332&cc=GB>, Reckitt Benckiser Group plc, September 25, 2012. Web. May 17, 2013.

Dated: May 31, 2013.

Janet Woodcock,

Director, Center for Drug Evaluation and Research.

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2013-N-0012]

"Script Your Future" Medication Adherence Campaign

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of grant funds for the continuing support of a national effort to promote the importance of medication adherence to enhance the health of Americans. Medication adherence is taking medicine as directed to treat an illness or disease in order to get the best health outcome possible for each patient. Nearly three out of four Americans report that they do not take their medication as directed. One in three people never fill their prescriptions. The annual price tag for medication adherence failure is estimated to be \$290 billion, and the impact on the medical system and patients from this lack of adherence may result in relapses or recurrences of medical symptoms, increases in hospital visits, or even death. FDA is committed to addressing this issue, which has enormous implications for public health and the U.S. economy, by, in part,

continuing its financial and other contributions to a carefully planned, well-executed effective national campaign begun in 2010 by the National Consumers League (NCL) called "Script Your Future".

To continue and enhance this important public health initiative, the Division of Health Communications (DHC)/Office of Communications (OCOMM)/Center for Drug Evaluation and Research (CDER) in FDA seeks to assist the National Consumers League in the development of new online resources and tools for patients, engagement of public and private partners to build on and complement existing medication adherence programs, education of health care professionals with strategies to share with patients, continuous evaluation of the campaign to enhance and improve it, expansion of public-private partnerships, strengthening of this national forum focused on informing consumers about medication adherence, and tailoring messaging to subpopulations of consumers who may need adaptations or special efforts to inform and educate them.

DATES: Important dates are as follows:

1. The application due date is July 1, 2013.
2. The anticipated start date is August 2013.
3. The opening date is the date this announcement is published in the **Federal Register**.
4. The expiration date is July 2, 2013.

ADDRESSES: Submit the paper application to: Gladys Melendez, Grants Management (HFA-500), Food and Drug Administration, 5630 Fishers Lane, Rm. 2032, Rockville, MD 20857; and a copy to Elaine Frost, Center for Drug Evaluation and Research, Food and Drug Administration, 10001 New Hampshire Ave., Rm. 1140, Silver Spring, MD 20903. For more information, see section III of the **SUPPLEMENTARY INFORMATION** section.

FOR FURTHER INFORMATION CONTACT: Paula Rausch, Center for Drug Evaluation and Research, Food and Drug Administration, 10001 New Hampshire Ave., Rm. 4110, Silver Spring, MD 20903, 301-796-3121; or Gladys Melendez, Grants Management Branch (HFA-500), Food and Drug Administration, 5630 Fishers Lane, Rm. 2032, Rockville, MD 20857, 301-827-7175.

For more information on this funding opportunity announcement (FOA) and to obtain detailed requirements, please obtain the full FOA from gladys.bohler@fda.hhs.gov.

SUPPLEMENTARY INFORMATION:

I. Funding Opportunity Description

Request for Application: FDA-RFA-13-027.

Catalog of Federal Domestic Assistance: 93.103

A. Background

In order to fulfill FDA's mission to protect public health by assuring the safety, efficacy, and security of human drugs; and helping the public to obtain the accurate, science-based information they need to use medications in ways that maintain and improve their health, FDA seeks to continue its participation in a national campaign aimed at promoting the importance of medication adherence to enhance the health of Americans.

FDA recognizes medication adherence as a formidable health problem that results in health system and human costs that adversely impact our nation. FDA has a responsibility as a public health agency to educate and inform the public and health professionals about the importance of medication adherence. Since 2010, FDA has been a key government stakeholder in the NCL's initiative, along with other major government agencies and private and nonprofit organizations, to address the issue of poor medication adherence. FDA is committed to educating and informing the public about this issue, including key subpopulations such as those with low literacy and health literacy, or that faces health disparities or is economically disadvantaged.

The NCL is the nation's oldest consumer organization. With FDA and its other government partners, NCL launched its nationwide "Script Your Future" campaign in 2010 to address the issue of poor medication adherence. NCL possesses an extensive research and evaluation framework from past medication outreach efforts that helped ensure the campaign's medication adherence messages and materials are based on sound communication science. In addition, NCL assembled a coalition of more than 130 public-private partners to mobilize resources that can increase awareness and outreach to the public far beyond what FDA would be able to do alone to promote increased understanding and positive actions among the general public and health professionals related to this critical issue. Future NCL plans are in sync with FDA goals for a national medication adherence campaign and FDA seeks to enhance this carefully designed communications intervention. FDA has been and remains a key partner with NCL on issues pertaining to the safe use of medicines.