



ANDA 207338

**ANDA APPROVAL**

Actavis Laboratories FL, Inc.  
2945 West Corporate Lakes Blvd., Suite B  
Weston, FL 33331  
Attention: Janet Vaughn  
Senior Director of Regulatory Affairs

Dear Madam:

This letter is in reference to your abbreviated new drug application (ANDA) received for review on June 19, 2014, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) for Fentanyl Sublingual Tablets, 100 mcg, 200 mcg, 300 mcg, 400 mcg, 600 mcg and 800 mcg.

Reference is also made to the complete response letter issued by this office on July 28, 2016, and to any amendments thereafter.

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 Office of Bioequivalence has determined your Fentanyl Sublingual Tablets, 100 mcg, 200 mcg, 300 mcg, 400 mcg, 600 mcg and 800 mcg, to be bioequivalent and, therefore, therapeutically equivalent to the reference listed drug (RLD), Abstral Sublingual Tablets, 100 mcg, 200 mcg, 300 mcg, 400 mcg, 600 mcg and 800 mcg, of Sentyln Therapeutics Inc. (Sentyln).

The RLD upon which you have based your ANDA, Sentyln's Abstral Sublingual Tablets, 100 mcg, 200 mcg, 300 mcg, 400 mcg, 600 mcg and 800 mcg, is subject to periods of patent protection. The following patents and expiration dates are currently listed in the Agency's publication titled *Approved Drug Products with Therapeutic Equivalence Evaluations* (the "Orange Book"):

<u>U.S. Patent Number</u>	<u>Expiration Date</u>
6,759,059 (the '059 patent)	September 24, 2019
6,761,910 (the '910 patent)	September 24, 2019
7,910,132 (the '132 patent)	September 24, 2019

Your ANDA contains paragraph IV certifications to each of the patents under section 505(j)(2)(A)(vii)(IV) of the FD&C Act stating that the patents are invalid, unenforceable, or will not be infringed by your manufacture, use, or sale of Fentanyl Sublingual Tablets, 100 mcg,

200 mcg, 300 mcg, 400 mcg, 600 mcg and 800 mcg, under this ANDA. You have notified the Agency that Actavis Laboratories FL, Inc. (Actavis) complied with the requirements of section 505(j)(2)(B) of the FD&C Act and that litigation was initiated within the statutory 45-day period against Actavis for infringement of the '059, '910 and '132 patents in the United States District Court for the District of New Jersey [Orexo AB v. Actavis Laboratories FL, Inc., Andrx Corporation, Actavis, Inc., and Actavis Pharma, Inc., Civil Action No. 3:15-cv-00826(PGS-DEA)]. You have also notified the Agency that this case was dismissed.

With respect to 180-day generic drug exclusivity, we note that Actavis was the first ANDA applicant for Fentanyl Sublingual Tablets, 100 mcg, 200 mcg, 300 mcg, 400 mcg, 600 mcg and 800 mcg, to submit a substantially complete ANDA with a paragraph IV certification. Therefore, with this approval, Actavis may be eligible for 180 days of generic drug exclusivity for Fentanyl Sublingual Tablets, 100 mcg, 200 mcg, 300 mcg, 400 mcg, 600 mcg and 800 mcg. This exclusivity, which is provided for under 505(j)(5)(B)(iv) of the FD&C Act, would begin to run from the date of the commercial marketing identified in section 505(j)(5)(B)(iv). The Agency notes that Actavis failed to obtain tentative approval of this ANDA within 30 months after the date of which the ANDA was filed. See section 505(j)(5)(D)(i)(IV) of the FD&C Act (forfeiture of exclusivity for failure to obtain tentative approval). The Agency is not, however, making a formal determination at this time of Actavis' eligibility for 180-day generic drug exclusivity. It will do so only if a subsequent paragraph IV applicant becomes eligible for full approval (a) within 180 days after Actavis begins commercial marketing of Fentanyl Sublingual Tablets, 100 mcg, 200 mcg, 300 mcg, 400 mcg, 600 mcg and 800 mcg, or (b) at any time prior to the expiration of the '059, '910 and '132 patents if Actavis has not begun commercial marketing. Please submit correspondence to this ANDA notifying the Agency within 30 days of the date of the first commercial marketing of this drug product or the RLD. If you do not notify the Agency within 30 days, the date of first commercial marketing will be deemed to be the date of the drug product's approval. See 21 CFR 314.107(c)(2).

Under section 506A of the FD&C 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 (REMS) REQUIREMENTS**

Section 505-1 of the FD&C Act 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)]. In accordance with section 505-1(i) of the FD&C Act, a drug that is the subject of an ANDA under section 505(j) is subject to certain elements of the REMS required for the applicable listed drug.

The details of the REMS requirements were outlined in our REMS notification letter dated January 20, 2015. In that letter, you were also notified that pursuant to section 505-1(i) of the FD&C Act, 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 (ETASU), unless FDA waives that requirement.

Your final proposed REMS, referenced in Drug Master File 027320 is approved. The REMS is posted to the FDA REMS website, available at <http://www.fda.gov/rems>. The REMS consists of a Medication Guide, ETASU, and an implementation system.

Your REMS must be fully operational before you introduce Fentanyl Sublingual Tablets into interstate commerce.

The Transmucosal Immediate – Release Fentanyl (TIRF) REMS uses a shared system for the ETASU and the REMS assessments. This shared system REMS Program currently includes the products listed on the FDA REMS website, available at <http://www.fda.gov/rems>. Other products may be added in the future if additional NDAs or ANDAs are approved.

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

We remind you that you must include an adequate rationale to support a proposed REMS modification for the addition, modification, or removal of any goal or element of the REMS, as described in section 505-1(g)(4) of the FD&C Act.

We also remind you that section 505-1(f)(8) of the FD&C Act prohibits holders of an approved covered application from using any element to assure safe use 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 any submission containing a REMS assessment or proposed modifications of the REMS with the following wording in bold capital letters at the top of the first page of the submission as appropriate:

**ANDA 207338 REMS ASSESSMENT**

**NEW SUPPLEMENT FOR ANDA 207338/S-000  
CHANGES BEING EFFECTED IN 30 DAYS  
PROPOSED MINOR REMS MODIFICATION**

*or*

**NEW SUPPLEMENT FOR ANDA 207338/S-000  
PRIOR APPROVAL SUPPLEMENT  
PROPOSED MAJOR REMS MODIFICATION**

*or*

**NEW SUPPLEMENT FOR ANDA 207338/S-000  
PRIOR APPROVAL SUPPLEMENT  
PROPOSED REMS MODIFICATIONS DUE TO SAFETY LABELING  
CHANGES SUBMITTED IN SUPPLEMENT XXX**

Should you choose to submit a REMS revision, prominently identify the submission containing the REMS revisions with the following wording in bold capital letters at the top of the first page of the submission:

**REMS REVISION FOR ANDA 207338**

To facilitate review of your submission, we request that you submit your proposed modified REMS and other REMS-related materials in Microsoft Word format. If certain documents, such as enrollment forms, are only in PDF format, they may be submitted as such, but the preference is to include as many as possible in Word format.

**REPORTING REQUIREMENTS**

Postmarketing reporting requirements for this ANDA are set forth in 21 CFR 314.80-81 and 314.98 and at section 506I of the FD&C Act. The Office of Generic Drugs should be advised of any change in the marketing status of this drug or if this drug will not be available for sale after approval. In particular, under section 506I(b) of the FD&C Act, you are required to notify the Office of Generic Drugs in writing within 180 days from the date of this letter if this drug will not be available for sale within 180 days from the date of approval. As part of such written notification, you must include (1) the identity of the drug by established name and proprietary name (if any); (2) the ANDA number; (3) the strength of the drug; (4) the date on which the drug will be available for sale, if known; and (5) the reason for not marketing the drug after approval.

**PROMOTIONAL MATERIALS**

You may request advisory comments on proposed introductory advertising and promotional labeling materials prior to publication or dissemination. Please note that these submissions are voluntary. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the package insert (PI), Medication Guide, and patient PI (as applicable) to:

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

Alternatively, you may submit a request for advisory comments electronically in eCTD format. For more information about submitting promotional materials in eCTD format, see the draft Guidance for Industry (available at:

<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM443702.pdf>).

You must also submit final promotional materials and package insert(s), accompanied by a Form FDA 2253, at the time of initial dissemination or publication [21 CFR 314.81(b)(3)(i)]. Form FDA 2253 is available at

<http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf>.

Information and Instructions for completing the form can be found at

<http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf>.

For more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see

<http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm>.

### **ANNUAL FACILITY FEES**

The Generic Drug User Fee Amendments of 2012 (GDUFA) (Public Law 112-144, Title III) established certain provisions<sup>1</sup> 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<sup>st</sup> 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.

### **CONTENT OF LABELING**

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.

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<sup>1</sup> Some of these provisions were amended by the Generic Drug User Fee Amendments of 2017 (GDUFA II) (Public Law 115-52, Title III).

The Electronic Common Technical Document (eCTD) is CDER's standard format for electronic regulatory submissions. Beginning May 5, 2017, ANDAs must be submitted in eCTD format and beginning May 5, 2018, drug master files must be submitted in eCTD format. Submissions that do not adhere to the requirements stated in the eCTD Guidance will be subject to rejection. For more information please visit: [www.fda.gov/ectd](http://www.fda.gov/ectd).

Sincerely yours,

*{See appended electronic signature page}*

For Vincent Sansone, Pharm.D.  
Deputy Director  
Office of Regulatory Operations  
Office of Generic Drugs  
Center for Drug Evaluation and Research



Sarah  
Kurtz

Digitally signed by Sarah Kurtz

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