



NDA 020747/S-041

**SUPPLEMENT APPROVAL**

Cephalon, Inc.  
41 Moores Road  
P.O. Box 4011  
Frazer, PA 19355

Attention: Baldev B. Rana  
Manager, Regulatory Affairs

Dear Ms. Rana:

Please refer to your Supplemental New Drug Application (sNDA) dated May 21, 2014, received May 21, 2014, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for ACTIQ (oral transmucosal fentanyl citrate).

We acknowledge receipt of your amendments dated November 26, and December 11, 2014. We also refer to the May 20, November 25, and December 10, 2014, submissions to DMF (b) (4) which contain the proposed modifications to your shared risk evaluation and mitigation strategy (REMS) program.

This "Prior Approval" supplemental new drug application provides for modifications to the approved REMS for ACTIQ (oral transmucosal fentanyl citrate), which is part of the single shared system REMS, the Transmucosal Immediate-Release Fentanyl (TIRF) REMS Access Program.

We have completed our review of this supplemental application, as amended. It is approved, effective on the date of this letter.

**RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS**

The REMS for TIRF Products, of which ACTIQ (oral transmucosal fentanyl citrate) is a member, was originally approved on December 28, 2011, and the most recent REMS modification was approved on November 7, 2013. The REMS consists of a Medication Guide, elements to assure safe use, an implementation system, and a timetable for submission of assessments of the REMS.

Your proposed modifications to the TIRF REMS, including appended REMS materials as applicable, consist of the following:

1. Removal of NDC Numbers from the following:
  - i. Independent Outpatient Pharmacy Enrollment Form
  - ii. Chain Outpatient Pharmacy Enrollment Form

- iii. TIRF REMS Website
2. Removal of reference to generic equivalents of specific products and replacement with a footnote in the following:
  - i. Education Program for Prescribers and Pharmacists
  - ii. TIRF REMS Website
3. Removal of “Attachment 1: List of TIRF Medicines Available Only through the TIRF REMS Access Program,” and replacement with a hyperlink to the new TIRF REMS Webpage in the following:
  - i. TIRF REMS Document
  - ii. Overview for Prescribers
  - iii. Prescriber Enrollment Form
  - iv. Overview for Patients and Caregivers
  - v. Independent Outpatient Pharmacy Overview
  - vi. Chain Outpatient Pharmacy Overview
  - vii. Closed System Outpatient Pharmacy Overview
  - viii. Independent Outpatient Pharmacy Enrollment Form
  - ix. Chain Outpatient Pharmacy Enrollment Form
  - x. Closed System Outpatient Enrollment Form
  - xi. Inpatient Pharmacy Enrollment Form
  - xii. Distributor Enrollment Form
  - xiii. TIRF REMS Website and Website Landing Page
4. Revised criteria for inactivation of Patient-Prescriber Agreement Form (PPAF) in the TIRF REMS Document
5. Revisions to enhance knowledge about conversion of TIRF Medicines in the following:
  - i. Education Program for Prescribers and Pharmacists
  - ii. TIRF REMS Website
6. Information clarifying the process to electronically transmit TIRF REMS Cash Claims in the following:
  - i. TIRF REMS Document
  - ii. TIRF REMS Access Program Frequently Asked Questions (FAQ)
  - iii. Independent Outpatient Pharmacy Overview
  - iv. Chain Outpatient Pharmacy Overview
  - v. Closed System Outpatient Pharmacy Overview

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.

Your proposed modified REMS, submitted on May 21, 2014, amended on December 11, 2014, and appended to this letter, is approved.

The TIRF REMS Access Program currently includes the products listed on the FDA REMS website, available at <http://www.fda.gov/downloads/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/UCM309784.pdf>

Other products may be added to the TIRF REMS Access Program in the future if additional TIRF NDAs or ANDAs are approved.

The timetable for submission of assessments of the REMS will remain the same as that approved on June 5, 2012. There are no changes to the revised REMS assessment plan attached to our August 21, 2014, REMS Assessment Acknowledgment/REMS Assessment Plan Revisions letter.

In addition to the assessments submitted according to the timetable included in the approved REMS, you must submit a REMS assessment when you submit a supplemental application for a new indication for use as described in section 505-1(g)(2)(A) of the FDCA. Also, under section 505-1(g)(2)(C), 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.

If the assessment instruments and methodology for your REMS assessments are not included in the REMS supporting document, or if you propose changes to the submitted assessment instruments or methodology, you should update the REMS supporting document to include specific assessment instrument and methodology information at least 90 days before the assessments will be conducted. Updates to the REMS supporting document may be included in a new document that references previous REMS supporting document submission(s) for unchanged portions. Alternatively, updates may be made by modifying the complete previous REMS supporting document, with all changes marked and highlighted. Prominently identify the submission containing the assessment instruments and methodology with the following wording in bold capital letters at the top of the first page of the submission:

**NDA 020747 REMS CORRESPONDENCE  
(insert concise description of content in bold capital letters, e.g.,  
UPDATE TO REMS SUPPORTING DOCUMENT - ASSESSMENT  
METHODOLOGY)**

An authorized generic drug under this NDA must have an approved REMS prior to marketing. Should you decide to market, sell, or distribute an authorized generic drug under this NDA, contact us to discuss what will be required in the authorized generic drug REMS submission.

Prominently identify any submission containing the REMS assessments 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:

**NDA 020747  
REMS ASSESSMENT**

**NEW SUPPLEMENT FOR NDA 020747  
PROPOSED REMS MODIFICATION**

**NEW SUPPLEMENT (NEW INDICATION FOR USE)  
FOR N 020747  
REMS ASSESSMENT  
PROPOSED REMS MODIFICATION (if included)**

If you do not submit electronically, please send 5 copies of REMS-related submissions.

**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 Kimberly Compton, Senior Regulatory Project Manager, at 301-796-1191.

Sincerely,

*{See appended electronic signature page}*

Judith A. Racoosin, MD, MPH  
Deputy Director for Safety  
Division of Anesthesia, Analgesia, and  
Addiction Products  
Office of Drug Evaluation II  
Center for Drug Evaluation and Research

Enclosure:  
REMS

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**This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.**  
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/s/  
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JUDITH A RACOOSIN  
12/24/2014