Office of Prescription Drug Promotion

Internal Consults

****Pre-decisional Agency Information****

Please Note: The following review is for DRISK only and should not be used to provide comments to the sponsor.

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Date: June 27, 2017

Re: MF 027320
Transmucosal Immediate Release Fentanyl (TIRF) Products
Comments on draft Risk Evaluation and Mitigation Strategies (REMS) Materials [Submission date: June 9, 2017 (Sequence: 0029, 0030)]

Materials Reviewed

OPDP has reviewed the following proposed REMS materials for the TIRF Products:

- Healthcare Provider (HCP) REMS Materials:
  - Dear Healthcare Provider Letter: Safety Update
  - Chain Outpatient Pharmacy Enrollment Form

- Overview for Chain Outpatient Pharmacies
- Closed System Outpatient Pharmacy Enrollment Form
- Overview for Closed System Outpatient Pharmacies
- Wholesaler/Distributor Enrollment Form
- Education Program for Prescribers and Pharmacists
- Frequently Asked Questions
- Independent Outpatient Pharmacy Enrollment Form
- Overview for Independent Outpatient Pharmacies
- Inpatient Pharmacy Enrollment Form
- Overview for Inpatient Pharmacies
- Knowledge Assessment
- Patient-Prescriber Agreement Form
- Prescriber Enrollment Form
- Overview for Prescribers

- Direct-to-Consumer (Patient) REMS Materials:
  - Overview for Patients and Caregivers

- Websites
  - TIRF REMS Access Program: Web Prototype

The version of the draft REMS materials used in this review can be found at: \\CDSESUB1\evsprod\MF027320\027320.enx

OPDP offers the following comments on these draft REMS materials for the TIRF products.

General Comment

Please remind the sponsors that REMS materials are not appropriate for use in a promotional manner.

OPDP notes the link **www.TIRFREMSaccess.com** and toll free numbers such as 1-866-822-1483. OPDP recommends that these items represent a direct link to only REMS related information and not be promotional in tone.

REMS Materials

OPDP does not object to including the following materials in the REMS program (please see Specific Comment[s] below):

- Healthcare Provider (HCP) REMS Materials:
  - Dear Healthcare Provider Letter: Safety Update
  - Chain Outpatient Pharmacy Enrollment Form
  - Overview for Chain Outpatient Pharmacies
  - Closed System Outpatient Pharmacy Enrollment Form

- Overview for Closed System Outpatient Pharmacies
- Wholesaler/Distributor Enrollment Form
- Education Program for Prescribers and Pharmacists
- Frequently Asked Questions
- Independent Outpatient Pharmacy Enrollment Form
- Overview for Independent Outpatient Pharmacies
- Inpatient Pharmacy Enrollment Form
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- Knowledge Assessment
- Patient-Prescriber Agreement Form
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Specific Comment[s]

OPDP considers the following statement[s] promotional in tone and recommends revising or deleting them from the REMS piece:

- Dear Healthcare Provider Letter: Safety Update

  - **Risk**
    - "Life-threatening respiratory depression could occur at any dose in opioid non-tolerant patients. Deaths have occurred in opioid non-tolerant patients treated with some TIRF medicines"

      The inclusion of this risk statement under the presentation of the Indication for these products minimizes the importance of this risk information. Consider revising the letter to include this information under the Contraindications header in a manner consistent with the approved PI.

      - "**Do not use TIRF medicines in opioid non-tolerant patients; death can occur**

        TIRF medicines are contraindicated for acute or post-operative pain management…"(bolded emphasis original)

        The utilization of bolded font for these risk statements may imply that these risk statements are more important than the remaining risk information presented under the Contraindications header. Consider

revising to present the information under this header in a similar text throughout the presentation. In addition, consider utilizing a separate bullet for each contraindication listed, similar to the presentation in the approved PI.

- Education Program for Prescribers and Pharmacists

  - **Risk**
    - "TIRF medicines are contraindicated in opioid non-tolerant patients because life-threatening respiratory depression and death could occur at any dose in patients not taking chronic opioids" (page seven)

    The inclusion of this risk statement under the presentation of the Indication minimizes the importance of this risk information. Consider revising this REMS piece to include this information under the Contraindications header on page nine, in a manner consistent with the approved PI.

- TIRF REMS Access Program: Web Prototype

  - Please apply our comments for the above presentations to similar presentations in the Web Prototype REMS document.

We have no additional comments on these proposed REMS materials at this time.

Thank you for your consult.

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

/s/

LATOYA S TOOMBS
06/27/2017