CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

22-266

MEDICAL REVIEW(S)

FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH
DIVISION OF, ANALGESIA, ANESTHESIA, AND RHEUMATOLOGY PRODUCTS
10903 New Hampshire Avenue, Building 22, Silver Spring, MD 20993

Clinical REMS Review

Application:	NDA 22-266
Drug Name:	Fentanyl Buccal Soluble Film (Onsolis™)
Sponsor:	Bio Delivery Sciences International (BDSI)
Submission Type:	Risk Evaluation and Mitigation Strategy (REMS) Document
Date:	6/11/09
Reviewer:	Elizabeth Kilgore, M.D.
Team Leader:	Ellen Fields, M.D., MPH
Project Manager:	Kimberly Compton

Background: Onsolis™ is a transmucosal formulation of fentanyl developed for the management of breakthrough pain (BTP) in opioid tolerant cancer patients. It is indicated only for patients 18 years of age and older who are already receiving opioid therapy for underlying persistent cancer pain. The drug would be available in five dosage strengths: 200, 400, 600, 800, and 1200 mcg.

The Sponsor submitted a proposed Onsolis Risk Minimization Action Plan (RiskMAP) on October 31, 2007, with subsequent amendments to the RiskMAP on March 20, April 11, and May 7, 2008.

Title IX, Subtitle A, Section 9901 of FDAAA amends the FDCA to authorize FDA to require the submission of a Risk Evaluation and Mitigation Strategy (REMS) if the Secretary determines that such a strategy is necessary to ensure that the benefits of a drug outweigh the risks (section 505-1(a)(1).

A Complete Response (CR) letter was issued to the Sponsor on 8/25/08 notifying them that NDA 22-266 (including amendments) could not be approved without a REMS to ensure that the benefits of Onsolis (analgesia) outweigh the risks (overdose, abuse, and accidental exposure). The Sponsor was further informed that the elements of the REMS must include a Medication Guide, a Communication Plan, Methods to Assure Safe Use, and a Timetable for Submission of Assessment of the REMS.

The Sponsor subsequently submitted their proposed REMS and REMS Supporting Document on 12/9/08.A final review is to be completed by OSE. This clinical review will address the Sponsor's proposed REMS as it pertains to clinical issues.

Overview of Onsolis REMS

I. Goals:

- [redacted]
- [redacted]
- [redacted]

b(4)

II. REMS Elements:

- **Medication Guide (MG)**
  - Onsolis will be packaged in child-resistant foil packages supplied in cartons containing 30 films.
  - Three copies of the MG will be distributed with every carton (one copy as part of the Prescribing Information and two extra copies will be separated from the combined Prescribing Information/Medication Guide by perforations).
  - If less than 30 films are dispensed, the Program pharmacist will separate a perforated MG and supply it to the patient.

- **Communication Plan**
  - "Dear Prescriber Letter", "Dear Pharmacist Letter" b(4)
  - [redacted]

- **Elements to Assure Safe Use**
  - Enrollment forms for prescriber, patient, wholesaler and pharmacy
  - Healthcare providers who **prescribe** Onsolis are educated and enrolled in the Onsolis specific program and must attest to certain elements of understanding regarding the drug

- Each patient **treated** with Onsolis is to be counseled and enrolled in the Onsolis program for documentation of safe use conditions and must attest to understanding certain elements of the drug
- [redacted] b(4)
- Pharmacies, practitioners, or healthcare settings that **dispense** Onsolis are educated and enrolled in the program and must attest to following certain procedures for dispensation of the drug, including auditing and reporting.

III. Implementation System:

- [redacted], receive Onsolis program enrollment faxed forms; answer questions b(4)
- Onsolis program database will be available of all enrolled participants including prescribers, patients, wholesalers, and pharmacies
- Distribution and prescription data monitoring plan will be available
- [redacted] b(4)

IV. Timetable for Submission of Assessments:

- The program is to be assessed every 6 months for the [redacted] after approval of the NDA and annually thereafter b(4)
- Assessments are to be submitted to FDA within 60 days after the close of the respective assessment interval

V. Information Needed for Assessments:

- The Sponsor submitted this information in the REMS Supporting Document and identified the following components as necessary for assessments
  - Knowledge, attitude and behavior (KAB) surveys
  - Prescriber and pharmacy education and enrollment report from the Onsolis Program database
  - Program effectiveness report
  - Medication Guide for Onsolis distribution and dispensing report
  - Distribution and dispensing failures report

Discussion: There have been ongoing negotiations between the Sponsor and the Agency regarding the content of the REMS. The final negotiated form is acceptable to the Division. The REMS will be sent to SWAT and Safety Review Team (SRT) for final Agency clearance.

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/s/

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6/11/2009 03:42:16 PM
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/s/

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6/11/2009 12:58:59 PM
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