Compton, Kimberly

From: Compton, Kimberly
Sent: Friday, April 03, 2009 6:41 PM
To: 'David T. Wright'
Subject: FU on Onsolis items

Hi Dave,

I just wanted to give you some feedback on a few items from our TC yesterday and then let you know a few new things that came up today on Onsolis.

From yesterday:

1. TM, copyright, etc. symbols in the PI--according to the guidelines for PLR and SPL formatting provided by our SEALD TEAM the "TM", "R" and other symbols should not be used after drug names in Highlights or the Table of Contents. They may be used only once in the content of labeling (Full Prescribing Information). We have edited this into the version of the PI we will be clearing with Dr. Rappaport upon his return and so you will see it reflected there when we email that to you.

2. Regarding working on just the text version of the letter(s) discussed yesterday and submitting the web-based mock-up after agreement on the content is reached, it will be acceptable to work on the text-only version of the letter(s) in question, but before final agreement is reached, a mock-up of the web-version of the document will need to be reviewed as well. Please submit the proposed letter(s) for review as soon as possible.

3. OSE estimates they will have preliminary carton/container label feedback in the next week or so.

4. The nonclincial team plans to review the proposed label change to the pregnancy section you emailed us yesterday by next week.

New items:

1. As there is very limited time remianing in the rvw cycle, we would like to request that BDSI go ahead and submit whatever materials or pieces they have as soon as they are ready (i.e., don't hold pieces to group together, await additional Agency input, etc.)

2. To facilitate final review and negotiation of the REMS, we plan to schedule one-hour mtgs once weekly (beginning in approximately two weeks) which we will use only on an as needed basis to discuss any remaining or outstanding issues either internally or with BDSI. We respectfully ask that BDSI set aside these times to be available to interact with the Agency on the REMS and finalization of the product review duirng the designated times (I will email you a list once I develop it. Probably early next week.)

3. Please clarify when the patients and prescribers are actually registered in the program (i.e., once the form is sent? Rec'd? Scored? Once 100% correct answers are rec'd?, etc.)

I hope you have a nice weekend,
Kim

Kimberly Compton

Kimberly Compton, R.Ph.
Regulatory Project Manager
Division of Anesthesia, Analgesia and
Rheumatology Products (HFD-170)
301-796-1191

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

/s/

Kimberly Compton
4/8/2009 05:46:01 PM
CSO

Compton, Kimberly

From: Compton, Kimberly
Sent: Monday, March 16, 2009 8:03 PM
To: David T. Wright
Cc: Stradley, Sara
Subject: REMS comments and questions for Onsolis
Attachments: N 22-266 OSE Comments and questions sent to firm 3-16-09 .doc

Hi again Dave,

OSE has forward us a set of questions and comments they have regarding the REMS submission and we are forwarding that on here.

Again, please share this with your team and provide a response (this time it should be a formal amendment to the NDA) as soon as it is ready. As many of the REMS items are inter-related and inter-dependent on one another, we prefer a response to all items mentioned in this attachment at one time, rather than receiving pieces separately.

Please let us know if you have any questions about our requests.

<<N 22-266 OSE Comments and questions sent to firm 3-16-09 .doc>>

Thanks

Kim

Kimberly Compton

Kimberly Compton, R.Ph.

Regulatory Project Manager

Division of Anesthesia, Analgesia and

Rheumatology Products (HFD-170)

301-796-1191

FDA Comments on ONSOLIS REMS Proposal

Sponsor: Biodelivery (NDA 22-266)

Submission Date: December 12, 2009

We have the following preliminary comments on the proposed REMS for Onsolis. We expect to have additional comments as the review of your application progresses.

Comments on Proposed REMS

I. **Goal** – Revise the goals to be clear and concise in describing the ultimate REMS goal. An example is provided below:

To mitigate the risk of overdose, abuse, addiction, and serious complications due to medication errors by:

A. Ensuring proper patient selection, including avoidance of use of ONSOLIS in opioid non-tolerant patients;
B. Preventing exposure to ONSOLIS in persons for whom it was not prescribed, including accidental exposure in children.
C. Training healthcare prescribers, pharmacists, and patients about proper dosing and administration

II. **REMS ELEMENTS**

A. **Medication Guide** – The language in the REMS is acceptable; the medication guide will need to be revised. Comments on the Medication Guide will be sent separately (these were included in the version of the PI/MG emailed on 3-16-09).

B. **Communication Plan** –

a. Provide a description of the target population for the communication at the time of market launch; use modified language from the REMS supporting document: healthcare providers in the following specialties who prescrib[redacted]of the total prescriptions for oral transmucosal fentanyl products: pain management specialist who are comprised of anesthesiologist, physical medicine and rehabilitation physicians, general practitioners and oncologist and oncology nurse practitioners will receive FOCUS program materials and list the materials. b(4)

b. List the materials that will be distributed at launch, such as[redacted]Pharmacist letter. b(4)

c. List all education materials and enrollment forms in the "Elements to Assure Safe Use" in the REMS and REMS supporting document.

C. **Elements to Assure Safe Use**

1. **Include the following in prescriber enrollment and certification:**

- prescribers must complete the prescriber enrollment form and fax the form the FOCUS program,
- prescriber enrollment must include verification that the prescriber understands the risk (s) of ONSOLIS and the FOCUS Program components. This should be accomplished through a "quiz" at the completion of the prescriber education with a required percentage for successful completion,
- prescribers are required to be re-educated and re-enrolled following substantial changes in the FOCUS program or at an interval of at least every year, whichever occurs first.
- BDSI will maintain a database of all certified prescribers in FOCUS. BDSI must monitor to ensure that only certified prescribers are prescribing ONSOLIS
- The prescriber education materials and enrollment forms for prescribers should be listed in the proposed REMS under this element and should also be appended to the REMS.

2. **Include the following in documentation of safe use conditions:**

- the prescriber and patient will be required to complete the patient enrollment form and the prescriber faxes the prescription to the FOCUS program,
- the patient is given a unique patient identifier
- b(4)
- the hard-copy of the prescription is received by the FOCUS pharmacy before the prescription is dispensed and
- patients are required to re-counseled and re-enrolled following substantial changes in the FOCUS program or at an interval of at least every year, whichever occurs first. If the patient transfers to another prescriber, the patient and new prescriber will complete a new FOCUS enrollment form.

- describe the procedure for putting a patient in an inactive status

- The patient education materials and enrollment form for patients should be listed in the proposed REMS under this element and appended to the REMS.

3. **Include the following in pharmacy enrollment and certification:**

   - BDSI has designed a controlled distribution system to deliver ONSOLIS using the following pharmacies for dispensing ONSOLIS: a central, nationwide, specialty mail-order FOCUS pharmacy (ies) and regional, large oncology practice FOCUS pharmacies. Prescriptions will only be dispensed after confirmation that the prescriber and patient are enrolled and active and that the hard-copy of the prescription has been received. Prescriptions will be shipped by traceable courier with adult signature required;

   - pharmacies are required to provide a medication guide with each shipped prescription

   - pharmacies are required to be re-educated and re-enrolled following substantial changes in the FOCUS program or at an interval of at least every year, whichever occurs first.

   - The pharmacist education materials and enrollment form for pharmacies should be listed in the proposed REMS under this element and appended to the REMS.

D. **Program Implementation** – revise your Implementation System to include the following:

   - [illegible]

   - monitor for any potential gaps in therapy related to the procedures for dispensing the drug.

   - the FOCUS program database should be an integrated, computerized, validated database that captures enrollment, patient tracking and drug distribution data;

Comments on the REMS Supporting Document – The proposed REMS supporting document is incomplete and will need additional details as noted above and below in order for us to complete our review.

Regarding the Elements Elements to Assure Safe Use:

- Provide your proposal for testing prescribers at the time of enrollment.

- Explain how pharmacists will be trained and enrolled; we propose that you have each pharmacy keep documentation of pharmacist training. The pharmacy enrollment form should be signed by the administrator of the pharmacy.

- Explain how many large oncology practices will be enrolled; provide a listing of these practices in the supporting document.

- Describe how seriously incapacitated patients will be counseled and obtain their prescription from the large oncology practice pharmacies. Include this procedure in the supporting document.

- Clarify how medication will be provided for hospitalized and hospice patients (discussed in March 6, 2009 telecon; follow-up pending from BDSI).

- [redacted] b(4)

- Describe the monitoring system which triggers re-training of prescribers (section 6.3.1).

- Describe the monitoring system which triggers re-training of patients (section 6.3.2).

- Clarify how BDSI will be notified when a patient is transferred to another prescriber.

- Describe what information the pharmacies will provide in the FOCUS program report and how often that report will be sent (section 6.3.4).

- Clarify if the pharmacies will use a check list to ensure that all the conditions for prescribing have been met – enrollment of prescriber and patient, counseling of the patient (initial prescription only), and medication guide provided to patient (each prescription).

- Describe when and how patients will receive their medication guides in relation to the counseling. Note, they should receive a medication guide with each prescription.

- Describe the corrective action taken for late delivery of prescriptions.

- Clarify if there will be a procedure for patients to obtain a prescription if their prescriber is inactivated.

Regarding the Information Needed for Assessment (section 6.6 of supporting document) –provide the following additional information necessary for the assessment; address the issues included below:

- Reports on the status of the training and enrollment of prescribers, patients, and clinical administration sites; cumulative and for the reporting period.

- Reports on periodic assessments of the distribution and dispensing of the Medication Guide in accordance with 21 CFR 208.24; section 6.6.4 states that FOCUS program will list any prescriptions that have been filled without an accompanying MG, how will that information be obtained?

- Reports on the status of FOCUS counseling of patients before receiving ONSOLIS and how this information on counseling will be obtained

- A report on periodic audits of the pharmacies and wholesalers

- A report on the extent of use by pharmacy site; central FOCUS pharmacy versus regional, large oncology practice FOCUS pharmacies

General Comments

- Submit your proposed REMS and other materials in WORD format. It makes review of these materials more efficient and it is easier for the web posting staff to make the document 508 compliant. It is preferable that the entire REMS and appended materials be a single WORD document. 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 be in a single WORD document.

- For posting purposes, submit the revised REMS documents in WORD, electronically. The "old" revised material will be extracted and replaced with the revised document(s) as part of the entire REMS. You do not need to resubmit the entire REMS. For each Word document you provide you should submit a corresponding PDF including both clean and track changes versions.

- Comments on the educational materials, surveys, and enrollment forms will be coming in the next few weeks

- **ONSOLIS Program Website** – The website should stand-alone and should only include REMS approved materials. The website should not reference or link to external websites. The website may provide links or display the approved educational materials, approved MG, and approved package insert. The website should not be a means to promote ONSOLIS or any other BDSI product.

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

/s/

Kimberly Compton
4/8/2009 05:41:54 PM
CSO