Compton, Kimberly

From: Compton, Kimberly
Sent: Friday, April 17, 2009 7:39 PM
To: 'David T. Wright'
Cc: Compton, Kimberly
Subject: RE: NDA 22-266 - ONSOLIS REMS Review Teleconferences
Attachments: N 22-266 REMS educational materials comments 4-17-09.doc

Hi Dave,

Attached please find a copy of our most recent set of comments on the REMS materials, while only some of the changes are in track mode, I believe the others are described well enough so BDSI can locate them in the specific documents. Please let me know if you have any trouble with them.

Thanks for the labeling, I will share it with the team.

Thanks,
Kim

From: David T. Wright [mailto:DTWright@bdsinternational.com]
Sent: Friday, April 17, 2009 4:20 PM
To: Compton, Kimberly
Subject: RE: NDA 22-266 - ONSOLIS REMS Review Teleconferences

Thanks for your rapid reply Kim!

We look forward to further discussions and hopefully reaching agreement on the PI/MG next Wednesday. In this regard, please find attached now additional BDSI tracked changes in the version attached to your email yesterday.

Regarding the additional REMS comments you mention below, will these be sent in MS Word tracked changes to the documents provided in NDA Sequence 0033?

Regarding the pediatric development plan, prior to our teleconference next Wednesday, I hope to be able to provide a brief response to each of your 3 points below.

Have a nice weekend!

Best regards, Dave

David T Wright, PhD, RAC
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From: Compton, Kimberly [mailto:Kimberly.Compton@fda.hhs.gov]
Sent: Thursday, April 16, 2009 5:05 PM
To: David T. Wright
Subject: RE: NDA 22-266 - ONSOLIS REMS Review Teleconferences

Hi Dave,

I was just about to email you. We have a lot to convey today.

1st off, yes, we would like to utilize our TC for next Wed 4-22 at 3 PM. We are happy to discuss the PI/MG (I have attached our latest version with changes shown). As you observe we do only have a few points that seem to be outstanding, however, we will not be able to make final agreement until Sr. Mgmt is able to rvw the final label and give their OK. So, after we iron out those couple of points you mention, we will present Sr. Mgmt with a clean copy of the label and (hopefully) get their OK. If they have changes however, we will FWD those along and have discussion on them as needed.

In addition, I will be sending you (I believe they will be ready tomorrow) additional comments on the REMS materials (mostly the educations components, etc) and will be prepared to discuss those during our TC next week also.

I think a good topic to discuss in the TC is how the order of/ how the team envisions reaching agreement on all the REMS pieces.

In addition, we are working on the other aspects of the review that will prepare the application for approval if we reach agreement on all the pieces and that includes the pediatric plan/materials, etc. In that vein we need to come to agreement on a pediatric plan/studies for Onsolis and present it to our internal Pediatric Research and Review Committee. Therefore, please review the below and submit the requested materials as soon as possible.

> In order to fulfill the pediatric study requirements under PREA, studies must be based on the proposed/approved adult indication.
>
> In general, the PREA requirements are that you carry out a study(ies) to assess the pharmacokinetics, safety, and efficacy in the pediatric population for the *proposed indication*.
>
> The study in the Written Request issued 28 June 2007 could fulfill the requirements for PREA. The Pediatric Plan, as agreed upon between the Division and the Sponsor must be presented to the Pediatric Research and Review Committee (by the Division) prior to Approval.

We therefore request you submit the following by as soon as possible:

1. A commitment to study the pharmacokinetics, efficacy and safety of ONSOLIS in the pediatric population older than [redacted] (You do not need to submit protocols at this time.)

2. A timeline that includes: dates of protocol submissions, dates of start of studies, dates of study completion, and dates of submission of final study reports to the Agency.

3. Inform us whether you plan to use the study outlined in the Written Request in order to fulfill your PREA commitment.

We note your requests for a partial waiver for study in patients [redacted] and younger, and for deferral of the initiation of studies, which both appear acceptable at this time.

b(4)

b(4)

We're happy to use the BDSI call in info you set up and provided below.

Thanks,
Kim

From: David T. Wright [mailto:DTWright@bdsinternational.com]
Sent: Thursday, April 16, 2009 4:35 PM
To: Compton, Kimberly
Subject: NDA 22-266 - ONSOLIS REMS Review Teleconferences

Kim:

When will you be able to confirm whether or not our REMS review teleconference, tentatively scheduled for Wednesday, 22 April at 3:00 PM, will take place?

Is it reasonable to plan on reaching agreement on the prescribing information / medication guide during our first REMS review teleconference? Since there are only two remaining tracked change concepts in the version I emailed to you last Thursday (ie, the inclusion of 1-877-4ONSOLIS and the reproductive toxicology coverage text), is it reasonable to expect that we can also discuss Agency comments on the REMS enrollment forms and/or other REMS documents during this meeting?

Since the REMS, REMS supporting document, and REMS supporting document appendices are comprised of 17 individual documents, what is the planned order for discussing and reaching agreement on these documents?

Should we plan on using the following BDSI teleconference numbers for our REMS review teleconferences:
- 866.519.2804, and
- passcode – 433416?

We look forward to talking to you and your team soon!

Thanks in advance for your reply.

Best regards, Dave

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FDA Comments on ONSOLIS REMS Proposal

Sponsor: Biodelivery (NDA 22-266)

Submission Date: December 12, 2009

Date of Comments: April 9, 2009

We have the following preliminary comments on the proposed REMS educational materials and other materials that have been submitted as part of the REMS.

The following documents for the Onsolis REMS have been reviewed:

- Dear Prescriber Letter
- Dear Pharmacist Letter
- b(4)
- Program Overview
- Prescriber Enrollment Form
- Patient Enrollment Form
- Wholesaler Enrollment Form
- Pharmacy Enrollment Form
- HCP Website
- b(4)
- Prescriber Enrollment Confirmation
- Patient Enrollment Confirmation
- Pharmacy Enrollment Confirmation
- Patient Record Status Form

I. General comments

- Specialty pharmacy education is lacking for this program. The REMS Supporting Document lists the same materials for both prescriber and pharmacist training but it's not clear how the pharmacy is trained on the actual procedures, for example how they verify that prescribers and patients are enrolled, how they ensure patients have been counseled. If the web based program and word document program are to be used to educate the pharmacist, the Pharmacy Enrollment form will need to be added to the web based program.

- All changes made to the materials listed above will need to be resubmitted for review. Submit these materials in a Word format to allow for more efficient review.

- REMS materials are not appropriate for use in a promotional manner.

- Modify the REMS Goals so they are consistent in all educational materials to read:

    1. Preventing use of Onsolis in opioid non-tolerant patients.

    2. Preventing misuse, abuse and overdose of Onsolis.

3. Preventing exposure to Onsolis in persons for whom it was not prescribed, particularly children.

- Physicians and patients will be re-enrolled in the program once a year and following substantial changes in the FOCUS Program.

- Define the concept "substantial changes" in regard to the FOCUS Program.

- Reflect comments on the materials in the proposed REMS and REMS Supporting Document.

II. Comments on the *Dear Prescriber Letter* and the *Dear Pharmacist Letter*

The Prescriber and Pharmacist Letters are not well organized and contain a lot of promotional language. The most important safety information and safety messages should follow the introductory paragraph describing the drug. This should then be followed by a description of the FOCUS Program with an explanation of the reason the FOCUS Program is being implemented. Below are specific comments on some of the language in the letters.

- Remove the statement "[redacted]" This information is already covered in the letter and is promotional. This can be replaced by another letter heading such as "Important Prescribing Information About Onsolis (fentanyl buccal soluble film)." b(4)

- The statement "[redacted]" is promotional in tone. Remove this statement from the first paragraph. We recommend language such as "MEDA Pharmaceuticals is introducing Onsolis, a new treatment indicated only for breakthrough pain in patients with cancer, 18 years of age and older. Onsolis can be used in patients who are already receiving and who are tolerant to opioid therapy for their underlying persistent cancer pain." b(4)

- We do not believe it is necessary to include a picture of the actual tablet sizes. If you want to include this information, it should be included closer to the end of the letter.

- Revise the below-indicated paragraphs as follows (strikethrough indicates text deletion, underlining indicates text addition):

b(4)

[redacted] b(4)

- The statement, ' [redacted] is promotional in tone. Remove this statement from the fourth paragraph. b(4)

- Under the section **Important Safety Information**, remove the percentages behind the adverse events. The percentage symbol is not consistent with the prescribing information.

- The following statements minimize the risks of the drug. Revise them accordingly:

[redacted] b(4)

III. Comments on *the Focus Program for ONSOLIS (Prescriber Training Guide)*

- Clarify whether this material is to be used to train prescribers, pharmacists, or both. Your submission indicates that this is prescriber training, however the REMS Supporting Document lists this and other materials as training materials for both prescribers and pharmacists.

- Page 2 - revise the promotional claim in bolded text on Page 2 of this document as follows:

[redacted] b(4)

- Page 2 - In the section titled "Complete Patient Counseling and Enrollment" revise the bullets as follows:

[redacted] b(4)

- Page 2 - In the section titled "Initiate Delivery Process" describe how the prescribers receive the pre-paid, pre-addressed courier envelopes.

- Page 3 – see changes as shown below:

b(4)

- Page 4 – see changes as shown below:

b(4)

- Page 11 – Provide an explanation about how the pharmacy verifies that both the prescriber and patient are enrolled

- Page 11 – revise the following statements as follows:

  - [redacted]
  - [redacted]

b(4)

IV. Comments on the *Program Overview*

- See first, second, third, and fourth comments under # 3 above.

V. Comments on the *Prescriber Enrollment Form*

- Include the following introductory statement to form: "I understand that Onsolis is available only through the FOCUS Program and I agree to comply with the program requirements and acknowledge that:"

- Delete the statement [redacted]

- Revise the below-indicated statements as follows:

b(4)

b(4)

VI. Comments on the *Patient Enrollment Form*

- Revise the below-indicated statements as follows:

b(4)

- Add the following language to Statement 1 in the patient information section- "I have asked my prescriber all the questions I have about my Onsolis therapy."
- Statement on 2 in the patient section states [redacted] b(4) This statement is misleading as there are also serious risks to patients who do take Onsolis as directed. Revise this statement so it is not so misleading.
- Under the Patient Authorization for Disclosure and Use of Health Information Statement—
    - Clarify in patient-friendly language what it means to de-identify their health information.
- [redacted] b(4)

- Patients should automatically receive a copy of the Authorization form after signing the consent form.

VII. Comments on the *Wholesaler Enrollment Form*

- The form, as currently written, is not directed to designated individual with authority to sign for the wholesale. Identify who (e.g., Sales Director, etc.) will sign the form. Change the signature authority to better represent the responsible party.

- Describe what is meant by [redacted] Onsolis shipping reports to be sent to the FOCUS Program. b(4)

VIII. Comments on the *Pharmacy Enrollment Form*

- Identify who 'I' is referring to in the confirmation statements. The form, as currently written, is directed to the pharmacy instead of a pharmacist. Clarify whether the pharmacy is enrolled or the whether the program requires individual pharmacist enrollment. If the former, identify who will be able to receive and sign the form, and describe how the individual signing the form will ensure that relevant staff are adequately trained and educated about the FOCUS Program.

  - If individual pharmacists are required to sign the form, remove the first confirming statement. Replace with the following statement: 'I have reviewed the training and educational material for the FOCUS Program and understand the risk and benefits of chronic opioid therapy.'

  - If pharmacies are enrolled, revise sentence #1 to read: " I will ensure and document that all pharmacists at this site are educated about the FOCUS program for Onsolis"

  - If the individual pharmacists are enrolling, statements 2 and 3 are okay, if the pharmacy is enrolled, the statement needs to be revised so that the responsible pharmacist is attesting that he/she "will ensure that the staff pharmacists will only dispense Onsolis" or "will not substitute", etc. In other words, the responsible pharmacist needs to acknowledge or confirm these statements for the pharmacy/staff pharmacists not only for his or herself.

- Include the following introductory statement to form: "I understand that Onsolis is available only through the FOCUS Program and I agree to comply with the program requirements and acknowledge that:"

- Regarding statements under #2:

  - Regarding a- it would be helpful to include who the pharmacist/pharmacy contacts to obtain verification

  - Regarding b and c- clarify if the pharmacy is required to counsel the patient or whether their role is only to ensure that counseling has occurred e.g., by the [redacted] or the prescribing physician
  - Regarding d- the Medication Guide is generally dispensed with the prescription. It is not usually provided ahead of every prescription. Revise this statement as a separate statement, for example - [redacted] b(4)

- Change signature authority to better represent the responsible party; for example "Pharmacy Manager Signature"

IX. Comments on the *HCP Website*

- Provide the following changes to the Program objectives wherever they are listed on the website. The FOCUS Program for Onsolis will: 1) ***Provide education to*** prescribers, patients and caregivers regarding the safe use of ONSOLIS 2) ***Facilitate access*** to Onsolis educational material and 3) Provide information and prescriber support for Onsolis by calling 1-877-4ONSOLIS (1-877-466-7654) or visiting www.Onsolis.com.

- Remove the promotional statement that [redacted] b(4)

- In general the information on this website is very dense (particularly the sections on proper patient selection, risks, and dosing and administration); written in paragraphs rather than bulleted comments. Please revise the materials to make them less dense and easier to follow.

- In the section, "Risks of Onsolis," there are links to Consensus Statement and Substance Abuse in Brief Fact Sheet; as you will have no control over the content of these documents, you will need to ensure that the links are properly maintained.

- The HCP website materials will need to reflect the previous comments on other materials (above).

- Remove the statement, [redacted] from the top of each page of the website. DDMAC is concerned that this claim implies that the REMS program is guaranteed to make the drug inherently safer, when this is not the case. Furthermore, DDMAC is concerned that the use of the term [redacted] implies that the REMS program will make it easier for patients to get the drug. b(4)

- On the Prescriber Education and Registration page titled *Prescriber Education and Enrollment*, change the introductory sentence to read, "Before you can enroll in the FOCUS Program for ONSOLIS **or prescribe Onsolis,**" you must complete the Prescriber Education.

- On the first page of the Dosing and Administration section (under Appropriate product dosing and administration), remove the promotional statement [redacted] b(4)

- On the first page of the "Risks of ONSOLIS" section, delete the following promotional claim in bolded text: [redacted] b(4

X. Comments on [redacted] b(4)

b(4)

b(4)

b(4)

b(4)

XI. Comments on [redacted]

b(4)

XII. Comments on the Prescriber Enrollment Confirmation Form

- Remove the promotional statement that ' [redacted] ' from the section for Patient Registration. b(4)

XIII. Comments on the Patient Enrollment Confirmation Form

- Under the Second and Subsequent Prescriptions, indicate that a prepaid, pre-addressed courier envelope is provided to send the courier the hardcopy of the prescription to the FOCUS pharmacy to stay consistent with the information provided in The FOCUS Program for Onsolis training manual's 3-Step Focus Program Process.

XIV. Comments on the Pharmacy Enrollment Confirmation Form

- If the response to #9 above is that individual pharmacists need to enroll, change the heading of the form to Pharmacist Enrollment Confirmation.

XV. We have reviewed these documents and do not have comments on the following materials at this time:

- Patient Record Status
- Prescriber Enrollment Request for Missing Information Form
- Prescriber Enrollment Request
- Patient does not meet FOCUS Program Requirement
- Pharmacy Enrollment Request for Missing Information
- Patient Discontinuation Confirmation
- Prescriber FOCUS Program Non-Compliance
- Pharmacy FOCUS Program Non-Compliance
- Wholesaler FOCUS Program Non-Compliance

As we continue our review, additional comments on these all REMS materials will be sent to you.

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
4/24/2009 04:45:40 PM
CSO