Compton, Kimberly

From: Compton, Kimberly
Sent: Friday, May 01, 2009 6:54 PM
To: 'David T. Wright'
Cc: Compton, Kimberly
Subject: May 1 Comments for N 22-266

Hi Dave,

Below is today's set of comments on Onsolis. There were a few outstanding points from that we did not get to in our TC on 4/27/09 and then some comments on the surveys.

General Comments of the REMS and/or REMS Supporting Document

Regarding your replies sent Apr 9, 2009; page 10

i. Item b: Explain how pharmacists will be trained and enrolled, we propose that your have each pharmacy keep documentation:
The answer provided on page 11 does not address this.

ii. Item k: Clarify if the pharmacies will use a check list…
There was not answered

- Page 12 reports of status of training and enrollment should be cumulative and for the reporting period, that is not noted in section 6.6.2.

- **Page 42, section 6.6: Include language about your plans to analyze and summarize surveillance and monitoring activities for abuse, misuse and overdose and any intervention taken resulting from signals of abuse, misuse and overdose (in CR letter).**

- **Page 50, section 6.6.3.2: Remove [redacted] from list** b(4)

Regarding Timetable for Assessment, assessments should be completed at 6 months, one year, and annually thereafter.

Comments on Surveys

Physician survey:

The method you propose to define adequate comprehension of the education materials does not appear to be capable of demonstrating whether specific educational messages are being conveyed to the respondents. The evaluation is intended to assess the effectiveness of conveying specific educational messages about Onsolis and the FOCUS Program to the physicians. A more appropriate method to assess the effectiveness of conveying the specific educational messages would be to look at individual questions and determine if a pre-specified percentage of respondents answered that question correctly. Specify what percentage of total respondents has to get an individual question correct.

[redacted] b(4)

[redacted] A more appropriate method would be to use multiple

choice questions with specific correct answers. This method eliminates the interviewer trying to interpret the respondent's answer. Therefore, re-write the proposed questions into a multiple choice format, with an instruction to "Select all that apply" where applicable. The questions should be non-leading and non-biased. The proposed answer choices should be non-obvious and include an option of "I don't know".

Respondents who participate in the survey receive re-education. This can lead to a bias if they are surveyed again. To eliminate potential bias, respondents who have completed the survey should not be surveyed in any subsequent REMS evaluations. Add a statement to the "Control for bias" section in the methodology that states respondents who have completed the survey will not be surveyed again.

Patient survey:

The method you propose to define adequate comprehension of the education materials does not appear to be capable of demonstrating whether specific educational messages are being conveyed to the respondents. The evaluation is intended to assess the effectiveness of conveying specific educational messages about Onsolis and the FOCUS Program to the paitents. A more appropriate method to assess the effectiveness of conveying the specific educational messages would be to look at individual questions and determine if a pre-specified percentage of respondents answered that question correctly. Specify what percentage of total respondents has to get an individual question correct.

[redacted] A more appropriate method would be to use multiple b(4)
choice questions with specific correct answers. This method eliminates the interviewer trying to interpret the respondent's answer. Therefore, re-writethe proposed questions into a multiple choice format, with an instruction to "Select all that apply" where applicable. The questions should be non-leading and non-biased. The proposed answer choices should be non-obvious and include an option of "I don't know".

- Add a question to the survey that asks if a patient received the counseling call. For example:
    - Did you receive a counseling call from the FOCUS Program?
        a) Yes
        b) No
        c) I don't remember

- Add questions to the survey that ask if a patient received, read and understood the Medication Guide. For example:

    - Who gave you the Medication Guide for Onsolis? (Select all that apply)
        a) A doctor or someone in the doctor's office
        b) A pharmacist or someone at the pharmacy
        c) I did not get a Medication Guide for Onsolis

    - Did you read the Medication Guide?
        a) All
        b) Most
        c) Some
        d) None

    - Did you understand what you read in the Medication Guide?
        a) All

b) Most
c) Some
d) None

- Did someone offer to explain to you the information in the Medication Guide?
  a) Yes, my doctor or someone in my doctor's office
  b) Yes, my pharmacist or someone at the pharmacy
  c) No

- Did you accept the offer? Yes or No

- Did you understand the explanation that was given to you?
  a) All
  b) Most
  c) Some
  d) None

- Did or do you have any question about the Medication Guide? Yes or No (If Yes, list your question below) Note: This is an open text field that should be grouped/coded by the sponsor prior to submitting to FDA

- In the feedback text for question #1, add the following, "Onsolis should only be used one time per episode, and doses should be separated by at least 2 hours."

Respondents who participate in the survey receive re-education. To eliminate potential bias, respondents who have completed the survey should not be surveyed in any subsequent REMS evaluations.

- Add a statement to the "Control for bias" section in the methodology that states respondents who have completed the survey will not be surveyed again.

Thanks,
Kim

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

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/s/

Kimberly Compton
5/4/2009 12:51:42 PM
CSO

Compton, Kimberly

From: Compton, Kimberly
Sent: Thursday, April 30, 2009 7:07 PM
To: 'David T. Wright'
Cc: Compton, Kimberly
Subject: Onsolis Carton Labeling re: MG Statement

HI Dave,

I now have the feedback from our CMC and OSE groups on the Carton and Container labeling for Onsolis.

The only comment the team has at this time is that while the Medication Guide statement does appear on the carton labeling, it is not prominent and conspicuous in its current location and it does not utilize the current standard language for these statements. Therefore, revise the statement

[redacted] to read "Dispense the enclosed Medication Guide to each patient". b(4)

And, relocate the statement to the principal display panel.

Other than that I believe the carton and container labeling are acceptable. Please make the above revision and submit an amendment with the new versions to the NDA as soon as you're able.

Thanks
Kim

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

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/s/

Kimberly Compton
4/30/2009 07:10:32 PM
CSO

Compton, Kimberly

From: Compton, Kimberly
Sent: Thursday, April 16, 2009 5:05 PM
To: 'David T. Wright'
Subject: RE: NDA 22-266 - ONSOLIS REMS Review Teleconferences
Attachments: N 22-266 PI-MG -from FIRM 3-25-09 --USE FOR EDITS.doc

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. [redacted] b(4)
>
> 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 ———— (You do not need to submit protocols at this time.) b(4)

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 ———— and younger, and for deferral of the initiation of studies, which both appear acceptable at this time. 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

David T Wright, PhD, RAC
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28 Page(s) Withheld

_____ Trade Secret / Confidential (b4)

✓ Draft Labeling (b4)

_____ Draft Labeling (b5)

_____ Deliberative Process (b5)

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/s/

Kimberly Compton
4/24/2009 04:47:30 PM
CSO