

Compton, Kimberly

From: Compton, Kimberly
Sent: Thursday, March 20, 2008 11:01 AM
To: 'David T. Wright'
Cc: Safarik, Michelle; Compton, Kimberly
Subject: FW: check out the BEMA website

Hi Dave,

Our team has noted the following on BDSI's BEMA website as of today, March 20, 2008:

BDSI's Current BEMA Products In Development

BEMA Fentanyl (Breakthrough Pain in Patients on Opioids)

There is a clear need for additional narcotic agents in alternative dosage forms to provide rapid pain relief.

BEMA Fentanyl is expected to meet the need for new narcotics and will be ideal for:

- breakthrough pain in opioid-tolerant patients
- post-operative patients following step-down from IV narcotics; hospitalized patients or outpatients without IV access
- emergency rooms patients where available IV lines are limited or impractical

We have the following questions in regard to this:

1. How long has this been posted on your website?
2. What are your plans for this website and will you be posting any corrective messages?
3. How will you assess the potential for off-label use this has created in the scheme of your RiskMAP?
4. What elements of your risk minimization program will provide corrective actions to ensure that the postoperative and emergency room uses will be understood as dangerous and potentially fatal?
5. How will you measure the success of these corrective actions?
6. Has the information presented on your website promoting postoperative and emergency room use been presented in any other program, materials, or meetings?

We have also shared this information and our request for response with our colleagues in DDMAC and they may contact you directly with additional follow-up.

We require a full response to these questions in no more than one week.

Thank you,
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
3/25/2008 06:46:01 PM
CSO

Compton, Kimberly

From: Lostritto, Richard T
Sent: Wednesday, February 27, 2008 3:14 PM
To: Ysem, Xavier J
Cc: Al Hakim, Ali H; Compton, Kimberly; Harapanhalli, Ravi S; Mille, Yana R
Subject: RE: Established Name for NDA 22-266 drug product.

Hi Xavier,

I reviewed the materials that you and Kim sent me. Thank you both for the comprehensive and timely input.

After some internal discussion my feeling is that the closest data elements we have to describe this drug product's ESTABLISHED name using CDER's Data Standards Manual (DSM) is **(fentanyl buccal soluble film)**. That captures the drug name, the route of administration, and the dosage form (using the closest currently acceptable term of soluble film). We can quibble if it would be "film soluble" or "soluble film" in the established name.

As we discussed, "patch" does not seem to fit this case because the dosage form is bioerodible in something like 30 minutes. Patches don't do that; so patch seems out. **b(4)**

The term "BEMA" designation (as the abbreviation or spelled out) is too proprietary and inappropriate for use in the established name.

The term is not defined in the DSM and cannot be used in this case. **b(4)**

If this terminology of the established name is unacceptable to you and/or the OND Division, let's continue to work the problem through a meeting (one should do). There are options in terms of changing the DSM, but such things require a fair amount of time, effort, and planning.

Please include Ravi and Yana Mille on any such meeting.

Thanks,

Rik

From: Ysem, Xavier J
Sent: Tuesday, February 26, 2008 10:19 AM
To: Lostritto, Richard T
Cc: Al Hakim, Ali H; Compton, Kimberly
Subject: Established Name for NDA 22-266 drug product.

Rik,

Regarding the established name for NDA 22-266 DP I do favor the name 'Fentanyl Buccal Bioerodible Patch' instead of 'fentanyl bioerodible mucoadhesive proposed by the applicant. The considerations for this choice are given below. **b(4)**

According to the CDER Data Standard Manual, version 008, a patch is defined as "A drug delivery system that often contains an adhesive backing that is usually applied to an external site on the body. Its ingredients either passively diffuse from, or are actively transported from, some portion of the patch. Depending upon the patch, the ingredients are either delivered to the outer surface of the body or into the body. A patch is sometimes synonymous with the terms 'extended release film' and 'system'."

Based on that definition, which does not exclude application to an internal site on the body such as buccal application and sometimes synonymous of the term 'system' ("system" is not defined as a type of dosage form in the CDER Data Standard Manual), the dosage form of NDA 22-266 should be classified as patch. A name such as 'fentanyl buccal bioerodible patch' (compared to applicant's proposed 'fentanyl bioerodible mucoadhesive') seems in my opinion a better defined and concise established name for the proposed drug product.

b(4)

Notice that the use of BEMA™ Fentanyl as proprietary name is not considered here; only the appropriateness of the established name is discussed.

Please let me know your/NLC opinion.

Thanks,

Xavier

Xavier Ysern, PhD
FDA/ CDER/ OPS
Office of New Drug Quality Assurance
Division of Pre-Marketing Assessment I
10903 New Hampshire Ave.
Bldg. 21, Rm. 2550 Phone: (301) 796-1779
Silver Spring, MD 20993-0002 Fax: (301) 796-9747

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/s/

Kimberly Compton
3/25/2008 06:42:37 PM
CSO



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

FILING COMMUNICATION

NDA 22-266

BioDelivery Sciences International, Inc.
801 Corporate Center Drive
Suite 210
Raleigh, NC 27607

Attention: David T. Wright, PhD, RAC
Director, Regulatory Affairs

Dear Dr. Wright:

Please refer to your new drug application (NDA) dated and received October 31, 2007, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act, for TRADENAME (fentanyl bioerodible mucoadhesive _____, oral transmucosal 200, 400, 600, 800, and 1200 mcg

b(4)

We also refer to your submission dated November 21, 2007.

We have completed our filing review and have determined that your application is sufficiently complete to permit a substantive review. Therefore, this application is considered filed 60 days after the date we received your application in accordance with 21 CFR 314.101(a). The review classification for this application is **Standard**. Therefore, the user fee goal date is August 31, 2008.

At this time, we are notifying you that, we have not identified any potential review issues. Please note that our filing review is only a preliminary evaluation of the application and is not indicative of deficiencies that may be identified during our review.

All applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred. We note that you have not fulfilled the requirements. We acknowledge receipt of your request for a waiver of pediatric studies for this application for pediatric patients less than _____. And we acknowledge receipt of your request for a deferral of pediatric studies for this application for pediatric patients: _____

b(4)

NDA 22-266

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If you have any questions, call Kimberly Compton, Regulatory Project Manager, at (301) 796-1191.

Sincerely,

{See appended electronic signature page}

Bob A. Rappaport, M.D.

Director

**Division of Anesthesia, Analgesia, and
Rheumatology Products**

Office of Drug Evaluation II

Center of Drug Evaluation and Research

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/s/

Sara Stradley
1/11/2008 07:52:18 AM
for Bob Rappaport, MD

DSI CONSULT: Request for Clinical Inspections

Date: December 7, 2007

To: Constance Lewin, M.D., M.P.H, Branch Chief, GCP1, HFD-46

From: Kimberly Compton, Regulatory Health Project Manager
Division of Anesthesia, Analgesia, and Rheumatology Products,
HFD-170

Subject: **Request for Clinical Site Inspections**
Application: NDA-22-266
Sponsor: BDSI
Drug: BEMA Fentanyl (Fentanyl BioErodable Mucoadhesive) b(4)

Protocol/Site Identification:

The following protocols/sites essential for approval have been identified for inspection.

Site # (Name,Address)	Protocol #	Number of Subjects	Indication
Rohit Kapoor, MD Invisions Consultant, LLC 12602 Toepperwein, Suite 202 San Antonio, TX 78233	FEN-201 FEN-202	27 26	Management of breakthrough pain in cancer patients who are opioid tolerant
James North, MD Center for Clinical Research 145 Kimel Park Drive, Suite 330 Winston Salem, NC 27103	FEN-201 FEN-202	16 13	Management of breakthrough pain in cancer patients who are opioid tolerant

Domestic Inspections:

We have requested inspections because (please check all that apply):

- Enrollment of large numbers of study subjects
- High treatment responders (specify):
- Significant primary efficacy results pertinent to decision-making

- There is a serious issue to resolve, e.g., suspicion of fraud, scientific misconduct, significant human subject protection violations or adverse event profiles.
- Other (specify):

International Inspections:

We have requested inspections because (please check all that apply):

- There are insufficient domestic data
- Only foreign data are submitted to support an application
- Domestic and foreign data show conflicting results pertinent to decision-making
- There is a serious issue to resolve, e.g., suspicion of fraud, scientific misconduct, or significant human subject protection violations.
- Other (specify):

Goal Date for Completion:

We request that the inspections be performed and the Inspection Summary Results be provided by (inspection summary goal date) ***July 31, 2008***. We intend to issue an action letter on this application by ***August 29, 2008***. The PDUFA due date for this application is ***August 29, 2008***

Should you require any additional information, please contact Kim Compton at Ph: (301) 796-1191

Concurrence: (as needed)

Sharon Hertz, MD, Deputy Director
Ellen Fields, MD, Medical Reviewer

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/s/

Kimberly Compton
12/19/2007 06:57:02 PM