From:	Marchione, Carol </O=CEPHALON/OU=US01 ADMINISTRATIVE GROUP/CN=RECIPIENTS /CN=CMARCHIO>
To:	Levin, Penny; Napoletano, Matthew; Thibodeau, Laurie; Larijani, Susan; Narayana, Arvind; Richards, Suzanne
CC:	Floyd, Eric
Sent:	3/13/2007 9:36:58 PM
Subject:	Response from FDA Regarding Actiq Patient Testimonials
Attachments:	040929 20747-FAX FROM DDMAC ACT208.pdf

Please see second page on Misleading Presentation of Information. I think the Fentora patient case studies need to be evaluated in light of this. Carol

PLAINTIFFS TRIAL EXHIBIT
P-16318_00001

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

TRANSMITTED BY FACSIMILE

Tracie A. Parker
Senior Manager
Regulatory Affairs
Cephalon, Inc.
145 Brandywine Parkway
West Chester, PA 19380-4245

RE: NDA # 20-747
Actiq® (oral transmucosal fentanyl citrate)
MACMIS ID # 12674

Dear Ms. Parker:

This letter responds to Cephalon, Inc's (Cephalon) submission dated August 26, 2004 requesting comments on proposed promotional material for Actiq® (oral transmucosal fentanyl citrate). The Division of Drug Marketing, Advertising, and Communications (DDMAC) provides comments on the following proposed promotional material:

- Actiq Patient Profiles (ACT 208)

Since many claims and representations are similar or closely related, DDMAC's comments on a particular claim or representation apply to similar claims or representations in these and future promotional materials for Actiq.

Unsubstantiated Comparative Claims

You present multiple claims under the header, "Managing breakthrough pain," such as, "Prior treatment: Ibuprofen and Percocet" and "Prior treatment: MSIR®" in addition to claims that compare Actiq with "regular rescue medication." Such claims are misleading because they imply that there are other agents approved for the same indication as Actiq, when such is not the case. Therefore, DDMAC recommends deletion of any claims that make this misleading implication. We refer to our comments dated June 17, 2004 where we addressed this specific issue.

Lack of Important Contextual Information

You present claims such as, "'Now, if the pain breaks through an interrupts my homework, I use ACTIQ to help manage it'," "'At school, when I felt the pain coming on, I'd excuse myself to take an ACTIQ,'" and "Frequency: 5-6 breakthrough pain episodes per day." These and similar claims are misleading because they imply that it is appropriate for patients to consume

as many Actiq units as needed to control all episodes of breakthrough cancer pain per day, when such is not the case. The PI specifically states, "Once a successful dose has been found..., patients should limit consumption to four or fewer units per day." Therefore, DDMAC recommends including adequate and prominent context to avoid this misleading implication. We refer to our comment letter dated January 26, 1999 regarding a similar claim.

Misleading Presentation of Information

Throughout this proposed promotional piece, you present multiple claims based upon patient reported outcomes. For example, you present claims such as, "Pain used to ruin my appetite...until I started ACTIQ," "Uncontrolled pain deepened depression and anxiety," and "ACTIQ works...especially at night. It relieves the pain enough for me to go to sleep." These and other claims are misleading because they overstate the efficacy of Actiq by implying that Actiq has a positive impact on physical, role, and mental functioning, sleep, appetite, general health perception, and psychological well-being. Such claims need to be substantiated with adequate and well-controlled clinical trials using well-developed and validated instruments to assess the effects of Actiq treatment on physical, role, and mental functioning, sleep, appetite, general health perception, and psychological well-being.

You present the claim, "Regardless of pain pathophysiology, patients in clinical studies titrated to the same mean dose of 600 mcg." This claim is misleading because it implies that patients in all clinical studies titrated to a mean dose of 600 mcg, which is inconsistent with the PI. The PI specifically states that in a double-blind placebo controlled crossover study, patients were titrated to a mean Actiq dose of 789 ± 468 mcg.

You present the claim "Within 15 minutes of starting medication, patients using ACTIQ rated their pain relief at 67%...." This claim is misleading because it implies that onset of action will occur at any time period following commencement of administration, which is inconsistent with the PI. We refer to our comment letter dated March 4, 2004 regarding a similar claim.

Overstatement of Efficacy

You present the claim, "Portability, convenience and control." This claim of "control" is misleading because it implies that all patients will experience control of their breakthrough cancer pain with Actiq, which thereby overstates the efficacy of Actiq. We refer to our comment letter dated August 29, 2002 regarding this issue.

If you have any questions, please contact me by facsimile (301) 594-6771, or write to me at the Division of Drug Marketing, Advertising, and Communications, HFD-42, Room 8B-45, 5600 Fishers Lane, Rockville, MD 20857. DDMAC reminds you that only written communications are considered official.

In all future correspondence regarding this particular matter, please refer to MACMIS ID # 12674 in addition to the NDA number.

Sincerely,

{See appended electronic signature page}

Jialynn Wang, Pharm.D.
LT, USPHS
Regulatory Review Officer
Division of Drug Marketing,
Advertising, and Communications

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

/s/

Jialynn Wang
9/29/04 10:33:43 AM

TOTAL P.05

FAX COVER SHEET

DIVISION OF DRUG MARKETING, ADVERTISING AND COMMUNICATIONS
CENTER FOR DRUG EVALUATION AND RESEARCH
FOOD AND DRUG ADMINISTRATION
5600 Fishers Lane, HFD #42
Rockville, MD 20857

Date: September 29, 2004

To: Tracie A. Parker
Senior Manager
Regulatory Affairs
Cephalon, Inc.

Fax: 610-738-6642 **Phone:** 610-738-6339

From: Jialynn Wang, Pharm.D.
LT, USPHS
Regulatory Review Officer
Division of Drug Marketing, Advertising, and Communications

Fax: 301-594-6771 **Phone:** 301-827-2831

No. of Pages without cover sheet: 4

THIS DOCUMENT IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS ADDRESSED AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL AND PROTECTED FROM DISCLOSURE UNDER APPLICABLE LAW. If you are not the addressee, or a person authorized to deliver the document to the addressee, you are hereby notified that any review, disclosure dissemination, copying, or other action based on the content of this communication is not authorized and may be in violation of law. If you have received this document in error, please immediately notify us by telephone and return it to us by U.S. mail to: HFD-42; 5600 Fishers Lane, Rockville, MD 20857.