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January 12, 2007

OVERNIGHT COURIER 1/12/07

Division of Dockets Management
Food and Drug Administration (HFA-305)
Department of Health and Human Services
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Citizen Petition

Dear Sir or Madam:

The undersigned submits this petition, in quadruplicate, pursuant to Section 505(j)(2)(C) of the Federal Food, Drug and Cosmetic Act, and in accordance with 21 CFR 10.30 on behalf of a client requesting the Commissioner of the Food and Drug Administration to declare that the drug product, Oral Transmucosal Fentanyl Citrate, 1000 mcg and 1400 mcg, is suitable for consideration in an abbreviated new drug application (ANDA).

A. Action Requested

The petitioner requests that the Commissioner of the Food and Drug Administration declare that Oral Transmucosal Fentanyl Citrate, 1000 mcg and 1400 mcg, are suitable for submission as an ANDA. The listed reference drug product (RLD), upon which this petition is based, is Actiq® (oral transmucosal fentanyl citrate), 400 mcg, NDA 20-747 held by Cephalon, Inc. Actiq® is also approved in the 200 mcg, 600 mcg, 800 mcg, 1200 mcg and 1600 mcg strengths. All of the products are manufactured by Cephalon, Inc. (See copy of the page from the current Electronic Edition of the Approved Drug Products with Therapeutic Equivalence Evaluations, Attachment 1.) Therefore, the petitioner seeks a change in strength (from the approved strengths of 200 mcg, 400 mcg, 600 mcg, 800 mcg, 1200 mcg, and 1600 mcg to include the intermediate strengths of 1000 mcg and 1400 mcg) from that of the listed drug product to allow for the ability to titrate the patient to a dose between two currently approved doses.

B. Statement of Grounds

The Federal Food, Drug and Cosmetic Act provides for the submission of an Abbreviated New Drug Application for a drug product that differs in dosage strength from that of the listed drug provided the FDA has approved a petition that proposed filing such an application.

The RLD, Actiq® by Cephalon, Inc. is an oral transmucosal product that is currently approved in the strengths of 200 mcg, 400 mcg, 600 mcg, 800 mcg, 1200 mcg, and 1600 mcg of Fentanyl Citrate. The proposed drug product also represents an oral transmucosal dosage form, but containing the intermediate strengths of 1000 mcg or 1400 mcg of Fentanyl Citrate. The petition is thus seeking a change in strength (from approved doses of 200 mcg, 400 mcg, 600 mcg, 800 mcg, 1200 mcg, and 1600 mcg to include the intermediate strengths of 1000 mcg and 1400 mcg) from that of the RLD. Please note that the proposed change in strengths represent dosage strengths between the currently approved strengths of Oral Transmucosal Fentanyl Citrate.

2007 P-0022

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The acceptability of the proposed 1000 mcg and 1400 mcg strengths are clearly contemplated in the labeling of the listed drug. The current dosing instructions in the approved labeling of the RLD are as follows:

"ACTIQ should be individually titrated to a dose that provides adequate analgesia and minimizes side effects (see **Dose Titration**).

Dose Titration

Starting Dose: The initial dose of ACTIQ to treat episodes of breakthrough cancer pain should be 200 mcg. Patients should be prescribed an initial titration supply of six 200 mcg ACTIQ units, thus limiting the number of units in the home during titration. Patients should use up all units before increasing to a higher dose.

From this initial dose, patients should be closely followed and the dosage level changed until the patient reaches a dose that provides adequate analgesia using a single ACTIQ dosage unit per breakthrough cancer pain episode....

Increasing the Dose: If treatment of several consecutive breakthrough cancer pain episodes requires more than one ACTIQ per episode, an increase in dose to the next higher available strength should be considered. At each new dose of ACTIQ during titration, it is recommended that six units of the titration dose be prescribed. Each new dose of ACTIQ used in the titration period should be evaluated over several episodes of breakthrough cancer pain (generally 1-2 days) to determine whether it provides adequate efficacy with acceptable side effects. The incidence of side effects is likely to be greater during this initial titration period compared to later, after the effective dose is determined.

Daily Limit: Once a successful dose has been found (i.e., an average episode is treated with a single unit), patients should limit consumption to four or fewer units per day. If consumption increases above four units/day, the dose of the long-acting opioid used for persistent cancer pain should be reevaluated....

Generally, the ACTIQ dose should be increased when patients require more than one dosage unit per breakthrough cancer pain episode for several consecutive episodes. When titrating to an appropriate dose, small quantities (six units) should be prescribed at each titration step. Physicians should consider increasing the around-the-clock opioid dose used for persistent cancer pain in patients experiencing more than four breakthrough cancer pain episodes daily."

The 1000 mcg would permit administration of an intermediate dose for those patients that may require greater than 800 mcg, but less than 1200 mcg for relief of symptoms. Similarly, the 1400 mcg strength would permit administration of an intermediate dose for those patients that may require greater than 1200 mcg, but less than 1600 mcg for relief of symptoms. The approved labeling clearly indicates that the dose should be titrated to adequate analgesia with minimal adverse effects. Because this drug product is not without the potential for significant adverse reactions, the proposed new intermediate strengths of the product would give the healthcare practitioner greater flexibility in selecting the most appropriate dose to provide adequate analgesia for the patient while minimizing potential adverse events.

There are no proposed changes in labeling with the exception of the obvious changes in strength sought in this petition. The uses, indications, warnings and directions for use will remain the same as that of the RLD. Draft labeling for the proposed product is included in Attachment 2, and the RLD's approved labeling is provided in Attachment 3.

Therefore, the petitioner's request for the Commissioner to find that a change in strengths from the approved 200 mcg, 400 mcg, 600 mcg, 800 mcg, 1200 mcg, and 1600 mcg strengths to the intermediate strengths of 1000 mcg and 1400 mcg for Oral Transmucosal Fentanyl Citrate should raise no questions of safety or effectiveness, and the Agency should approve the petition.

C. Environmental Impact

The petitioner claims a categorical exclusion under 21 CFR 25.31.

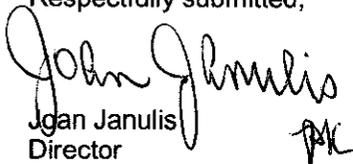
D. Economic Impact

The petitioner does not believe that this is applicable in this case, but will agree to provide such an analysis, if requested by the Agency.

E. Certification

The undersigned certifies, that to the best knowledge and belief of the undersigned, this petition includes all information and views on which the petition relies, and that it includes representative data and information known to the petitioner, which are unfavorable to the petition.

Respectfully submitted,


John Janulis
Director

JJ/pk

- Attachments:
1. Approved Drug Products with Therapeutic Equivalence Evaluations, accessed November 12, 2006
 2. Draft Labeling Proposed for Fentanyl Citrate Troche / Lozenge
 3. Labeling for Actiq[®] approved September 6, 2006

cc: Craig Kiester (OGD)

Actiq[®] is a registered trademark of Cephalon, Inc.

M03JD7012