

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

022377Orig1s000

OTHER ACTION LETTERS



NDA 22-377

King Pharmaceuticals, Inc.
Attention: Mr. Greg Carrier
501 Fifth Street
Bristol, TN 37620

COMPLETE RESPONSE

Dear Mr. Carrier:

Please refer to your new drug application (NDA) dated July 16, 2008, received July 17, 2008, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for sumatriptan injection.

We acknowledge receipt of your submissions dated the following: August 13, 2008, August 14, 2008, February 19, 2009, March 26, 2009, April 21, 2009 and April 27, 2009.

We have completed the review of your application, as amended, and have determined that we cannot approve this application in its present form. We have described below our reasons for this action and, where possible, our recommendations to address these issues.

INSUFFICIENT INFORMATION ABOUT THE DRUG TO DETERMINE WHETHER THE PRODUCT IS SAFE FOR USE UNDER THE CONDITIONS PRESCRIBED, RECOMMENDED, OR SUGGESTED IN ITS PROPOSED LABELING (21CFR § 314.125 (B)(4)).

We believe that a proprietary name is necessary to assure safe and effective use of your product, and prevent medication errors, for the following reasons:

Your 6 mg sumatriptan succinate auto-injector differs from the previously approved Imitrex 6 mg (sumatriptan succinate) auto-injector in that your product, among other things, is a preassembled single use disposable injector. It is operated by grasping the device in the middle and applying pressure to push the needle end against the injection site. By contrast, the Imitrex auto injector is a reusable device that must be individually loaded before each use. It operates by pushing a button at the end of the device. Your proposed labeling, and the approved labeling of the Imitrex auto-injector, include statements directing prescribers to instruct patients on the proper use of the product prior to first use in a medically unsupervised situation. Given that patients instructed on the use of another sumatriptan auto-injector may be unable to use your product without prior training, and vice versa, inadvertent substitution may lead to failed use of the product during a migraine attack, or to a safety risk to the patient.

As communicated to you during the review cycle, both proposed proprietary names were found unacceptable by the Agency. As you have not proposed an alternative acceptable proprietary name, or evidence that your product is safe for use without a proprietary name, the application can not be approved.

LABELING

We note that you have agreed to the following revisions regarding your container labels, carton labeling, and instructions for use:

A. General Comments on the Container Labels and Carton Labeling

1. The word “Auto-Injector” appears next to the established name, sumatriptan injection. Auto-Injector is a descriptor of the device and is not an approved USP dosage form. Thus, relocate the word Auto-Injector away from both the proprietary and established names (i.e., away from [TRADENAME] Injection).
2. The net quantity volume is not identified on the carton labeling or container label. Revise the product strength (6 mg) to include the volume in each injection (e.g., 6 mg/0.5 mL).

B. Container Label (Active drug)

1. The route of administration does not appear on the label. In accordance with 21 CFR 201.100 (b)(3), include the route of administration.
2. The order of important information on the labels and labeling is difficult to follow. Specifically, the proprietary name, established name, dosage form, and product strength are not presented in the usual format. Relocate the product strength from above the proprietary name to appear juxtapose to the established name and dosage form.

C. Carton Labeling

1. Include the route of administration statement on the principle display panel. We note that it is present on the side panel, but recommend that it also appear on the principal display panel in order to make this information more readily identifiable.
2. The order of important information on the labels and labeling is difficult to follow. Specifically, the proprietary name, established name, dosage form, and product strength are not presented in the usual format. Relocate the product strength so that it does not appear in the blue wave, but is juxtapose to the established name and dosage form.

E. Instructions for Use (Active drug)

1. The light green box holds important information (e.g. the blue safety release should not be removed until you are ready to use the auto-injector, the orange

needle end should never be touched, etc.). As currently presented, the only statement that stands out is “Keep out of reach of children before and after use.” There are other important messages that need to be just as prominently displayed. The use of a light green colored text on a white background to highlight important information reduces the readability and is not very prominent. Improve the color contrast so that it is more prominent and will stand out to highlight important information to ensure users will read and not overlook this information before using the device (e.g., the Attention! box at the beginning of the instructions and other statements highlighted in light green in the instructions for use).

2. In the “How to Use” section, “Preparing the Auto-Injector” subsection, the second picture shows the auto-injector sliding into the user’s hand. We understand the intent of this graphic. However, when attempting this step, we believe the user will use their thumb or other part of the hand to stop the auto-injector when sliding into the hand. This contradicts the second bullet in “Holding the Injector” section to “Never put the thumb on either end” of the auto-injector. In fact, in the picture shown, it appears as though the user is using their thumb at the blue cap on the injector. Revise the picture and/or directions to clarify these instructions.

3. In the How to Use section, “Disposing of the Auto-Injector” subsection, the first step is to “Hold the auto-injector on a flat surface”. However, the picture shows the auto-injector being held in the air. Modify the picture and/or the situation to more explicitly convey what the patient should do in order to minimize the potential for needle-sticks.

4. In the “Storage/Disposal Case” section, the first bullet instructs the user to “Always store and carry the auto-injector in the storage/disposal case.” (b) (4)
(e.g., Always store and carry the [TRADENAME] auto-injector in the storage/disposal case). (b) (4)

Submit draft labeling that incorporates revisions in the attached labeling. In addition, submit updated content of labeling [21 CFR 314.50(l)(1)(i)] in structured product labeling (SPL) format as described at <http://www.fda.gov/oc/datacouncil/spl.html>. To facilitate review of your submission, provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should include annotations with the supplement number for previously-approved labeling changes.

Additionally, we have the following comment, which is not a reason for this action, but which you should address in your response:

We recommend that the (b) (4)

OTHER

Within one year after the date of this letter, you are required to resubmit or take one of the other actions available under 21 CFR 314.110. If you do not take one of these actions, we will consider your lack of response a request to withdraw the application under 21 CFR 314.65. A resubmission must fully address all the deficiencies listed. A partial response to this letter will not be processed as a resubmission and will not start a new review cycle.

Under 21 CFR 314.102(d), you may request a meeting or telephone conference with us to discuss what steps you need to take before the application may be approved. If you wish to have such a meeting, submit your meeting request as described in the FDA Guidance for Industry *Formal Meetings With Sponsors and Applicants for PDUFA Products*, February, 2000 (<http://www.fda.gov/cder/guidance/2125fnl.htm>).

The drug product may not be legally marketed until you have been notified in writing that this application is approved.

If you have any questions, call Lana Chen, Regulatory Project Manager, at (301) 796-1056.

Sincerely,

{See appended electronic signature page}

Eric Bastings, MD
Deputy Director
Division of Neurology Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

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

/s/

Eric Bastings
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