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RESEARCH**

APPLICATION NUMBER:

020639Orig1s049

OTHER REVIEW(S)

**REGULATORY PROJECT MANAGER LABELING REVIEW
(PHYSICIAN LABELING RULE)**

Division of Psychiatry Products

Application Number(s): NDA 020639/S-049/S-054
NDA 022047/S-023/S-027

Name of Drug(s): Seroquel (quetiapine fumarate) Tablets
Seroquel XR (quetiapine fumarate) Extended-Release Tablets

Applicant: AstraZeneca

Material Reviewed:

Submission Date(s): NDA 020639/S-049 & NDA 02247/S-023
January 15, 2010, March 25, 2011, April 1, 2011

NDA 020639/S-054 & NDA 022047/S-027
March 22, 2011, May 27, 2011

Receipt Date(s): Same as above

Type of Labeling Reviewed: Word/PDF

20-639	049	PA	Seroquel (quetiapine fumarate) Tabs	Revisions to Highlights, sections 5.21 (Warnings and Precautions: use in Patients with Concomitant Illness), 7 (Drug Interactions), 8.1 (Pregnancy), 8.3 (Nursing) and 10 (Overdosage)
20-639	054	CBE	Seroquel (quetiapine fumarate) Tabs	Addition of term "hypothermia" to Section 6.3 (Postmarketing Experience)
22-047	023	PA	Seroquel XR (quetiapine fumarate) Tabs	Revisions to Highlights, sections 5.21 (Warnings and Precautions: use in Patients with Concomitant Illness), 7 (Drug Interactions), 8.1 (Pregnancy), 8.3 (Nursing) and 10 (Overdosage)
22-047	027	CBE	Seroquel XR (quetiapine fumarate) Tabs	Addition of term "hypothermia" to Section 6.3 (Postmarketing Experience)

Background and Summary

NDA 020639/S-049 & NDA 02247/S-023:

The March 25, 2011, submission constituted a complete response to our February 4, 2011 action letter the labeling submitted with the Complete Response was the same as that provided in the action letter. These "Changes Being Effected" supplemental new drug application propose revisions to include text regarding QT prolongation associated with quetiapine overdose in the Highlights section, sections 5.21

(Warnings and Precautions: Use in Patients with Concomitant Illness), 7 (Drug Interactions), and 10 (Overdosage), as well as editorial revisions throughout labeling. The sponsor accepted most of our proposed revisions. The clinical reviewer was in agreement with the alternative(s) proposed by the sponsor in the complete response.

NDA 020639/S-054 & NDA 022047/S-027:

New supplements submitted on March 22, 2011. These "Changes Being Effected" supplemental new drug applications provide for adding the term "hypothermia" to Section 6.3 Postmarketing Experience.

Review

This supplemental application provides for the following changes to product labeling:

- 1) Addition of the term "hypothermia" under Section 6.3 (Post Marketing Experience).
- 2) Revisions to include text regarding QT prolongation associated with quetiapine overdose in the Highlights section, sections 5.21 (Warnings and Precautions: Use in Patients with Concomitant Illness), 7 (Drug Interactions), and 10 (Overdosage).
- 3) Sections 8.1 (Pregnancy) and 8.3 (Nursing Mothers) of the Seroquel and Seroquel XR labels were revised to be consistent by combining language currently found separately in the labels.
- 3) Changes to Medication Guide:
 - a) "Abnormal heart beats or rhythm" added as a new bullet to the 'List of things to tell your healthcare provider' for consistency with new QT labeling text in Section 5.12
 - b) Seroquel only: bullet under 'What should I tell my healthcare provider before taking Seroquel?' regarding breast feeding was revised for consistency with the changes to Sections 8.1 and 8.3.
- 4) The 500-count bottle for all strengths was removed from Section 16 (How Supplied/Storage and Handling) because it is no longer available.
- 5) The submission was originally submitted as a CBE supplement, but the Complete Response included changes to the Medication Guide, therefore, supplements 020639/S-049 and 022047/S-023 were recoded as Prior Approval supplements in accordance with the regulations.
- 5) It should be noted that the proposed labeling includes language submitted under CBE supplements that are currently under review by the Division.

(b) (4)

Deficiencies

- 1) It was noted that SPL was not submitted. The following statement will be incorporated into the approval letter:
 - As soon as possible, but no later than 14 days from the date of this letter, submit, using the FDA automated drug registration and listing system (eLIST), the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format, as described at <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>, that is identical to the enclosed labeling (text for the package insert) and include the labeling changes proposed in any pending "Changes Being Effected" (CBE) supplements. Information on submitting SPL files using eLIST may be found in the guidance for industry titled "SPL Standard for Content of Labeling Technical Qs and As" at <http://www.fda.gov/downloads/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf>

Conclusions

1. These supplements provide for the labeling changes listed above when compared to the last approved labeling (approval letter dated May 17, 2011). The clinical review team reviewed the supplements and resubmission and has recommended the supplements for approval. No further labeling negotiation was required.
2. The supplements contain CBE language currently under review by the Division which is noted in the action letter.
3. Recommend an approval letter issue for these supplements.

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Supervisory Comment/Concurrence:

Paul David, RPH
Chief, Project Management Staff

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

/s/

KIMBERLY S UPDEGRAFF
06/30/2011

PAUL A DAVID
06/30/2011