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APPLICATION NUMBER:

202543Orig1s000

SUMMARY REVIEW

Cross-Discipline Team Leader Review

Date	11/1/11
From	Norman Hershkowitz, MD, PhD
Subject	Cross-Discipline Team Leader Review
NDA/BLA # Supplement#	202543
Applicant	HQ Speciality Pharma Llc
Date of Submission	1/13/11
PDUFA Goal Date	11/13/11
Requested Established Name / Approved Established names	(b) (4) levetiracetam in sodium chloride injection
Dosage forms / Strength	1. Levetiracetam in 0.82% NaCl injection (500mg/100 mL) 2. Levetiracetam in 0.75% NaCl injection (1000mg/100 mL) 3. Levetiracetam in 0.54% NaCl injection (1500mg/ 100 mL)
Proposed Indication(s)	1. Partial Onset Seizures 2. Myoclonic Seizures 3. Primary Generalized Tonic-Clonic Seizures
Recommended:	Approval

1. Background and Introduction

Levetiracetam is approved for partial, myoclonic and primary generalized seizures in children and adults under the proprietary product known as Keppra. A proprietary injectable formulation of Keppra, Keppra Injection, is available as a replacement for oral Keppra, when such a route is not possible. This formulation has the same indication except it is approved only in patients 16 years and older. This proprietary formulation requires pre-mixing before infusion, and is labeled to be administered over a period of 15 minutes with either 500 mg, 1,000 mg and 1500 mg doses diluted in 100 ml of a compatible diluent. The present Sponsor has submitted an NDA for three pre-mixed solutions of 500mg, 1,000mg and 1,500 mg of levetiracetam pre-diluted in a 100 ml of an isosmotic salt (NaCl) solution. This proposal is being submitted as a 505(b) (2), using the already marketed product of Keppra and Keppra Injection as a reference.

2. CMC

No CMC/DMEPA issues were identified other than carton and container issues, which have been resolved. For details on these see the CMC and the DMEPA reviews by Dr. Clafey and Ms. Merchant, respectively.

3. Nonclinical Pharmacology/Toxicology

No phram/tox issues were raised, as the degradation and impurity profile of this product is similar to that of Keppra.

4. Clinical Pharmacology/Biopharmaceutics

The Sponsor has requested a biowaiver. This request was reviewed by Dr. Dorantes of ONDQA. The reviewer recommended that the biowaiver be granted. As a result no new pharmacokinetic studies have been performed.

5. Clinical Microbiology

Initial microbiology product review by Dr. Pawar identified a number of deficiencies (e.g. endotoxin limit). These were corrected and Dr. Pawar finds that the application can be approved.

6. Clinical/Statistical- Efficacy and Safety

Dr Rusinowitz, medical officer, performed the efficacy and safety review. No clinical studies are included in this application. As a 505(b) (2) the review team has concluded that the already approved products, Keppra and Keppra Injection, support the efficacy and safety of this product. Moreover, the Sponsor provided additional published information that indicated no new safety labeling is required.

7. Advisory Committee Meeting

None.

8. Pediatrics

PREA is not triggered as this is neither new active ingredient; new indication; new dosage form; new dosing regimen; or new route of administration.

9. Other Relevant Regulatory Issues

DMEPA identified a number of issues including those dealing with the established name, cartoon and container, and labeling, which were all resolved.

10. Labeling

See final label.

11. Recommendations/Risk Benefit Assessment

There are no risk benefit issues. Approval is recommended.

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/s/

NORMAN HERSHKOWITZ
11/01/2011