CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

206030Orig1s000

SUMMARY REVIEW

Summary Review for Regulatory Action

Date	(electronic stamp)
From	Eric Bastings, MD. Deputy Director.
Subject	Division Director Summary Review
NDA/BLA # **Supplement #**	206,030
Applicant Name	Lundbeck
Date of Submission	4/8/16
PDUFA Goal Date	10/8/16
Proprietary Name / **Established (USAN) Name**	Carnexiv/carbamazepine
Dosage Forms / Strength	Intravenous
Proposed Indication(s)	Replacement therapy for oral carbamazepine formulations, when oral administration is temporarily not feasible, in adults with the following seizure types: • Partial seizures with complex symptomatology • Generalized tonic-clonic seizures • Mixed seizure patterns which include the above, or other partial or generalized seizures
Action	Approval

Material Reviewed/Consulted OND Action Package, including:	**Names of discipline reviewers**
CDTL Review	Norman Hershkowitz
CMC/Drug Product	Andrei Ponta
CMC/Facility	Viviana Matta/Ruth
CMC/ Regulatory Business	Martha Heimann
Clinical Review	Steven Dinsmore
OSE/DMEPA	Dhara Shah

1. Introduction and Background

NDA 206,030 is a 505(b)(2) application for carbamazepine injection (Carnexiv), an intravenous formulation of carbamazepine. Carbamazepine is an anticonvulsant approved for the treatment of partial onset seizures and generalized tonic-clonic seizures. Carnexiv is proposed as a replacement therapy when oral carbamazepine administration is temporarily not feasible. Carnexiv uses sulfobutylether beta-cyclodextrin sodium salt (Captisol) as solubilizing agent. The application references NDA 16,608 (Tegretol 200 mg IR tablets) and NDA 20,234 (Tegretol 400 mg XR tablets).

The application was issued a Complete Response letter in the first cycle, because of product quality issues. These included missing critical information on extractables from storage of the drug product in diluent bags, and a failed visual inspection (b) (4) for the batch analysis of the commercial scale carbamazepine injection lot. In addition, the proposed acceptance limit for osmolality of the drug product was not acceptable. There were no clinical or nonclinical issues in the original submission.

I refer the reader to my first cycle summary review for a description of the basis for the regulatory action, and a discussion of the reviews findings for the original submission.

2. CMC/Device

I concur with the conclusions reached by the chemistry reviewer that the applicant has addressed all deficiencies identified in the Complete Response letter. Manufacturing site inspections were acceptable. There are no outstanding issues.

3. Nonclinical Pharmacology/Toxicology

No new nonclinical information was part of this submission. I refer to reader to my first cycle summary review.

4. Clinical Pharmacology/Biopharmaceutics

No new clinical pharmacology information was part of this submission. I refer to reader to my first cycle summary review.

5. Clinical Microbiology

Not applicable.

6. Clinical/Statistical-Efficacy

No new clinical efficacy information was part of this submission. I refer to reader to my first cycle summary review.

7. Safety

No new clinical safety information was part of this submission. I refer to reader to my first cycle summary review.

8. Advisory Committee Meeting

No advisory committee meeting was necessary for this application, which is for a new dosage form of an already approved active moiety.

9. Pediatrics

PREA was not triggered because this product has an orphan designation.

10. Other Relevant Regulatory Issues

There are no other unresolved relevant regulatory issues.

11. Labeling

The applicant changed the proprietary name of this product from Carbella to Carnexiv after they discovered that a medication was recently approved with a similar sounding name, Kybella. The new name was found acceptable by the DMEPA reviewer.

There are no other unresolved labeling issues.

12. Decision/Action/Risk Benefit Assessment

This application was issued a Complete Response letter in the first cycle because of product quality deficiencies. As these deficiencies have been adequately addressed, I will issue an approval letter for this application.

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/s/

ERIC P BASTINGS
10/07/2016