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APPLICATION NUMBER:
NDA 22-253 & 22-254

**CLINICAL PHARMACOLOGY AND
BIOPHARMACEUTICS REVIEW(S)**

MEMORANDUM TO FILE

Dissolution Specification or Lacosamide Tablets (NDA 22-253 and NDA ~~_____~~)

b(4)

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|--|--|
| NDA number (submission date) | NDA 022-253 and _____ (September 28, 2007) |
| Drug name, substance, dosage form and strength | Vimpat, Lacosamide film-coated tablets (50-, 100-, 150-, 200-, 250- and 300-mg) |
| Sponsor | Schwarz Biosciences, Inc. Research Triangle Park, NC |
| Clinical Division | Division of Neurology Products and Division of Anesthesia, Analgesia and Rheumatology Products |

b(4)

The purpose of this memorandum to file is to clarify and consolidate the ONDQA recommendation for dissolution specification for the lacosamide tablets.

In my April 4, 2008, dated review of this submission, I had provided the following section to support dissolution specification for lacosamide tablets:

The Sponsor has shown in multiple media that lacosamide tablets are highly soluble (pH range 1 to 7.5) and based on the submitted data, the following dissolution method for the lacosamide tablets is acceptable:

USP Apparatus 2 (Paddle)
Test medium: 0.1 N HCl, 900 mL
Temperature: 37° C ± 0.5°C
Paddle rotation speed: 50 rpm
Q: ~~_____~~ at 30 min

b(4)

For the CMC review including complete product quality assessment and specification for the lacosamide dosage forms, please see Dr. Prafull Shiromani's review.

In the NDA, although lacosamide dissolution testing was carried out at 50 rpm paddle rotation speed, the Sponsor proposes ~~_____~~ rpm for the dissolution specification, however, consistent with the submission, the Sponsor should maintain the original paddle speed of 50 rpm for dissolution testing.

b(4)

Consistent with the above comments, the primary quality reviewer, Dr. Prafull Shiromani, had also requested additional information from the Sponsor (including those related to dissolution and stability testing of the lacosamide tablets).

The Sponsor responded to the IR letter on April 29, 2008. Dr. Shiromani's May 20, 2008, dated review, encompassing evaluation of the updated dissolution test results obtained at both 50 rpm and — rpm (as part of the updated 24 month stability data from twelve primary stability batches and additional supportive data), indicates that the Q value of — at 30 min with a paddle speed of 50 rpm is acceptable for ensuring product quality.

b(4)

This reviewer agrees with Dr. Prafull Shiromani's extensive chemistry review of the dissolution test results obtained from stability batches. The Q value of — at 30 min is acceptable (instead of — at 30 min) based on dissolution test results that indicate that as long as the test is carried out with a — paddle speed (50 rpm vs. — rpm) and according to the above test conditions (USP Apparatus 2, and 900 mL of 0.1 N HCl media), the dissolution test is suitable for quality assessment of the lacosamide tablets.

b(4)

For product specification of the lacosamide tablets, including in vitro dissolution, please see Dr. Shiromani's May 20, 2008, dated Chemistry Review.

Signature:


Arzu Selen, Ph.D.
Associate Director, Biopharmaceutics
Office of New Drug Quality Assessment

**This is a representation of an electronic record that was signed electronically and
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/s/

Arzu Selen
6/27/2008 11:15:26 AM
BIOPHARMACEUTICS

CLINICAL PHARMACOLOGY REVIEW

NDA: 22-253, — b(4)
Submission Dates: 9/28/2007; 11/26/2007; 12/13/2007; 5/27/2008
Type: 505(b)(1)
Generic Name: Lacosamide
Brand Name: VIMPAT
Drug Class: Other antiepileptics
Proposed Indications: **NDA 22-253:** For the treatment of Epilepsy as adjunctive therapy in patients with partial onset seizures aged 16 years and older
NDA — For the management of neuropathic pain associated with diabetic peripheral neuropathy b(4)
Clinical Divisions: **NDA 22-253:** Neurology Products (DNP)
NDA — Anesthesia, Analgesia and Rheumatology Products (DAARP)
OCP Division: Clinical Pharmacology 2 (DCP2)
Reviewers: Lei Zhang, Ph.D.
Emmanuel O. Fadiran, R.Ph., Ph.D.
Team Leader: Suresh Doddapaneni, Ph. D.
PM Reviewer: Hao Zhu, Ph.D.
PM Team Leader: Joga Gobburu, Ph.D.
Dosage Form: Film Coated Tablets
Strengths: 50, 100, 150, 200, 250, and 300 mg
Route of Administration: Oral
Proposed Dosing regimens: **NDA 22-253:** Starting dose is 100 mg (50 mg twice daily) and the recommended maintenance dose of lacosamide is 200-400mg per day. Maximum dose is — mg/day.
 b(4)
Applicant: Schwarz Biosciences, Inc
Relevant IND: IND —
Type of Submission; Code: 505 (b)(1); 1S b(4)

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