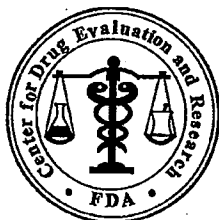


**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*  
**NDA 22-253 & 22-254**

**RISK ASSESSMENT and RISK MITIGATION  
REVIEW(S)**



Department of Health and Human Services  
Public Health Service  
Food and Drug Administration  
Center for Drug Evaluation and Research  
Office of Surveillance and Epidemiology

Date: October 17, 2008

To: Russell Katz, M.D., Director  
Division of Neurology Products

Through: Jodi Duckhorn, M.A., Team Leader  
Patient Labeling and Education Team  
Division of Risk Management (DRISK)

From: Sharon R. Mills, BSN, RN, CCRP  
Patient Product Information Specialist  
Patient Labeling and Education Team  
Division of Risk Management (DRISK)

Subject: Memo to file Re: Review of Patient Labeling (Medication Guide)

Drug Name(s) and Application  
Type/Number(s):

- VIMPAT (lacosamide) Tablet, Film Coated for Oral use, NDA 22-253
- VIMPAT (lacosamide) Injection for Intravenous Use, NDA 22-254
- \_\_\_\_\_

Applicant/sponsor: Schwartz Biosciences

OSE RCM #: 2008-847

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Schwartz Biosciences submitted parallel original New Drug Applications for:

- NDA 22-253 for lacosamide tablets,  
“For the treatment of Epilepsy as adjunctive therapy in patients with partial onset seizures aged 16 years and older”  
“For the management of neuropathic pain associated with diabetic peripheral neuropathy.”
- NDA 22-254 lacosamide Injection,  
“For the treatment of Epilepsy as adjunctive therapy in patients with partial onset seizures aged 16 years and older when oral administration is temporarily not feasible.”

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OSE reviewed a Class Medication Guide (MG) for Antiepileptic Drugs, drafted by the Division of Neurology Products (DNP) in March 2008, which was modeled after the Class Antidepressant MG. Following a joint meeting of the Peripheral and Central Nervous System Drugs Advisory Committee (PCNS) and Psychopharmacologic Drugs Advisory Committee on July 10, 2008 to discuss the results of FDA's meta-analysis and issues related to antiepileptic drugs and suicidality, the review division decided to develop Class labeling for the Professional Information and MGs for these products. The review division worked in collaboration with the Patient Labeling and Education Team in DRISK in developing the MG template for the Antiepileptic Drugs.

This memo serves to document our findings and close out our consult request.

The Tradename VIMPAT has been accepted by FDA for lacosamide. VIMPAT (lacosamide) requires a MG because it is part of the Antiepileptic Class of drugs. The Patient Labeling and Education Team was requested to review the proposed MG for VIMPAT; however, the review division has decided that the MG for VIMPAT will only contain the class-specific language regarding suicidality that has been agreed upon by DNP and DRISK, and will not contain product specific language. See attached. Therefore, no further review is necessary at this time.

We have made two minor changes at the end of the VIMPAT MG as follows:

/ / / /

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Please let us know if you have any questions.

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✓ Draft Labeling (b4)

       Draft Labeling (b5)

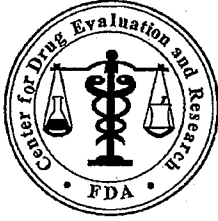
       Deliberative Process (b5)

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/s/  
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Sharon Mills  
10/17/2008 09:33:41 AM  
DRUG SAFETY OFFICE REVIEWER

Jodi Duckhorn  
10/17/2008 09:44:40 AM  
DRUG SAFETY OFFICE REVIEWER



Department of Health and Human Services  
Public Health Service  
Food and Drug Administration  
Center for Drug Evaluation and Research  
Office of Surveillance and Epidemiology

Date: May 15, 2008

To: Russell Katz, MD, Director  
Division of Neurology Products  
Bob Rappaport, MD, Director  
Division of Anesthesia, Analgesia and Rheumatology Products

Thru: Kellie Taylor, PharmD, MPH, Team Leader  
Denise Toyer, PharmD, Deputy Director  
Division of Medication Error Prevention

From: Judy Park, PharmD, Safety Evaluator  
Division of Medication Error Prevention

Subject: Labeling Review

Drug Name(s): Vimpat (Lacosamide) Tablets, \_\_\_\_\_ and Injection

Application Type/Number: NDA 22-253, NDA 22-254. \_\_\_\_\_

Applicant: Schwarz Biosciences, Inc.

OSE RCM #: 2008-633

b(4)

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## EXECUTIVE SUMMARY

The results of the Label and Labeling Risk Assessment found that the presentation of information and design of the proposed carton and container labels appears to be vulnerable to confusion that could lead to medication errors. The Division of Medication Error Prevention believes the risks we have identified can be addressed and mitigated prior to drug approval, and provides recommendations in Section 5.2 that aim at reducing the risk of medication errors.

## 1 BACKGROUND

### 1.1 INTRODUCTION

This consult was written in response to a request from the Division of Neurology to evaluate the container labels and carton labeling of Vimpat for its potential to contribute to medication errors. The proprietary name, Vimpat, and the insert labeling were evaluated under a separate review (OSE Review #2007-1611).

### 1.2 PRODUCT INFORMATION

Vimpat (Lacosamide) is a new molecular entity indicated for partial-onset seizures as adjunctive therapy in patients aged 16 years and older, as well as for management of neuropathic pain associated with diabetic peripheral neuropathy. The recommended dose for partial onset seizures is 100 mg per day twice daily initially, then increased to 200 mg per day to 400 mg per day. The recommended initial dose for diabetic peripheral neuropathic pain is \_\_\_\_\_

\_\_\_\_\_ The maximum daily dosage of Vimpat is \_\_\_\_\_ mg per day. When switching from oral to intravenous dose, the initial total daily intravenous dosage should equal the oral total daily dosage and frequency. The parenteral formulation of Vimpat can be administered without further dilution or may be mixed in a compatible diluent and should be administered intravenously over at least \_\_\_\_\_ Vimpat will be available in 50 mg, 100 mg, 150 mg, 200 mg, 250 mg, and 300 mg tablets, \_\_\_\_\_ and 10 mg/mL solution for injection: \_\_\_\_\_ is indicated for neuropathic pain. For partial seizure indication, tablets, \_\_\_\_\_ and injectables are indicated.

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## 2 METHODS AND MATERIALS

This section consists of two sections which describe the methods and materials used by the Division of Medication Error Prevention staff conducting a label, labeling, and/or packaging risk assessment. The primary focus of the assessments is to identify and remedy potential sources of medication error prior to drug approval. The Division of Medication Error Prevention defines a medication error as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer.<sup>1</sup>

The label and labeling of a drug product are the primary means by which practitioners and patients (depending on configuration) interact with the pharmaceutical product. The container labels and carton labeling communicate critical information including proprietary and established

<sup>1</sup> National Coordinating Council for Medication Error Reporting and Prevention.  
<http://www.nccmerp.org/aboutMedErrors.html>. Last accessed 10/11/2007.



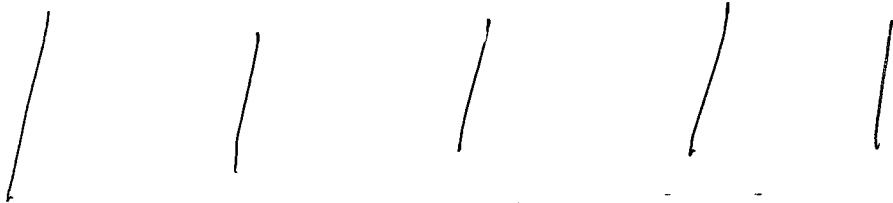
name, strength, form, container quantity, expiration, and so on. The insert labeling is intended to communicate to practitioners all information relevant to the approved uses of the drug, including the correct dosing and administration.

Given the critical role that the label and labeling has in the safe use of drug products, it is not surprising that 33 percent of medication errors reported to the USP-ISMP Medication Error Reporting Program may be attributed to the packaging and labeling of drug products, including 30 percent of fatal errors.<sup>2</sup>

Because our staff analyze reported misuse of drugs, our staff are able to use this experience to identify potential errors with all medication similarly packaged, labeled or prescribed. We use FMEA and the principles of human factors to identify potential sources of error with the proposed product labels and insert labeling, and provided recommendations that aim at reducing the risk of medication errors.

For this product the Applicant submitted on April 9, 2008 following labels and labeling for our review (see Appendices A, B, C, D, E, F, and G for images):

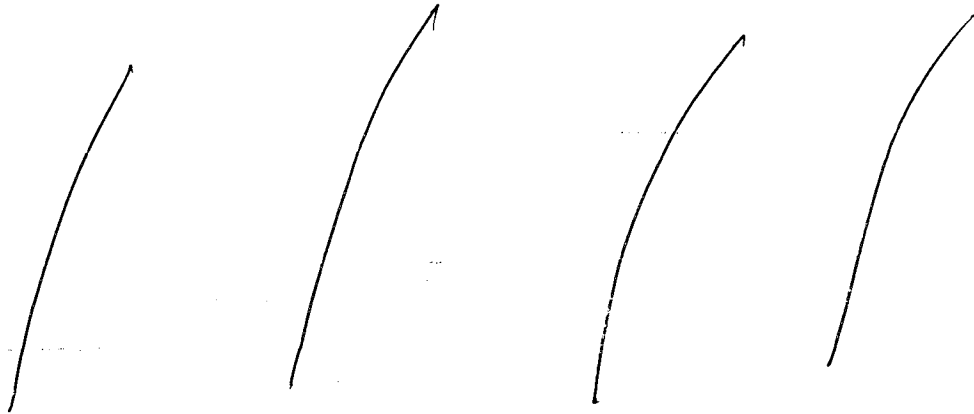
- Retail Container for Injection: 10 mg/mL (20 mL vial)
- Retail Carton for Injection: 10 mg/mL (20 mL vial)



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- Retail Container for Tablets : 50 mg, 100 mg, 150 mg, 200 mg, 250 mg, and 300 mg (60, 180, \_\_\_\_\_ counts)

### 3 RESULTS



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<sup>2</sup> Institute of Medicine. Preventing Medication Errors. The National Academies Press: Washington DC. 2006. p275.

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## 5 CONCLUSIONS AND RECOMMENDATIONS

The Label and Labeling Risk Assessment findings indicate that the presentation of information and design of the proposed container labels and carton labeling introduces vulnerability to confusion that could lead to medication errors. We believe the risks we have identified can be

addressed and mitigated prior to drug approval, and provides recommendations in Section 5.2 that aim at reducing the risk of medication errors.

**5.1 COMMENTS TO THE DIVISION**

Based upon our assessment of the labels and labeling, we have identified areas needed of improvement. We have provided recommendations in Section 5.2 and request this information be forwarded to the Applicant.

We would appreciate feedback on the final outcome of this review. Please copy us on any communication to the Applicant with regard to this review. We would be willing to meet with the Division for further discussion, if needed. If you have further questions or need clarifications, please contact Daniel Brounstein, Project Manager, at 301-796-0674.

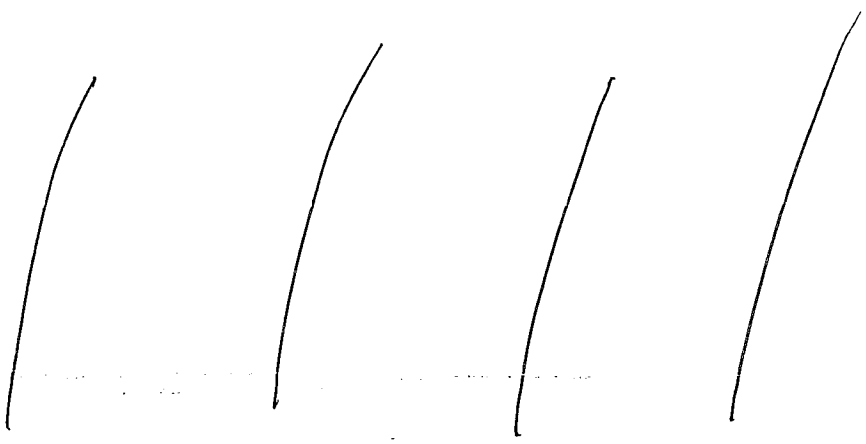
**5.2 COMMENTS TO THE APPLICANT**

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       Deliberative Process (b5)

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/s/  
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Judy Park  
5/15/2008 10:11:10 AM  
DRUG SAFETY OFFICE REVIEWER

Kellie Taylor  
5/15/2008 10:45:46 AM  
DRUG SAFETY OFFICE REVIEWER

Denise Toyer  
5/15/2008 12:35:59 PM  
DRUG SAFETY OFFICE REVIEWER