CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

022255Orig1s000

CHEMISTRY REVIEW(S)

Vimpat® (lacosamide) Oral Solution
NDA 22-255
Branch Chief Review
Chemistry, Manufacturing, and Controls

Applicant: Schwarz Biosciences, Inc.
8010 Arco Corporate Drive, Suite 100
Raleigh, NC 27617

Indication: adjunctive treatment of partial-onset seizures in patients with epilepsy, aged 17 years and older

Presentation: Immediate-release oral solution containing 10 mg/mL of lacosamide and the following excipients: glycerin, carboxymethylcellulose sodium, sorbitol solution, polyethylene glycol, sodium chloride, anhydrous citric acid, acesulfame potassium, methylparaben (b) (4) strawberry flavor, masking flavor, and water. The drug product is packaged in (b) (4) (b) (4) polyethylene terephthalate bottles sealed with white, child-proof, tamper-evident (b) (4) caps.

EER Status: Acceptable 15-JUL-2008

Consults: Microbiology – Approval 30-MAR-2010
EA – OPS No significant impact 15-MAY-2008
Methods Validation – Revalidation by Agency not requested.

Resubmission: 16-OCT-2009

Post-Approval Agreements: None

Drug Substance: The applicant referenced NDA 22-253 for all information concerning the chemistry, manufacturing, and control of lacosamide drug substance. We approved NDA 22-253 on 28-OCT-2008.

Conclusion: Drug substance is acceptable.

Drug Product: This resubmission is in response to the DMEPA request for the sponsor to reformulate the oral solution so that standard dosing measurements and devices could be used for administration. The original oral solution concentration was (b) (4). Based on DMEPA's request, Schwarz proposed a 10 mg/mL formulation. The 10 mg/mL formulation is similar to the original (b) (4) formulation with slight modifications in excipient amounts. Schwarz removed the (b) (4) based on comments received from the European Union. Schwarz confirms that this reformulation does not require any changes in the drug product manufacturers, manufacturing process, analytical methods, or impurity profile. All analytical methods remain appropriate for use and validated with respect to the new 10 mg/mL formulation. (b) (4) .

Each bottle of drug product contains lacosamide (10.0 mg/mL), glycerin USP (b) (4) carboxymethylcellulose sodium USP (b) (4) sorbitol solution USP ((b) (4) polyethylene glycol (b) (4) USP (b) (4) sodium chloride USP (b) (4) anhydrous citric acid USP (b) (4) (b) acesulfame potassium NF (b) (4) methylparaben (b) (4) USP (b) (4) strawberry

flavor (b) (4)), masking flavor (b) (4)), and purified water USP (b) (4) (b) (4)

Specification of the drug product includes: appearance, contents, odor, color, clarity, identification by RP-HPLC and UV spectrophotometry, methylparaben content by RP-HPLC, pH, purity by RP-HPLC, impurities and related substances by RP-HPLC, assay by RP-HPLC, assay of methylparaben by RP-HPLC, and microbial limits. The lacosamide reference standard for drug product is the same as that for drug substance. All test methods are compendial or have been appropriately validated for their intended purpose. The drug product stability data supports the proposed 18 month expiry for drug product stored at controlled room temperature [25º C (77º F); excursion permitted to 15-30º C (59-86º F)], and packaged in the proposed commercial bottles, sealed with caps.

In accordance with 21 CFR 320.22, the data provided adequately support granting the biowaiver request. Based on these results and the fact that the drug substance in the oral solution formulation is in the dissolved state, a request for waiver of an *in vivo* bioequivalence study for the 10 mg/mL lacosamide oral solution is justified. The conclusions of the ONDQA Biopharmaceutics reviewer (23-FEB-2010) indicate that the data provided support granting the biowaiver request. The CMC microbiology team recommended approval (30-MAR-2010).

Conclusion: Drug product is acceptable.

Additional Items:
• The applicant agreed to conduct primary stability studies on the first three consecutive drug product batches, in all packaging configurations, to firmly establish the proposed drug product expiry.
• The applicant agreed to place one batch of drug product per year for each of the largest and smallest packaging configuration, stored upright, on stability at 25°C/60% RH (long term conditions) with testing throughout the commercial life of the drug product and submission of the stability results in the annual report.
• All associated Drug Master Files (DMFs) are acceptable or the pertinent information was adequately provided in the application.
• The applicant submitted a methods validation package containing all relevant documentation (tests, methods, and acceptance criteria) for the control of the drug substance and the drug product.

Overall Conclusion:

From a CMC perspective, the application is recommended for **Approval**.

Ramesh Sood, Ph.D.
Branch Chief
DPA I/ONDQA

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22255	ORIG-1	SCHWARZ BIOSCIENCES INC	VIMPAT

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

/s/

WENDY I WILSON
04/19/2010
Branch Chief Memo entered on behalf of Ramesh K. Sood, Branch Chief, DPA I, ONDQA

MARTHA R HEIMANN
04/19/2010
for Ramesh Sood

NDA 22-255
Quality Review #2

Vimpat® (lacosamide) Oral Solution
10 mg/mL

Schwarz Biosciences, Inc.

Wendy I. Wilson-Lee, Ph. D.
Office of New Drug Quality Assessment
For
Office of Neurology Drug Products

DOCKET ALARM

Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

Real-Time Litigation Alerts

Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

Advanced Docket Research

With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

Analytics At Your Fingertips

Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

LAW FIRMS
Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

FINANCIAL INSTITUTIONS
Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS
Sync your system to PACER to automate legal marketing.