

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:
201367Orig1s000

RISK ASSESSMENT and RISK MITIGATION
REVIEW(S)



Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research

Office of Compliance

REMS Modification Memorandum

TO: NDA 21-911, 201-367, TSI 547

THROUGH: Suzanne Barone, Ph. D., Team Leader
Compliance Risk Management and Strategic Problem Solving Team
Division of Compliance Risk Management and Surveillance
Office of Compliance

FROM: Kendra Biddick, CSO
Compliance Risk Management and Strategic Problem Solving Team
Division of Compliance Risk Management and Surveillance
Office of Compliance

SUBJECT: Office of Compliance review and comment on the adequacy of the proposed combined modified risk evaluation and mitigation strategy (REMS) for Banzel (rufinamide) tablets and oral suspension

Review summary

The Timetable for Submission of Assessments submitted by Eisai as part of this REMS modification request submitted December 14, 2010, should be accepted for both NDA 201367 and NDA 21911, in place of the timetable in the REMS approved November 8, 2010.

Background

The purpose of the current request for REMS modification is to add the approval of an oral solution (NDA 201367) to the existing approval for tablets (NDA 21911). The REMS for Banzel tablets was approved November 14, 2008, with a timetable for submission of assessments that met the approval standard at the time. The standard language and due dates have changed and the REMS should be modified accordingly. The goal of the REMS is to educate prescribers and patients about the potential serious risks of Banzel (rufinamide), including the increased risk of suicidal thoughts and behavior.

The original due date for the first REMS assessment was May 14, 2010. OND informed Eisai on April 2, 2010 and May 10, 2010 that the comprehensive Medication Guide was currently under review. Thus it was too early to assess the REMS at that time. On May 24, 2010, Eisai submitted a letter formally notifying the Division that it was too early to assess the REMS, but that the Medication Guide would be adequate with the proposed modifications to achieve its purpose. This was considered a status update. On October 28, 2010 Eisai submitted a modified REMS. On December 14, 2010 Eisai submitted to NDA 21911 another modified REMS which included the NDA 201367 for the oral suspension.

OC Observations

The submissions for the two NDAs are identical, including the NDA number (201367), thus there is no REMS submitted with the NDA number 21911.

The Timetable for Submission of Assessments submitted by Eisai as part of the request for modification of the REMS meets the current standards for language and due dates.

OC Recommendations

The Office of Compliance recommends that the Timetable for Submission of Assessments be accepted as submitted by Eisai, with specific due dates. This will clarify that the addition of the oral solution NDA to the REMS for Banzel does not change the assessment due date. OC also recommends that both applicable NDAs appear at the top of the REMS document. The text that follows the Timetable for Submission of Assessments in the version of the REMS that is on the web should be removed:

 (b) (4)

The correct language, as submitted in Eisai's December 14, 2010 submission is:

Eisai Inc. will submit REMS Assessments to the FDA 18 months, 3 years, and 7 years from the initial approval of the REMS (November 14, 2008) according to the schedule below:

1. FDAA Assessment: March 14, 2010 (18 months from approval)
2. FDAA Assessment: November 14, 2011 (3 years from approval)
3. FDAA Assessment: November 14, 2015 (7 years from approval)

To facilitate inclusion of as much information as possible while allowing reasonable time to prepare the submission, the reporting interval covered by each assessment should conclude no earlier than 60 days before the submission date for that assessment. Eisai will submit each assessment so that it will be received by the FDA on or before the due date.

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/s/

KENDRA A BIDDICK
02/16/2011

SUZANNE BARONE
02/16/2011

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

Date: February 10, 2011

To: Russell Katz, MD, Director
Division of Neurology Products (DNP)

Through: Claudia B. Karwoski, PharmD, Director
Division of Risk Management (DRISK)

From: Mary Dempsey BS, Risk Management Programs Coordinator, DRISK
Robin Duer, RN, MBA, Senior Patient Labeling Reviewer, DRISK
Melissa Hulett MSBA, BSN, RN, Acting TL, Patient Labeling
Reviewer, DRISK

Subject: Prior Approval Supplement; proposed REMS Modification for
NDA 021911; Proposed initial REMS for NDA 201367

Drug Name: Banzel (rufinamide) Tablet
Banzel (rufinamide) Oral Solution

Application NDA 021911
Type/ Number: NDA 201367

Applicant/Sponsor: Eisai Inc

OSE RCM #: 2009-848
2010-2635

1 Background

The Division of Neurology Products (DNP) requested the Division of Risk Management (DRISK) review the Banzel (rufinamide) Tablet proposed Risk Evaluation Mitigation Strategy (REMS) Modification for the New Drug Application (NDA) 021911 and the proposed initial REMS for Banzel (rufinamide) Oral Suspension NDA 201367 submitted by Eisai Inc. on December 14, 2010 to both NDA applications. This submission proposes to combine the approved Banzel Tablet label and REMS to incorporate the currently under review Banzel Oral Suspension. Following the approval of the Banzel Oral Suspension there will be one combined label and REMS for all Banzel (rufinamide) formulations.

The Banzel (rufinamide) Tablet REMS was initially approved November 14, 2008 with the following elements:

- Medication Guide
- Timetable for Submission of Assessments

2 Material Reviewed

- November 14, 2008 initial Banzel Tablets REMS approval
- November 8, 2010 Banzel Tablets REMS Modification to include comprehensive Medication Guide (this was not reviewed by DRISK)
- November 30, 2010 electronic communication from Su-Lin Sun, DNP Regulatory Project Manager, requesting Eisai Inc. submit a proposed REMS to NDA 201367 and a REMS Modification with assessment to NDA 021911
- December 14, 2010 proposed REMS Modification Amendment; REMS Assessment for approved Banzel tablets (NDA 021911)
- December 14, 2010 proposed initial REMS for Banzel Oral Suspension (NDA 201367)
- February 4, 2011 proposed REMS Amendment to include Patient Instruction for Use (IFU)

3 Proposed REMS Elements

The December 14, 2010 Banzel tablet's cover letter states the following:

“ Reference is made to the Banzel Risk Evaluation and Mitigation Strategy (REMS) , which was approved on 14 November 2008 and modified on 08 November 2010. Please also refer to the 30 November 2010 electronic

communication from Su-Lin Sun, PharmD, regulatory project manager, requesting Eisai Inc. submit a proposed REMS as an amendment to NDA 201367 and a REMS modification with assessment to NDA 21911.

Enclosed within this submission are the documents for the REMS modification: (1) a revised comprehensive Medication Guide that is consistent with the Medication Guide approved on 08 November 2010 and that includes the new oral suspension formulation which is pending review, (2) a revised REMS and (3) a revised REMS supporting document. These documents will also be submitted as a proposed REMS amendment to NDA 201367 under separate cover.

It is too early to assess the REMS. The Medication Guide would be adequate with the proposed modifications to achieve its purpose.”

4 Discussion and Conclusion

DRISK compared the proposed REMS Modification to the approved REMS and found the documents to be identical with the exception of the inclusion of the Oral Suspension information. However, since the original REMS approval, the REMS template has undergone revisions. (see appended REMS document)

DRISK reviewed the proposed Medication Guide which proposes inclusion of all Banzel formulations and it is appended to this review. During the labeling negotiation process DRISK discussed with DNP the addition of Patient Instruction for Use (IFU) for the oral suspension dosing. FDA then requested Eisai Inc. submit an IFU which they did February 4, 2011. It should be noted that the IFU is not an element of the REMS; however, would provide additional dosing clarity for the oral suspension formulation. DRISK reviewed the IFU in collaboration with the Division of Medication Error Prevention (DMEPA) and the IFU is appended to this document.

5. Recommendations

Approve the REMS, Medication Guide, and Patient Instructions for Use (IFU) as appended to this review.

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/s/

MARY J DEMPSEY
02/10/2011

CLAUDIA B KARWOSKI
02/10/2011
concur



Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research

Office of Compliance

REMS Modification Memorandum

TO: NDA 201-367, 21-911

THROUGH: Suzanne Barone, Ph. D., Team Leader
Compliance Risk Management and Strategic Problem Solving Team
Division of Compliance Risk Management and Surveillance
Office of Compliance

FROM: Kendra Biddick, CSO
Compliance Risk Management and Strategic Problem Solving Team
Division of Compliance Risk Management and Surveillance
Office of Compliance

SUBJECT: Office of Compliance review and comment on the adequacy of the proposed modified risk evaluation and mitigation strategy (REMS) for Banzel (rufinamide) oral suspension

Review summary

The Timetable for Submission of Assessments submitted by Eisai as part of this REMS modification request should be accepted in place of the timetable in the modified REMS approved November 8, 2010.

Background

The purpose of the current request for REMS modification is to add the approval of an oral solution (NDA 201367) to the existing approval for tablets (NDA 21911). The REMS for Banzel tablets was approved November 14, 2008, with a timetable for submission of assessments that met the approval standard at the time. The standard language and due dates have changed and the REMS should be modified accordingly. The goal of the REMS is to educate prescribers and patients about the potential serious risks of Banzel (rufinamide). These risks include including the increased risk of suicidal thoughts and behavior.

OC Observations

The submissions for the two NDAs are identical, including the NDA number (201367), thus there is no REMS submitted with the NDA number 21911.

The Timetable for Submission of Assessments submitted by Eisai as part of the request for modification of the REMS meets the current standards for language and due dates.

OC Recommendations

The Office of Compliance recommends that the Timetable for Submission of Assessments be accepted as submitted by Eisai, and that both applicable NDAs appear at the top of the REMS document. The text that follows the Timetable for Submission of Assessments in the version of the REMS approved November 11, 2008 should be removed:

[REDACTED] (b) (4)

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/s/

KENDRA A BIDDICK
01/19/2011

SUZANNE BARONE
01/19/2011