CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

022036Orig1s000

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:	March 1, 2010
To:	Russel Katz, M.D., Director **Division of Neurology Products (DNP)**
Through:	Claudia Karwoski, PharmD, Director **Division of Risk Management (DRISK)**
From:	Jessica M. Diaz, RN, BSN Patient Product Information Reviewer **Division of Risk Management**
Subject:	DRISK Review #2 of Proposed Risk Evaluation and Mitigation Strategy (REMS) Feedback for Sponsor Submission
Drug Name(s):	SILENOR (doxepin) tablets
Application Type/Number:	NDA 22-036
Applicant/sponsor:	Somaxon Pharmaceuticals, Inc.
OSE RCM #:	2008-1663

1 INTRODUCTION

This memorandum is in response to a request by the Division of Neurology Products (DNP) for the Division of Risk Management (DRISK) to review Somaxon Pharmaceuticals, Inc's Risk Evaluation and Mitigation Strategy (REMS) submission on February 4, 2010 in response to DRISK's review of the proposed REMS completed November 10, 2009.

2 MATERIAL REVIEWED

- Proposed SILENOR (doxepin) Risk Evaluation and Mitigation Strategy (REMS) with feedback submitted on February 4, 2010. (See Appendix A)

3 CONCLUSIONS AND RECOMMENDATIONS

DRISK concurs with the REMS submission from Somaxon Pharmaceuticals, Inc, the changes to the document are consistent with the recommendations proposed in the Memo dated November 10, 2009.

Please let us know if you have any questions.

Appendix A: Somaxon Pharmaceuticals Submission

risk-management-pla
ns-silenor-02-2010.p

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22036	ORIG-1	SOMAXON PHARMACEUTICALS INC	SILENOR (DOXEPIN HCL)

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/s/

JESSICA M DIAZ
03/01/2010

CLAUDIA B KARWOSKI
03/01/2010
concur

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:	November 10, 2009
To:	Russel Katz, M.D., Director **Division of Neurology Products (DNP)**
Through:	Claudia Karwoski, PharmD, Director **Division of Risk Management (DRISK)**
From:	Jessica M. Diaz, RN, BSN Patient Product Information Reviewer **Division of Risk Management**
Subject:	DRISK Review of Proposed Risk Evaluation and Mitigation Strategy (REMS)
Drug Name(s):	SILENOR (doxepin) tablets
Application Type/Number:	NDA 22-036
Applicant/sponsor:	Somaxon Pharmaceuticals, Inc.
OSE RCM #:	2008-1663

1 INTRODUCTION

This memorandum is in response to a request by the Division of Neurology Products (DNP) for the Division of Risk Management (DRISK) to review the proposed Risk Evaluation and Mitigation Strategy (REMS) for SILENOR (doxepin). Please send these comments to the Applicant and request a response within two weeks of receipt. Please let us know if you would like a meeting to discuss these comments before sending to the Applicant. The Medication Guide review was completed by DRISK under separate cover on November 9, 2009. The DRISK review of the methodology and survey instruments once submitted by the Applicant to evaluate the REMS will also be provided under separate cover.

2 MATERIAL REVIEWED

- Proposed SILENOR (doxepin) Risk Evaluation and Mitigation Strategy (REMS), submitted on November 11, 2008.

3 CONCLUSIONS AND RECOMMENDATIONS

DRISK does not concur with the elements of the REMS. While the REMS included a medication guide and timetable for submission of assessments, it also included a proposal by the company to (b) (4) DRISK did not review this letter because we do not consider it necessary for approval of the REMS. We defer to the DNP as to whether (b) (4) If, DNP agrees that it would be acceptable that the sponsor (b) (4)

Please note, the timetable for submission of the assessments is required to be approved as part of the REMS, but not the Applicant's proposed information about the details of the REMS evaluation (methodology/instruments). The methodology and instruments **do not** need to be reviewed or approved prior to approval of the REMS.

We have the following comments and recommendations for the Applicant with regard to the proposed REMS.

Comments to Somaxon:

See the appended SILENOR (doxepin) REMS proposal (Appendix A of this memo) for track changes corresponding to comments in this review.

a. GOAL

Revise your goal as follows:

The goal of this REMS is to inform patients about the serious risks associated with the use of Silenor.

b. We have some editorial comments for the Medication Guide distribution plan in this section of the proposed REMS.

c. We remind you of the required statement alerting the dispenser to provide the Medication Guide with the product to the patient. The statement must be on the carton and container of all strengths and formulations. We recommend the following language:

Unit of use:

"Dispense the enclosed Medication Guide to each patient."

Not Unit of Use:

(b) (4)

d. We acknowledge you have included a Communication Plan with this REMS however, a Communication Plan is not necessary for the approval of this REMS.

e. Your proposed timetable for submission of assessments 18 months, 3 years, and 7 years is acceptable.

We have some editorial comments in this section of the proposed REMS.

f. Please submit for review a detailed plan to evaluate patients' understanding about the safe use of SILENOR (doxepin). Your detailed plan should be submitted as part of the REMS supporting document. This information **does not** need to be submitted for FDA review prior to approval of your REMS, however it should be submitted at least 90 days before you plan to conduct the evaluation. The submission should be coded "REMS Correspondence." If you plan to conduct this assessment using a survey, your submission should include:

- All methodology and instruments that will be used to evaluate the patients' understanding about the safe use of SILENOR (doxepin). This should include, but not be limited to:
  - Sample size and confidence associated with that sample size
  - How the sample will be determined (selection criteria)
  - The expected number of patients to be surveyed
  - How the participants will be recruited
  - How and how often the surveys will be administered
  - Explain controls used to minimize bias
  - Explain controls used to compensate for the limitations associated with the methodology
- The survey instruments (questionnaires and/or moderator's guide).
- Any background information on testing survey questions and correlation to the messages in the Medication Guide.

Please let us know if you have any questions.

4 pages of Draft Labeling have been Withheld in Full as b4 (CCI/TS) immediately following this page.

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NDA-22036	ORIG-1	SOMAXON PHARMACEUTICALS INC	SILENOR (DOXEPIN HCL)

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/s/

JESSICA M DIAZ
11/10/2009

CLAUDIA B KARWOSKI
11/10/2009
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