CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

202763Orig1s000

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 Surveillance and Epidemiology
Office of Medication Error Prevention and Risk Management

Date: February 8, 2012

To: Julie Beitz, MD, (Acting) Director
Division of Reproductive and Urologic Products (DRUP)

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

From: Robert Shibuya, MD, (Acting) Deputy Director, DRISK

Subject: Addendum to REMS Review dated January 31, 2012

Drug Name: Testosterone Gel (topical)

Application Type/ Number: NDA 202763

Applicant/Sponsor: Teva Pharmaceuticals

OSE RCM #: 2011-229

DRISK was informed via email from Jeannie Roule, DRUP-RPM, that DRUP, Division of Medication Error Prevention Analysis (DMEPA), and Chemistry (CMC) jointly decided that this product will be referred to as testosterone gel (b) (4)

DRISK agrees with that decision and the resulting revisions to the Professional Labeling (PI, Medication Guide (MG), and REMS (b) (4)

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

/s/

ROBERT B SHIBUYA
02/16/2012

MEMORANDUM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: February 3, 2012

TO: NDA 202763

THROUGH: Jeannie Roule

SUBJECT: DRISK comments/ REMS document

APPLICATION NUMBER: NDA 202763 (testosterone gel)

Comments from DRISK concerning the REMS document wee emailed to the Sponsor.

Please see attached email correspondences for all of the details.

The Division of Risk Management (DRISK) has completed their review of your proposed Risk Evaluation Mitigation Strategy (REMS) for the New Drug Application (NDA) 202763 submitted by Teva Pharmaceuticals January 13, 2011.

Your agreed upon REMS document is attached.

A Supporting Document was not provided in this proposed REMS submission.

Regarding your Assessment Plan:

Submit for review the detailed plan you propose to use to evaluate patients' understanding about the safe use of testosterone gel. You may submit the proposed plan after approval of the REMS, however submit it at least 90 days before you conduct the evaluation. Code the submission "REMS Correspondence." If the plan is to conduct the required assessment using a survey, make sure the submission includes all methodology and instruments used to evaluate the knowledge about the risks associated with and safe use of testosterone gel.

1. Recruit respondents using a multi-modal approach. For example, you might recruit respondents through physicians' offices, pharmacies, managed care providers, consumer panels, or on-line.

   Explain how often you perform non-respondent follow-up or reminders. If you use an incentive or honorarium, provide details on what is offered and the estimated dollar value.

   Explain how you select recruitment sites.

   Submit for review any recruitment advertisements.

2. Define the sample size and confidence interval associated with that sample size. Describe the rationale for your sample size.

3. Define the expected number of people to be contacted to obtain the proposed sample size, and how the sample is determined (selection criteria).

4. Ensure the sample is demographically representative of the population who use the drug (patients), regardless of the condition for which they use or prescribe it.

5. When possible and appropriate, ensure the sample is diverse in terms of age, race, ethnicity, sex, socio-economic status, education level, and geographically.

6. List the inclusion criteria for patients. For example, eligible *patient* respondents must be:

- Age 18 or older
- Currently taking testosterone gel or have taken the drug in the past 3 months
- Not currently participating in a clinical trial involving testosterone gel

Submit any screener instruments, and describe any quotas of sub-populations used.

7. Explain how you administer surveys and the intended frequency.
   Offer respondents multiple options for completing the survey. Be sure to include an option for the lower literacy population. For example, respondents might complete surveys online or through email, in writing or by mail, over the phone, and in person.

   Explain how you train surveyors.

8. Explain how you control for limitations or bias associated with the methodology and survey instrument(s).

9. Submit for review the introductory text used to inform respondents about the purpose of the survey.

   Tell potential respondents that their answers will not affect their ability to receive or take (patients testosterone gel, and that their answers and personal information will be kept confidential and anonymous.

10. Clarify in your methodology that respondents are eligible for one wave of the survey only.

11. Analyze results on an item-by-item or variable-by-variable basis. You may present the data using descriptive statistics, such as sample size, mean, standard deviation, median, minimum and maximum (for continuous variables), and frequency distributions (for categorical variables).

    You may stratify the data by any relevant variable, and also in aggregate.

12. Submit all methodology and instruments utilized with your assessments.

WITH REGARD TO THE PATIENT SURVEY INSTRUMENT:

13. The assessment evaluates the effectiveness of the REMS in achieving the goal by evaluating patients' knowledge of the serious risks associated with use of the drug. The assessment does not evaluate consumer comprehension of the Medication Guide.

14. Respondents should not be offered an opportunity to read or see the Medication Guide, Package Insert, or any other related educational materials again prior to taking the survey.

15. Submit for review the survey instruments (questionnaires and/or moderator's guide), including any background information on testing survey questions and correlation to the messages in the Medication Guide.

16. Ensure the patient knowledge survey includes questions that ask about the specific risks or safety information conveyed in the Medication Guide to determine if the patient understands the information and knows what to do if they experience an adverse event.

    Derive the risk-specific questions from information located in the "What is the Most Important Information I should know about testosterone gel?" section of the Medication Guide.

    Ensure the risk-specific questions are not biased or leading, and that multiple choice questions include an instruction to "select all that apply." Answer options should include an appropriate number of foils. Ensure that each question has an "I don't know" answer option.

    Randomize the order of the multiple choice responses on each survey.

17. Order questions so the risk-specific questions are asked first, followed by questions about receipt of the Medication Guide. Collect demographic questions last or as part of any screener questions.

    Do not allow respondents the opportunity or ability to go back to previous questions in the survey.

    Explain if and when any education will be offered for incorrect responses.

18. Include questions about receipt of the Medication Guide in the patient survey as a way to fulfill the obligation to report on the distribution of the Medication Guide.

19. Prior to the questions about receipt of the Medication Guide, include text that describes a Medication Guide. For example, Now we are going to ask you some questions about the Medication Guide you may have received with testosterone gel. The Medication Guide is a paper handout that contains important information about the risks associated with use of testosterone gel and how to use testosterone gel safely. Medication Guides always include the title "Medication Guide" followed by the word testosterone gel and its pronunciation. The Medication Guide usually has sections titled "What is the most important information I should know about testosterone gel," "What is testosterone gel," and "Who should not take testosterone gel."

20. Use the following (or similar) questions to assess receipt and use of the Medication Guide.

- Who gave you the Medication Guide for testosterone gel? (Select all that apply)
  - a) My doctor or someone in my doctor's office
  - b) My pharmacist or someone at the pharmacy
  - c) Someone else - please explain: _____
  - d) I did not get a Medication Guide for [Testosterone gel]

- Did you read the Medication Guide?
  - a) All,
  - b) Most,
  - c) Some,
  - d) None

- Did you understand what you read in the Medication Guide?
  - a) All,
  - b) Most,
  - c) Some,
  - d) None

- Did someone offer to explain to you the information in the Medication Guide?
  - a) Yes, my doctor or someone in my doctor's office
  - b) Yes, my pharmacist or someone at the pharmacy
  - c) Yes, someone else – please explain: _____
  - d) No

- Did you accept the offer? Yes or No

- Did you understand the explanation that was given to you?
  - a) All,
  - b) Most,
  - c) Some,
  - d) None

- Did or do you have any questions about the Medication Guide? Yes or No (If Yes, list your question(s) below) Note: Group/code this open text field prior to submitting to FDA

From: Roule, Jeannie
Sent: Friday, February 03, 2012 3:04 PM
To: 'Jane Frahn'; 'Aglaye Metellus'; Robert Vincent
Subject: REMS comments

Attachments: REMS comments from DRISK to Sponsor Feb 2012.doc; REMS doc from Sponsor Feb 2 2012.doc

Hello,

I have attached a word document that contains the comments concerning your REMS document that you have agreed to.
I have attached that document as well. The version that you sent back to me had deleted the top line. I have included it in this version.

Please accept the change and return the REMS document (only) back to me as soon as possible

Regards,
Jeannie


REMS comments from DRISK to Sp...


REMS doc from Sponsor Feb 2 20...

Jeannie Roule
Regulatory Project Manager
Division of Reproductive and Urologic Products
Center for Drug Evaluation and Research
Food and Drug Administration
Phone: (301) 796-2130 (main)
Direct Line: (301) 796-3993
Fax: (301) 796-9897
Email: jeannie.roule@fda.hhs.gov

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

/s/

JEANNIE M ROULE
02/03/2012

Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Surveillance and Epidemiology
Office of Medication Error Prevention and Risk Management

Date:	January 31, 2012
To:	Julie Beitz, MD, (Acting) Director Division of Reproductive and Urologic Products (DRUP)
Through:	Claudia B. Karwoski, PharmD, Director Division of Risk Management (DRISK)
From:	Robert Shibuya, MD, (Acting) Deputy Director, DRISK
Subject:	REMS Review
Drug Name:	Testosterone Gel 1% (topical)
Application Type/ Number:	NDA 202763
Applicant/Sponsor:	Teva Pharmaceuticals
OSE RCM #:	2011-229

1 Background

The Division of Reproductive and Urologic Products (DRUP) requested the Division of Risk Management (DRISK) review the topical Testosterone Gel 1% proposed Risk Evaluation Mitigation Strategy (REMS) for the New Drug Application (NDA) 202763 submitted by Teva Pharmaceuticals January 13, 2011.

The Medication Guide review by Division of Medical Policy Programs (DMPP) was completed January 20, 2012 under separate cover. The subject of this review is the REMS document.

2 Material Reviewed

- January 13, 2011 proposed REMS

3 REMS Elements

There is agreement between DRUP and DRISK that in accordance with section 505-1 of the FDCA, a REMS is necessary for the testosterone class of products to ensure that the benefits of the drug outweigh the risk of secondary exposure of children to testosterone due to drug transfer from adult males using testosterone gel drug.

The REMS must include the following elements:

- Medication Guide
- Timetable for Submission of Assessments

4 Conclusion and Recommendation to DRUP

DRISK reviewed the topical Testosterone Gel 1% proposed REMS and finds it acceptable with minor revisions. The detail of the distribution of the Medication Guide is more appropriate for the REMS Supporting Document. It is now CDER policy to include dates on REMS in order to have the most recent version posted on the FDA web site. (See attached REMS)

Send the applicant the attached REMS and the below comments on their assessment plan.

Please let DRISK know if you have any questions.

Comments to Teva Pharmaceuticals

See the appended topical Testosterone 1% REMS proposal for tracked changes corresponding to comments in this review.

A Supporting Document was not provided in this proposed REMS submission.

Regarding your Assessment Plan:

Submit for review the detailed plan you propose to use to evaluate patients' understanding about the safe use of [Tradename]. You may submit the proposed plan after approval of the REMS, however submit it at least 90 days before you conduct the evaluation. Code the submission "REMS Correspondence." If the plan is to conduct the required assessment using a survey, make

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2 Pages of Draft Labeling have been Withheld in Full as b4 (CCI/TS) immediately following this page

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

/s/

ROBERT B SHIBUYA
01/31/2012

CLAUDIA B KARWOSKI
01/31/2012
concur