CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

22309Orig1s000

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:	April 11, 2011
To:	Scott Monroe, MD, Director **Division of Reproductive and Urologic Products (DRUP)**
Through:	Claudia Karwoski PharmD, Director **Division of Risk Management (DRISK)**
From:	Shawna Hutchins, MPH, BSN, RN Patient Labeling Reviewer **Division of Risk Management (DRISK)**
Subject:	DRISK Review of Proposed Risk Evaluation and Mitigation Strategy (REMS)
Drug Name(s):	ANDROGEL 1.62% (testosterone gel)
Application Type/Number:	NDA 22-309
Applicant/sponsor:	Abbott Products Inc.
OSE RCM #:	2010-2434

1. INTRODUCTION

This review is written in response to a request by the Division of Reproductive and Urologic Products (DRUP) for the Division of Risk Management (DRISK) to review the Applicant's proposed Risk Evaluation and Mitigation Strategy (REMS) and REMS Supporting Document for AndroGel 1.62% (testosterone gel).

Please send these comments to the Applicant and request a response within two weeks of receipt. Let us know if you would like a meeting to discuss these comments before sending to the Applicant.

The DRISK review of the Medication Guide will be provided under a separate cover. The DRISK review of the methodology and survey instruments to be submitted by the Applicant to evaluate the REMS will be provided under separate cover.

2. BACKGROUND

In May of 2009, the FDA announced that it was requiring the sponsors of two existing FDA approved topical testosterone products to include new safety information in the labeling for their testosterone products. The FDA also notified the sponsors that they were required to submit a proposed REMS and Medication Guide for these products. The new safety information referred to by the FDA were cases of secondary exposure of children to testosterone due to drug transfer from adult males using testosterone gel products, presumably resulting from the failure to follow appropriate instructions for use. The particular populations at risk of inadvertent transfer are children and adult females. The revised labels, FDA approved REMS and Medication Guides of the two marketed topical testosterone gel products were approved in September of 2009.

Abbott Products Inc. voluntarily submitted a proposed Risk Evaluation and Mitigation Strategy (REMS) for NDA 22-309 AndroGel 1.62% (testosterone gel) for topical use, as it believes the additional information for patients will assist in reducing the risk of inadvertent secondary exposure of testosterone to children. In particular, the sponsor believes the inclusion of a Medication Guide with the product will promote the correct adherence by patients to the directions for the use of AndroGel 1.62%, and inform the patient about known potential side effects with the product.

3. MATERIAL REVIEWED

- Proposed AndroGel 1.62% (testosterone gel) Risk Evaluation and Mitigation Strategy (REMS) and REMS Supporting Document, submitted on January 15, 2010, and received by DRISK on March 29, 2011.

4. RESULTS OF REVIEW

In our review of the proposed REMS, we have:

- Ensured it meets the statutory requirements under the Food and Drug Administration Amendments Act (FDAAA) of 2007.

5. CONCLUSIONS AND RECOMMENDATIONS

Based on the available data, DRISK and DRUP concur that a REMS is necessary for Androgel 1.62% (testosterone gel) to ensure that the benefits of a drug indicated for replacement therapy in adult males for conditions associated with the absence or deficiency of endogenous testosterone, either primary or secondary hypogonadism outweigh the risks of secondary exposure of others to testosterone. The REMS would include only a Medication Guide. (b) (4)

Please note, the timetable for submission of the assessment 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 Abbott Products Inc.:

See the appended AndroGel 1.62% (testosterone gel) REMS proposal (Appendix A of this memo) for track changes corresponding to comments in this review.

a. **GOAL**

Revise your goal as follows:

To inform patients about the serious risks associated with the use of AndroGel 1.62% (testosterone gel).

b. Your Medication Guide distribution plan appears to be acceptable. Your detailed plan for how you plan to distribute the Medication Guide in accordance with 21 CFR 208.24 is more appropriate for the REMS Supporting Document. See our editorial comments on this section of the proposed REMS (see Appendix A)

- We remind you that under 21 CFR 208.24, you are responsible for ensuring that sufficient numbers of Medication Guides are provided with the product such that a dispenser can provide one Medication Guide with each new or refilled prescription. You state that a copy of the Medication Guide will be placed in each carton, along with the PI. We find this unit-of-use distribution plan acceptable.

- We remind you that under 21 CFR 208.24, you are responsible for ensuring that the AndroGel 1.62% (testosterone gel) carton or container label contains a prominent statement that the Medication Guide should be dispensed to each patient. We suggest the following language if the product is enclosed in the carton. "Dispense accompanying Medication Guide to each patient."

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

We have some editorial comments on this section of the REMS.

d. Regarding your REMS Assessment Plan

The submitted methodology lacks sufficient detail to complete a review.

1. Submit for review the detailed plan that will be used to evaluate patients' understanding about the risks associated with and safe use of AndroGel 1.62% (testosterone gel). 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 the evaluation will be conducted. The submission should be coded "REMS Correspondence." If the plan is to conduct the required assessment using a survey, the submission should include all methodology and instruments that will be used to evaluate the patients' knowledge about the risks associated with and safe use of AndroGel 1.62% (testosterone gel).
2. We encourage you to recruit respondents using a multi-modal approach. For example, patients could be recruited online, through physicians' offices, through pharmacies, managed care providers, or through consumer panels.
   Explain how often non-respondent follow-up or reminders will be completed.
   Explain how an incentive or honorarium will be offered, and the intended amount.
   Explain how recruitment sites will be selected.
   Submit for review any recruitment advertisements.
3. Define the sample size and confidence intervals associated with that sample size.
4. Define the expected number of patients to be surveyed to obtain the final proposed sample size, and how the sample will be determined (selection criteria)
5. The patient sample should be demographically representative of the patients who use AndroGel 1.62% (testosterone gel).
   If possible and appropriate, sample should be diverse in terms of: age, race, ethnicity, sex, socio-economic status, education level, geography.
6. Explain the inclusion criteria; that is, who is an eligible respondent. For example, *patient* respondents might be:
   - Age 18 or older
   - Currently taking AndroGel 1.62% (testosterone gel) or have taken in past 3 months
   - Not currently participating in a clinical trial involving AndroGel 1.62% (testosterone gel)
   - Not a healthcare provider

   Submit any screener instruments, and describe if any quotas of sub-populations will be used.
7. Explain how surveys will be administered, and the intended frequency.
   We encourage you to offer respondents multiple options for completing the survey. This is especially important for inclusion of the lower literacy population.

For example, surveys could be completed online or through email, in writing or by mail, over the phone, or in person.
Explain how surveyors will be trained.

8. Explain controls used to compensate for the limitations or bias associated with the methodology.
9. Submit for review the introductory text that will be used to inform respondents about the purpose of the survey.
   Potential respondents should be told that their answers will not affect their ability to receive or take AndroGel 1.62% (testosterone gel), and that their answers and personal information will be kept confidential and anonymous.
10. Respondents should not be eligible for more than one wave of the survey.
11. The assessment is to evaluate the effectiveness of the REMS in achieving the REMS goal by evaluating patients' knowledge of the serious risks associated with use of AndroGel 1.62% (testosterone gel). The assessment is not to evaluate consumer comprehension of the Medication Guide.
    Other than when the patient received the Medication Guide at the time the prescription was filled/dispensed, respondents should not be offered an opportunity to read or see the Medication Guide again prior to taking the survey.
12. 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.
13. The patient knowledge survey should include a section with questions asking about the specific risks or safety information conveyed in the Medication Guide to see if the patient not only understands the information, but knows what to do if they experience the event.
    Most of the risk-specific questions should be derived from information located in the "What is the Most Important Information I should know about AndroGel 1.62%?" section of the Medication Guide. The questions should be about understanding the risk, the symptoms, and what to do if the event occurs.
    The risk-specific questions should be non-biased, non-leading, multiple choice questions with the instruction to "select all that apply." Each question should have an "I don't know" answer option.
    The order of the multiple choice responses should be randomized on each survey.
14. The order of the questions should be such that the risk-specific questions are asked first, followed by questions about receipt of the Medication Guide. Demographic questions should be collected last or as part of any screener questions.
    Respondents should not have 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.
15. 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.

16. Just 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 AndroGel 1.62% (testosterone gel). The Medication Guide is a paper handout that contains important information about the risks associated with use of AndroGel 1.62% (testosterone gel) and how to use AndroGel 1.62% (testosterone gel) safely. Medication Guides always include the title "Medication Guide" followed by the word AndroGel 1.62% (testosterone gel) and its pronunciation. The Medication Guide usually has sections titled "What is the most important information I should know about AndroGel 1.62%," "What is Androgel 1.62%," and "Who should not take AndroGel 1.62%."

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

- Who gave you the Medication Guide for AndroGel 1.62% (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 AndroGel 1.62% (testosterone gel)

- Did you read the Medication Guide?
    - All,
    - Most,
    - Some,
    - None

- Did you understand what you read in the Medication Guide?
    - All,
    - Most,
    - Some,
    - None

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

- Did you accept the offer? Yes or No

- Did you understand the explanation that was given to you?
    - All,
    - Most,
    - Some,
    - None

- Did or do you have any questions about the Medication Guide? Yes or No (If Yes, list your question(s) below) Note: This is an open text field that should be grouped/coded by the sponsor prior to submitting to FDA

18. Results should be analyzed on an item-by-item or variable-by-variable basis. The data may be presented using descriptive statistics, such as sample size, mean, standard deviation, median, minimum and maximum (for continuous variables), and frequency distributions (for categorical variables).
19. Data may be stratified by any relevant demographic variable, and also presented in aggregate. We encourage you to submit with your assessments all methodology and instruments that were used to evaluate the effectiveness of the REMS.

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/s/

SHAWNA L HUTCHINS
04/11/2011

CLAUDIA B KARWOSKI
04/11/2011
concur

NDA 22-309 AndroGel® (testosterone gel) 1.62% CIII

Proposed Risk Evaluation and Mitigation Strategy (REMS) Supporting Document

Drug Class and Formulation: Testosterone Gel Products

Abbott Products, Inc.
901 Sawyer Road
Marietta, GA 30062
1-800-241-1643

October 18, 2010

TABLE OF CONTENTS

1. BACKGROUND

AndroGel® (testosterone gel) 1.62% CIII is a prescription topical testosterone gel that is indicated for replacement therapy in adult males for conditions associated with absence or deficiency of endogenous testosterone, either primary or secondary hypogonadism. AndroGel 1.62% is a new testosterone gel formulation based on the AndroGel 1% formulation, which was approved by the FDA in February 2000 (NDA 21-015). This new product is proposed to be administered in the dose range of 1.25 g (20.3 mg testosterone) to 5.0 g (81 mg testosterone) and is intended to achieve eugonadal concentrations of testosterone in hypogonadal men while applying less testosterone to the skin surface and up to half the amount of gel to the site(s) of application when compared to AndroGel 1%. In addition to a reduced volume of application, this 1.62% testosterone gel has improved viscosity and (b) (4) compared to AndroGel 1%. These effects have been achieved by optimizing the levels of existing components of AndroGel 1%.

AndroGel 1.62% is applied once daily to the shoulders and upper arms (b) (4) Precautions in the product labeling instruct patients to wash their hands after applying AndroGel 1.62%, and to cover the skin with clothing in areas where the product was applied, in order to avoid secondary exposure of others to testosterone.

The professional labeling for AndroGel 1.62% includes information on secondary testosterone exposure as addressed in the REMS. Several approaches have been implemented to communicate the risks of secondary exposure. The first includes the boxed warning in the prescribing information, which specifically highlights children as a higher risk population. This boxed warning indicates that 1) virilization has been reported in children who were secondarily exposed to testosterone gel 2) children should avoid contact with unwashed or unclothed application sites in men using testosterone gel and 3) health care providers should advise patients to strictly adhere to recommended instructions for use. Healthcare providers should discuss the signs and symptoms of virilization with their patients at the time of prescribing AndroGel 1.62%. Important text

in both the highlights and the main body of the prescribing information has been bolded to draw heightened attention to the reader. The prescribing information has an enhanced emphasis on safe and appropriate use of the product and describes signs and symptoms of secondary exposure that a child or woman could experience.

Secondly, Abbott has developed a Medication Guide to communicate the information about the risk of secondary exposure to patients who are prescribed the product. The REMS is designed to follow the FDA March 2005 guidance document, Development and Use of Risk Minimization Action Plans (RiskMAP)[1], and principles of Risk Evaluation and Mitigation Strategies as described in the FDA Amendments Act of 2007.[2]

The REMS includes a plan to evaluate patient awareness and understanding of the risks of secondary exposure from testosterone gel, as communicated in the Medication Guide through use of Knowledge, Attitude and Behavior (KAB) surveys.

2. GOALS AND OBJECTIVES

2.1. Goal

The goal of the REMS is to inform patients about the risks of secondary exposure associated with the use of AndroGel 1.62%.

2.2. Objectives

The specific educational objectives to be achieved by the AndroGel 1.62% REMS are to inform and educate patients about the following:

- The risk of secondary transfer (secondary exposure) of testosterone gel to others
- The proper technique for application of AndroGel 1.62%
- Steps patients should take to minimize the risk of testosterone transfer to others
- Signs and symptoms of virilization which may appear in another person if repeated secondary exposure occurs over time
- What to do if secondary exposure occurs

3. SUPPORTING INFORMATION ON PROPOSED REMS ELEMENTS

The proposed REMS for AndroGel 1.62% includes a Medication Guide to reinforce key risk messages to patients.

3.1. Additional Elements

3.1.1. Medication Guide

AndroGel 1.62% is available in a multiple-dose pump. A Medication Guide will be dispensed with each AndroGel 1.62% prescription. The following trade presentation is available:

- Carton of one 75 g pump

The product will be sold in unit-of-use packaging whereby the U.S. package insert with Medication Guide will be included with each unit-of-use package. This will permit the authorized dispenser to provide a Medication Guide to each patient receiving a prescription for AndroGel 1.62%. A copy of the Medication Guide will also be placed in each sample carton. Therefore, Abbott has met the requirements of 21 CFR 208.24 for distribution and dispensing of the Medication Guide.

The Medication Guide provides information on the risk of secondary exposure to testosterone which can occur through contact with a person using AndroGel 1.62%. It focuses specifically on how patients should use the product in order to minimize the risk of secondary exposure. The Medication Guide also describes the signs and symptoms of virilization in women and children so that patients and their families will be aware of what to monitor. The Medication Guide will also provide instruction on what a patient should do if he suspects that he has inadvertently exposed another person.

Additional copies of the Medication Guide will be available via the product website (www.androgel.com).

3.2. Timetable for Assessment of the REMS

The Sponsor is committed to evaluating the effectiveness of the REMS for AndroGel 1.62% and reporting the results to FDA. Assessments of the REMS will be provided to the FDA 18 months after approval of the REMS, with additional reports to be provided 3 and 7 years after approval. The reporting interval covered by each assessment will conclude no earlier than 60 days before the submission date for that assessment time interval. Based upon the assumption of an April 2011 approval, the tentative reporting dates are as follows:

	Month/Year of Submission
1st REMS Assessment (18 months from approval date)	September 2012
2nd REMS Assessment (3 years from approval date)	April 2014
3rd REMS Assessment (7 years from approval date)	April 2018

The assessments will include an evaluation of the effectiveness of the risk minimization program and recommendations for program improvements or changes, if required.

4. INFORMATION NEEDED FOR ASSESSMENTS

The Sponsor will conduct periodic assessments of the extent to which the REMS elements are meeting the goals or whether the goals or particular elements should be modified. The following sections summarize the sources of information that will be used in conducting the assessments.

4.1. Knowledge, Attitude, and Behavior Surveys

Knowledge, Attitude, and Behavior (KAB) surveys will be conducted with patients in order to assess their awareness and understanding of the risks of AndroGel 1.62% as

described in the Medication Guide. The surveys will also assess patient receipt of the Medication Guide.

For each assessment interval, the execution of the survey will conclude no earlier than 60 days before the assessment submission date. The methodology and protocols for the KAB surveys, and the survey instruments, will be developed after the product labeling and Medication Guide are finalized. These documents will be provided to the FDA at least 90 days before the surveys are administered. The protocol will include:

- the expected sample size and confidence intervals associated with that sample size
- a description of the methodology for recruitment and selection of the sample
- the specific selection criteria for inclusion in the survey
- a description of how and when the survey will be administered
- an explanation of the design features and controls that will be included to minimize bias and compensate for any limitations in the methodology
- A copy of the survey questionnaire will be submitted with the protocol for review.

4.2. Adverse Event Monitoring, Analysis, and Reporting

The activities occurring under this REMS will be integrated with the Sponsor's pharmacovigilance program to ensure proper surveillance, monitoring, and reporting of adverse events. The Sponsor's pharmacovigilance staff has developed specialized data collection guidelines that will be used to collect information for adverse events that may represent secondary exposure to testosterone. The Sponsor's pharmacovigilance staff will collect as much information as possible about these events and will collect it in a standardized fashion. The pharmacovigilance program will be implemented through standard operating procedures (SOPs) to ensure a robust, systematic process for capturing, evaluating, investigating, responding to, and reporting adverse events. Adverse event reports will be individually reviewed and collectively evaluated to determine if changes to the REMS could help to further mitigate the risks.

4.3. Dispensing of the Medication Guide & Patient/HCP Behaviors

The KAB surveys described above will also assess this by querying patients about whether they received a Medication Guide when their prescription for AndroGel 1.62% was dispensed. Further, patients will be asked if they read the Medication Guide, and if their Healthcare provider offered to go over the Medication Guide with them. Analyses of these responses will be provided in the regular assessment reports for the REMS.

5. REFERENCES

1. U.S. Department of Health and Human Services. Food and Drug Administration. Center for Drug Evaluation and Research (CDER). Center for Biologics Evaluation and Research (CBER). Guidance for Industry. Development and Use of Risk Minimization Action Plans. March 2005; http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm071616.pdf

2. U.S. Food and Drug Administration Amendments Act 2007 http://frwebgate.access.gpo.gov/cgi-bin/getdoc.cgi?dbname=110_cong_public_laws&docid=f:publ085.110

Risk Evaluation and Mitigation Strategy (REMS) Memorandum

U.S. FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH
Office of Drug Evaluation III
Division of Reproductive and Urologic Products

NDA: 22-309
Product: AndroGel (testosterone gel) 1.62%
APPLICANT: Unimed Pharmaceuticals, LLC
FROM: George Benson, M.D.
DATE: March 9, 2010

Section 505-1 of the Federal Food, Drug, and Cosmetic Act (FDCA) authorizes FDA to require the submission of a Risk Evaluation and Mitigation Strategy (REMS) if FDA determines that such a strategy is necessary to ensure that the benefits of the drug outweigh the risks (section 505-1(a)). Section 505-1(a)(1) provides the following factors:

(A) The estimated size of the population likely to use the drug involved;
(B) The seriousness of the disease or condition that is to be treated with the drug;
(C) The expected benefit of the drug with respect to such disease or condition;
(D) The expected or actual duration of treatment with the drug;
(E) The seriousness of any known or potential adverse events that may be related to the drug and the background incidence of such events in the population likely to use the drug;
(F) Whether the drug is a new molecular entity (NME).

After consultations between the Office of New Drugs and the Office of Surveillance and Epidemiology, we have determined that a REMS is necessary for AndroGel (testosterone gel) 1.62% to ensure that the benefits of the drug outweigh the risk of secondary exposure of children to testosterone due to drug transfer from adult men using this product. In reaching this determination we considered the following:

A. It has been estimated that 4 to 5 million American men have hypogonadism of whom 5 percent receive testosterone therapy. While it is not possible to estimate the size of the population likely to use testosterone gel products, of which AndroGel (testosterone gel) 1.62% is a member of the class, these products have the largest market share among testosterone-containing products. In 2007 alone, approximately 2.5 million prescriptions were dispensed for all formulations of testosterone-containing products.

B. Hypogonadism in men is a serious disease resulting from a lack of endogenous testosterone. The aim of testosterone therapy in men with hypogonadism is to restore or normalize male secondary sexual characteristics (such as beard, body hair, voice) and male sexual behavior, and to promote normal male somatic development (muscle

mass, bone). The consequences of long term testosterone deficiency in hypogonadal men may include decreased muscle mass and strength, decreased sexual function and osteoporosis.

C. Based on the phase 3 trial, AndroGel (testosterone gel) 1.62% was demonstrated to be effective in producing serum total testosterone concentrations within the normal range in the majority of hypogonadal men studied.

D. AndroGel (testosterone gel) 1.62% will be used for replacement therapy in males with conditions associated with a deficiency or absence of endogenous testosterone. Treatment is expected to continue throughout the patient's lifetime.

E. In addition to postmarketing reports of secondary exposure of children to testosterone, testosterone gel products, of which AndroGel (testosterone gel) 1.62% is a member of the class, have been associated with various other adverse effects, including gynecomastia, edema, and sleep apnea. Additionally, exogenous administration of testosterone may lead to azoospermia.

F. AndroGel (testosterone gel) 1.62% is not a new molecular entity.

In accordance with section 505-1 of FDCA and under 21 CFR 208, FDA has determined that a Medication Guide is required for AndroGel (testosterone gel) 1.62%. FDA has determined that AndroGel (testosterone gel) 1.62% poses a serious and significant public health concern requiring the distribution of a Medication Guide. The Medication Guide is necessary for patients' safe and effective use of AndroGel (testosterone gel) 1.62%. FDA has determined that AndroGel (testosterone gel) 1.62% is a product for which patient labeling could help prevent serious adverse effects and has serious risks (relative to benefits) of which patients should be made aware because information concerning the risks could affect patients' decisions to use, or continue to use, AndroGel (testosterone gel) 1.62%.

The elements of the REMS will be a Medication Guide and a timetable for submission of assessments of the REMS.

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22309	ORIG-1	UNIMED PHARMACEUTICALS INC	ANDROGEL

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/s/

MARTIN E KAUFMAN
03/09/2010

GEORGE S BENSON
03/10/2010

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 06, 2009
To:	Scott Monroe, M.D., Director **Division of Reproductive and Urologic Products (DRUP)**
Through:	Claudia Karwoski, PharmD, Director **Division of Risk Management (DRISK)**
From:	Shawna Hutchins, BSN, RN, Patient Labeling Reviewer **Division of Risk Management (DRISK)**
Subject:	DRISK Review of Proposed Risk Evaluation and Mitigation Strategy (REMS)
Drug Name(s):	ANDROGEL (testosterone gel) 1.62%
Application Type/Number:	NDA 22-309
Applicant/sponsor:	Solvay Pharmaceuticals Inc.
OSE RCM #:	2009-334

1 INTRODUCTION

This memorandum is in response to a request by the Division of Reproductive and Urologic Products (DRUP) for the Division of Risk Management (DRISK) to review the proposed Risk Evaluation and Mitigation Strategy (REMS) for ANDROGEL (testosterone gel) 1.62%. 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 is being reviewed by DRISK and will be provided under separate cover. The DRISK review of the methodology and survey instruments submitted by the Applicant to evaluate the REMS will also be provided under separate cover.

2 MATERIAL REVIEWED

- ANDROGEL (testosterone gel) 1.62% Risk Evaluation and Mitigation Strategy (REMS) Notification Letter dated April 22, 2009
- Proposed ANDROGEL (testosterone gel) 1.62% Risk Evaluation and Mitigation Strategy (REMS) and REMS Supporting Document submitted September 02, 2009

3 CONCLUSIONS AND RECOMMENDATIONS

DRISK concurs with the elements of the REMS which includes a Medication Guide and a Timetable for Submission of Assessments. However, the Applicant has described plans, in the REMS Supporting Document, to use additional communication tools including (b) (4) . The Applicant did not include these elements in the REMS (enforceable document) but did submit them for review. DRISK did not review these materials because we do not consider them necessary for approval of the REMS. We defer to the DRUP as to whether the (b) (4) If you agree that it would be acceptable that the sponsor send these (b) (4) outside of the approved REMS, we suggest you consult DDMAC to review these letters.

With regard to the Patient Information Sheet, we would recommend that this not be provided to patients by their prescribers. The Medication Guide should be the primary medication information that the patient should receive. We recommend instead the Applicant send additional copies of the Medication Guide to prescribers to use in explaining the appropriate use of the product.

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 Solvay Pharmaceuticals Inc.:

See the appended ANDROGEL (testosterone gel) 1.62% REMS proposal (Appendix A of this memo) for track changes corresponding to comments in this review.

a. GOAL

   Your proposed goal is acceptable.

b. The Medication Guide distribution plan is generally acceptable. We have some editorial comments in this section of the proposed REMS.

c. Your REMS Supporting Document includes a proposal to send a Patient Informational Sheet to prescribers to use in explaining the appropriate use of the product to their patients. The Medication Guide should be the primary medication information that the patient receives. We recommend that you send the prescriber copies of the Medication Guide to use in counseling patients rather than a separate patient information sheet.

d. 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.

   We acknowledge your commitment to submit your KAB survey methodology to FDA at least 90 days before the surveys are administered. The submission should be coded "REMS Correspondence". (b) (4)

Please let us know if you have any questions.

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Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22309	ORIG-1	UNIMED PHARMACEUTICALS INC	ANDROGEL

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/s/

SHAWNA L HUTCHINS
11/06/2009

CLAUDIA B KARWOSKI
11/10/2009
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