

**Summary Minutes of the Drug Safety and Risk Management Advisory Committee Meeting  
December 13, 2012**

**Location: FDA White Oak Campus, Building 31, the Great Room, White Oak Conference  
Center  
(Rm. 1503), Silver Spring, MD**

**All external requests for the meeting transcripts should be submitted to the CDER, Freedom  
of Information office.**

**These summary minutes for the December 13, 2012 Meeting of the Drug Safety and Risk  
Management Advisory Committee of the Food and Drug Administration were approved on  
2/26/13 \_\_\_\_.**

**I certify that I attended the December 13, 2012 meeting of the Drug Safety and Risk  
Management Advisory Committee and that these minutes accurately reflect what transpired.**

\_\_\_\_\_/s/\_\_\_\_\_  
**Nicole Vesely, PharmD  
Acting Designated Federal Officer  
Drug Safety and Risk Management Advisory  
Committee**

\_\_\_\_\_/s/\_\_\_\_\_  
**Almut Winterstein, PhD  
Acting Chairperson**

**for**

**Kristina Toliver, PharmD  
Designated Federal Officer  
Drug Safety and Risk Management Advisory  
Committee**

The Drug Safety and Risk Management Advisory Committee of the Food and Drug Administration, Center for Drug Evaluation and Research met on December 13, 2012 at the FDA White Oak Campus, Great Room (Rm. 1503), White Oak Conference Center (Room 1503), 10903 New Hampshire Avenue, Silver Spring, Maryland. Prior to the meeting, members and temporary voting members were provided copies of the background material from the FDA. The meeting was called to order by Almut Winterstein, PhD (Acting Chairperson); the conflict of interest statement was read into the record by Kristina A. Toliver, PharmD (Designated Federal Officer). There were approximately 50 persons in attendance. There was one Open Public Hearing speaker.

**Issue:** The Food and Drug Administration Amendments Act of 2007 requires FDA to bring, at least annually, one or more drugs with Risk Evaluation and Mitigation Strategies (REMS) with Elements to Assure Safe Use (ETASU) before CDER's Drug Safety and Risk Management Advisory Committee (DSaRM). On December 13, 2012, the Agency presented information on the risk management of teratogens, some of which have REMS with ETASU. The committee discussed two common risk management tools used to minimize the risk of teratogens – contraception and pregnancy testing. The committee discussed considerations for standardizing recommendations for use of these two tools.

**Attendance:**

**Drug Safety and Risk Management Advisory Committee Members Present (Voting):**

Brian Erstad, PharmD; Sonia Hernandez-Diaz, MD, DrPH; Peter Kaboli, MD; David Madigan, PhD; Elaine Morrato, DrPH; Almut Winterstein, PhD; T. Mark Woods, PharmD

**Temporary Members (Voting):**

Susan Broyles (Patient Representative); Christina Chambers, PhD, MPH; Elizabeth Conover, MSN; Janet Cragan, MD; John J. DiGiovanna, M.D.; Elaine Francis, PhD; Michael Green, MD; Kathleen Hoeger, MD, MPH; James Liebmann, MD; Michael Menefee, MD; Janine Polifka, MD; Sonja Rasmussen, MD, MS; Robyn Shapiro, JD; Angelica Walden (Patient Representative); Amy Whitaker, MD, MS; Katherine Wisner, MD, MS; Michael Wolf, PhD, MPH (via phone)

**Acting Industry Representative to the Drug Safety and Risk Management Advisory Committee (Non-Voting):**

Howard Fingert, MD, FACP (Acting Industry Representative)

**Drug Safety and Risk Management Advisory Committee Members Not Attending:**

Patrizia Cavazzoni, MD (Industry Representative); William Cooper, MD; Sherine Gabriel, MD (Chairperson), Karen Hopkins, MD (Consumer Representative); Jeanmarie Perrone, MD, FACMT; Marjorie Shaw Phillips, MS, RPh, FASHP; Maria Suarez-Almazor, MD, PhD

**FDA Participants (Non-Voting):**

Mwango Kashoki, MD, MPH; Claudia Manzo, PharmD; Gary Slatko, MD, MBA; Melissa Tassinari, PhD; Lynne Yao, MD

**Guest Speaker (Non-Voting, Presenting Only):** Erica Mayer, MD, MPH

**Designated Federal Officer:**

Kristina A. Toliver, Pharm.D.

**Open Public Hearing Speakers:**

Melissa Papic – Speaking on behalf of Eleanor Bimla Schwarz, MD, MS

***The agenda was as follows:***

Call to Order and Opening Remarks Introduction of Committee	<b>Almut Winterstein, PhD</b> Acting Chairperson, Drug Safety and Risk Management Advisory Committee (DSaRM)
Conflict of Interest Statement	<b>Kristina A. Toliver, PharmD</b> Designated Federal Officer, DSaRM
Opening Remarks	<b>Claudia Manzo, PharmD</b> Director Division of Risk Management (DRISK) Office of Surveillance and Epidemiology (OSE), Center for Drug Evaluation and Research (CDER), FDA
<b>FDA Presentations</b>	
Overview of REMS standardization efforts at FDA	<b>Adam Kroetsch, MSPPM</b> Operations Research Analyst Office of Planning and Analysis Office of Planning and Informatics CDER, FDA
Clarifying Questions	
General overview of contraception and pregnancy testing information available to the Agency	<b>Leyla Sahin, MD, FACOG</b> Medical Officer Pediatric and Maternal Health Staff (PMHS) Office of New Drugs (OND), CDER, FDA
Overview of contraception use and pregnancy testing in management of teratogens	<b>Tammie B. Howard, RN MSN</b> Regulatory Reviewer PMHS/OND, CDER, FDA
Clarifying Questions for the Presenters	
<b>BREAK</b>	
<b>FDA Presentations (cont.)</b>	
Communicating with Providers and Patients about Teratogenic Medicines	<b>Kate Oswell, MA</b> Health Communication Analyst DRISK/OSE, CDER, FDA
<b><u>Special Presentation:</u></b>	
Overview of current practice re: pregnancy planning and prevention	<b>Erica Mayer, MD, MPH (Guest Speaker)</b> Director of Clinical Research

counseling and assessment of most helpful tools to best facilitate risk benefit discussions related to teratogenic products

Dana-Farber/Brigham and Women's Cancer Center at Faulkner Hospital  
Assistant Professor in Medicine  
Harvard Medical School  
Boston, Massachusetts

Clarifying Questions for the Presenters

Open Public Hearing

**LUNCH**

Questions to the Committee/  
Committee Discussion

**ADJOURNMENT**

## Questions to the Committee:

### Drug Safety and Risk Management Advisory Committee Questions: December 13, 2012

The Agency is seeking input from the Committee on issues related to management of teratogenic risk in female patients of reproductive potential, and female partners of male patients treated with teratogenic drugs. The following non-voting questions will be discussed by the committee members:

#### Contraception:

1. **(DISCUSSION)** Discuss whether or not FDA should be making contraception use recommendations for providers and patients in the labeling and, when applicable, in Risk Evaluation and Mitigation Strategies (REMS) for teratogenic drugs.
  - a. If you determine that FDA should not be making contraception use recommendations, provide your reasons as to why not.
  - b. If you determine that the FDA should be making contraception use recommendations, provide your reasons as to why FDA should do so.

***Committee Discussion:** The committee stated that since contraception could be viewed as a sensitive topic, inclusion of FDA recommendations for contraception use and counseling in product labeling ensures that patients and providers discuss these issues; otherwise people may avoid the topic. The committee stated that contraception failure rates should be included in the recommendations. The committee considered methods with a <1% failure rate to be ideal for use when taking a teratogenic drug, however various other contraception methods could also be recommended. The committee noted that combined use of two comparatively less effective methods does not equal one highly effective method. The committee recommended that labeled information on contraception use should be updated regularly. With regard to female partners of male patients taking teratogenic drugs, any recommendations for contraception may be premature, based on the limited information currently available about the teratogenic risk posed to female partners. Please see transcripts from December 12 and 13 for detailed discussion.*

2. **(DISCUSSION)** If you determine that the FDA should be making recommendations for contraception use, either in labeling or in a REMS:
  - a. Discuss what factors FDA should consider when determining its contraception use recommendations (for example, contraceptive effectiveness, potential patient burden, patient adherence), and which considerations should take priority.
  - b. Discuss what specific contraception information the FDA should provide to patients and providers. Include as part of your discussion the situations for which recommendation of use of two forms of contraception is important and/or indicated.
  - c. Discuss the information sources (for example, print materials, online resources, targeted training) that FDA might use to more effectively communicate contraception use information to providers and patients.
  - d. Discuss under what specific circumstances, if any, a patient taking a drug with teratogenic risk should be referred to a specialized counselor for contraceptive counseling.

***Committee Discussion:** The committee recommended that FDA employ effective communication about recommended contraceptive methods. The failure rate and safety associated with the different contraceptive methods should be made clear. The committee also stated that the information in labeling should mention that there are a lot of factors taken in to consideration when choosing the best method of*

contraception for an individual patient. With regard to recommendations on contraception use, it is important to explain why contraception is important and to detail the teratogenic risks of their treatment. The committee also stated that it may be helpful to use a tiered approach in the product label or REMS educational information materials for contraception recommendations, showing the most effective method as the best choice, and then, if use of that method is not possible, 2<sup>nd</sup> or 3<sup>rd</sup> choices as appropriate. The committee also expressed concern regarding how the contraception information used in labeling can be kept current. The committee suggested use of a clearing- house for contraception information that could be updated as science evolves, with a link to the clearing-house in labeling as a possible alternative to the inclusion of specific information to minimize the need for labeling revisions. It was recommended that the language used in labeling advise providers to offer referral to specialized counseling on contraception when the providers determine that additional counseling beyond their knowledge or expertise is indicated; the committee stated that the specialty of the counselor should be left open. The committee recommended using technology such as smart phone apps and visual aids to more effectively communicate to patients about types of contraceptives and how to select one. It was noted that the counseling and recommendations should not be disjointed; the treatment of the patient and any needed counseling should be a collaboration amongst providers. They also stated the importance of follow-up with patients. Please see transcript for detailed discussion.

#### Pregnancy Testing:

3. **(DISCUSSION)** Discuss whether or not FDA should be making pregnancy testing recommendations for patients in the labeling and, when applicable, in REMS for teratogenic drugs
  - a If you determine that FDA should not be making pregnancy testing recommendations, provide your reasons as to why not.
  - b If you determine that the FDA should be making pregnancy testing recommendations provide your reasons as to why FDA should do so.

**Committee Discussion:** *The committee stated that there should be recommendations about pregnancy testing in product labeling and REMS materials. This is because no contraceptive is 100% effective, therefore pregnancy testing aids in the prevention or minimization of fetal exposure. The committee noted that the recommendations about the timing and frequency of pregnancy testing, and the type of test used are dependent on the goal of teratogenic risk management and the level concern about the teratogenic risk of the drug. If the risk management goal is to prevent all fetal exposures or all unintended pregnancies, then the pregnancy testing recommendations should be more stringent. Please see transcript for detailed discussion.*

4. **(DISCUSSION)** If you determine that the FDA should be making recommendations for pregnancy testing either in labeling or in a REMS:
  - a. Discuss the period of time within which pregnancy testing should be performed (1) in advance of the start of drug therapy and (2) before refilling a prescription.
  - b. Discuss how the type of pregnancy test used influences your recommended timing of the pregnancy test relative to (1) initiation of drug therapy and (2) refilling a prescription
    - i. Consider your answers in the context of urine versus serum pregnancy tests
    - ii. Consider your answers in the context of home versus laboratory pregnancy tests

- c. For teratogenic drugs that are used chronically, provide your recommendations for the frequency of pregnancy testing.

***Committee Discussion:*** *The committee stated that monthly testing should continue when already recommended. The committee suggested that monthly or very frequent testing may not be necessary for patients on highly-effective methods of contraception. The committee determined that prior to initiation (or re-initiation) of therapy with a teratogenic drug, two pregnancy tests may be necessary in order to confirm that conception has not occurred. The committee discussed the sensitivities of laboratory and urine pregnancy testing. Please see transcript for detailed discussion.*

After discussion of the questions was finished, the committee members provided their concluding statements for the meeting, as requested by the chair.

The meeting adjourned at approximately 3:00pm.