

**MEMORANDUM**

**Department of Health and Human Services  
Public Health Service  
Food and Drug Administration  
Center for Biologics Evaluation and Research**

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Date: January 10, 2011

From: Loan Nguyen, Pharm.D, Regulatory Review Officer  
CBER/OCBQ/DCM/APLB, HFM-602

Through: Lisa Stockbridge, Ph.D., Branch Chief  
CBER/OCBQ/DCM/APLB, HFM-602

To: Helen Gemignani, RPM, OVRR/DVRPA/CMC2 (HFM-478)  
Daryll Miller, Committee Chair, OVRR/DVRPA/CMC2 (HFM-478)  
Lewis Schrager, Medical Officer, OVRR/DVRPA/CRB2 (HFM-475)

Subject: Labeling Review - Comments on updated product labeling (Full Prescribing Information [FPI], container, and package labels)

Product: **Adenovirus Type 4 and Type 7 Vaccines, Live, Oral**  
BLA STN: **125296/0**  
Sponsor: Teva Woman's Health, Inc. (formerly Duramed Research Inc.)

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**Background:**

On September 14, 2010, Teva Woman's Health, Inc. (Teva), formerly Duramed Research, Inc. (Duramed), provided a resubmission to BLA 125296, Adenovirus Type 4 and Type 7 Vaccine, Live, Oral, in response to a Complete Response (CR) letter from the Agency dated July 16, 2009. The application was originally submitted on September 30, 2008.

The PDUFA action date for the resubmission is March 16, 2011.

APLB previously reviewed proposed labeling submitted with the original application (see APLB's memos dated May 12, 2009 and June 26, 2009 for details). With the resubmission of the application, Teva updated the proposed labeling to include the change in manufacturer name and other information requested by OVRR.

APLB has reviewed the updated PI that uses two adverse reaction tables (submitted on December 17, 2010) and the container and package labels (submitted on September 14, 2010). The following comments and recommendations are provided to OVRR for consideration, concurrence, and conveyance, as appropriate, to the applicant.

**Comments:**

**A. Review of Container (bottle) and Package (carton) Labels:**

- Ensure that the bottle labels and the carton label contain the expiration date and the lot number or other lot identification of the product.

**B. Review of Prescribing Information (PI):**

### **Highlights**

- Initial U.S. Approval is the four-digit year in which FDA initially approves the product. If the product is approved this year, the year 2011.
- Delete the first paragraph under section USE IN SPECIFIC POPULATIONS. Lack of information for subgroup other than pregnancy should not be included in the highlights.
- This particular product is Pregnancy Category D because it has potential risk to the fetus, as stated in the warnings and precautions. We recommend that this information be cross referenced. For example, "*Pregnancy: May cause fetal harm (5.3). Pregnancy Registry Available (8.1).*"
- For a new BLA, the revision date will be the month/year that the application is approved. Please update before approval.

### **Table of Contents**

- The use of the subsection heading "Overall Adverse Reactions" for subsection 6.1 is not necessary. The overall adverse reaction information may be presented directly beneath the section header without the use of a subsection heading. Subsection 6.1 is usually reserved for the mandated "Clinical Trials Experience." (See comment for ADVERSE REACTIONS section in FPI below). We recommend revising subsection 6.1 to Clinical Trials Experience.
- Delete study identification number, e.g. NCT00382408. (See comments for ADVERSE REACTIONS section in FPI below)
- Subsections are not necessary for Section 17 Patient Counseling Information. Consider deleting listing of subsections 17.1, 17.2, and 17.3.

### **Full Prescribing Information (FPI)**

#### **DOSAGE FORMS AND STRENGTHS (3)**

- Do not include "How Supplied" (i.e. packaging) information under this heading.
- Please include the strength or potency of the vaccine if relevant. The DESCRIPTION section states "potency of no fewer than 32,000 tissue-culture infective doses per tablet."
- Revise the statement "One Oral Enteric Coated Tablet each of Type 4 and Type 7, supplied as one bottle of each type containing 100 tablets" to improve readability. For example:

*The vaccine is available as enteric coated tablet, each of Type 4 and Type 7.*

- *Adenovirus Type 4 tablet*  
*White to off-white, round, coated tablet with stylized b imprinted on one side.*
- *Adenovirus Type 7 tablet*  
*Light peach, round, coated tablet with stylized b imprinted on one side.*

#### **WARNINGS AND PRECAUTIONS (5)**

- In subsection 5.4 Shedding and Transmission, the cross reference for virus present in

the stool should be 12.2, not 12.1.

- Some people are allergic to FD&C Yellow #6 aluminum lake dye. Consider including allergy to ingredients, particularly the dye and other chemicals in the enteric coating, as a contraindication or a warning or precaution.

#### ADVERSE REACTIONS (6)

- Revise the heading for subsection 6.1 to Clinical Trials Experience.
- Present the required statement “*Because clinical studies are conducted under widely varying conditions, adverse reaction rates observed in the clinical studies of a vaccine cannot be directly compared to the rates in the clinical trials of another vaccine and may not reflect the rates observed in practice*” immediately beneath the subheading 6.1 Clinical Trials Experience.
- Delete study identification numbers (e.g. NCT00382408) anywhere they appear in the PI. Studies should be described by their characteristics rather than their identification numbers.
- Be consistent in using the term “adverse reaction.” Adverse reactions are thought to be or potentially to be associated with the product. Adverse event that are not obviously associated with the product should not be included in the label.
- The statement “No subject in either treatment arm discontinued the study due to adverse events” seems irrelevant considering there was only one dose of vaccine. We recommend that this statement be deleted.

#### NONCLINICAL TOXICOLOGY (13)

- This section is not a required section and may be omitted in this PI as there is no data relating to nonclinical toxicology.

#### CLINICAL STUDIES (14)

- Delete study identification number, e.g. NCT00382408.

#### PATIENT COUNSELING INFORMATION (17)

- Subsections are not necessary. The information can be presented in bulleted format.
- We recommend presenting information in command language for better compliance.

If you have any questions regarding this review, please contact Loan Nguyen, Pharm.D., Regulatory Review Officer at 301-827-6333.

Firm: Teva Woman's Health, Inc.

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Bcc: HFM-602 L. Nguyen  
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Concurrence box:

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