NDA 22-110 VIBATIV™ (telavancin)

[Lipoglycopeptide]

Theravance, Inc.
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RISK EVALUATION AND MITIGATION STRATEGY (REMS)

I. GOALS

The goal of the VIBATIV REMS is to avoid unintended exposure of pregnant women to VIBATIV by:

- Educating healthcare professionals (HCPs) and patients on the potential risk of fetal developmental toxicity if women are exposed to VIBATIV while pregnant.
- Informing HCPs that a serum pregnancy test should be performed before initiating therapy with VIBATIV in women of childbearing potential.
- Informing HCPs that women of childbearing potential, including those being treated in the outpatient setting, should be counseled about pregnancy prevention and use of effective contraception during VIBATIV use.
- Informing HCPs and patients about the Pregnancy Registry for patients exposed to VIBATIV during pregnancy.

II. REMS ELEMENTS

A. Medication Guide

Theravance will ensure that a Medication Guide will be distributed with each VIBATIV prescription in accordance with 21 CFR 208.24. VIBATIV is packaged as a single unit of use and the Medication Guide is inserted inside the carton.

Additional copies of the Medication Guide will also be available via sales and/or clinical representatives, the product website, and by request at 1-800-727-7003.

Please see appended Medication Guide.

B. Communication Plan

In accordance with FDCA 505-1(e)(3), Theravance will implement a communication plan to targeted healthcare providers and pharmacists to support the implementation of the VIBATIV REMS. The communication plan consists of the following:

1. A Dear Healthcare Provider (HCP) Letter describing the fetal effects of VIBATIV seen in animals and pregnancy prevention measures. The letter will include Pregnancy Registry Information. The letter will be accompanied by the VIBATIV Package Insert (PI) and the Medication Guide.

2. The Dear HCP Letter will be distributed to targeted HCPs and pharmacists at the specified timeframes:

    a. Prior to commercial distribution
    b. 6 months after product approval
    c. 1 and 2 years after product approval

3. The Dear HCP Letter will be distributed either through hardcopy mailings by U.S. mail or email to reach the target audience. The letter will also be available on the product website. The website will also include information about the Pregnancy Registry and the toll-free number to call to enroll in the Registry.

    The email will target physicians based on the American Medical Association database. The email distribution list for other healthcare providers will be based on other databases and secured through a private contractor.

    Providers that have an email address on file will receive the Dear HCP Letter via email. If the intended recipient does not open the Dear HCP Letter within 72 hours, the materials will be distributed hardcopy via U.S. mail. The healthcare providers on the target audience list who do not have an email on file will receive a hardcopy via U.S. mail.

    All distributions, hardcopy and electronic will include the designation "Important Drug Warning" according to 21 CFR 200.5.

4. The Dear HCP Letter will be sent to the following targeted Healthcare Providers:

    Physician Groups
    Infectious Disease
    Emergency Medicine
    Critical Care Medicine
    Hospitalist
    General Surgery
    Obstetrics and Gynecology
    Family Practice

    Other Healthcare Professionals
    Health System Pharmacists / Hospital Pharmacists
    Outpatient Infusion Providers

    Organizational Headquarters
    Infectious Disease Society of America
    American College of Emergency Physicians

Society of Critical Care Medicine
Society of Hospital Medicine
Surgical Infection Society
American Thoracic Society (critical care)
American College of Chest Physicians (critical care)
American College of Obstetrics and Gynecology
American Society of Health System Pharmacists
Society of Infectious Disease Pharmacists
American College of Clinical Pharmacists
Outpatient Parenteral Antimicrobial Therapy
American Medical Association
American Hospital Association
Premier
Federation of American Hospitals

The Dear HCP Letter will be distributed with the VIBATIV Package Insert and Medication Guide.

Please see appended Dear HCP Letter.

C. **Elements to Assure Safe Use**

VIBATIV can be approved without any elements to assure safe use.

D. **Implementation System**

VIBATIV can be approved without any elements to assure safe use, therefore an implementation system is not required.

E. **Timetable for Submission of Assessments**

Theravance will submit REMS Assessments at 18 months, 3 years, and 7 years following the approval of the REMS (see table below). To facilitate inclusion of as much information as possible while allowing reasonable time to prepare the submission, the reporting interval covered by each assessment should conclude no earlier than 60 days before the submission date for that assessment. Theravance will submit each assessment so that it will be received by the FDA on or before the due date.

Timetable for Submission of Assessments	
Assessment	Month/Year of Submission
1st Assessment (18 months from approval)	March 2011
2nd Assessment (3 years from approval)	September 2012
3rd Assessment (7 years from approval)	September 2016

astellas
Leading Light for Life

IMPORTANT DRUG WARNING

September 13, 2011

Dear Health Care Provider:

This letter is to remind you of the potential risk of birth defects associated with VIBATIV™ (telavancin). A recent survey showed that healthcare providers are not aware that women of childbearing potential should have a **serum pregnancy test** before VIBATIV administration. Women should be counseled about using effective contraception during VIBATIV therapy. In addition, health care providers did not know a Medication Guide must be provided to all patients. The Food and Drug Administration required Astellas to communicate this information to you.

→ **Obtain a SERUM pregnancy test prior to administering VIBATIV**

Animal data indicate that use of VIBATIV during pregnancy is associated with reduced fetal weights and increased rates of digit and limb malformations in offspring, although these malformations were infrequent.

- **Women of child bearing potential should have a serum pregnancy test prior to administration of VIBATIV.** Serum pregnancy tests can detect a pregnancy before a urine test. Patients should be counseled on the risks and benefits of VIBATIV. Consideration should be given to using an alternative course of therapy, if a positive test result is obtained.

- **The use of VIBATIV should be avoided during pregnancy** unless the potential benefit to the patient outweighs the risk to the fetus.

- **Women of childbearing potential should use effective contraception during VIBATIV therapy.** Patients should be instructed to notify their prescribing physician/healthcare provider if they become pregnant while taking VIBATIV.

A **Pregnancy Registry** has been established to collect information about the effects of VIBATIV use during pregnancy. You are encouraged to register pregnant patients, or pregnant women may enroll themselves. Call 1-888-658-4228 to report a pregnancy.

→ **Provide the Medication Guide for All Patients Treated with VIBATIV**

The VIBATIV **Medication Guide** explains the potential risk associated with pregnancy exposure as well as other risks and benefits of VIBATIV.

- All patients who receive a course of VIBATIV should receive the Medication Guide regardless of their childbearing potential.

- The Medication Guide is included in every unit carton of VIBATIV as a tear off attachment to the package insert.

- Additional copies are available via sales representatives, the product website and by request through Astellas at 1-800-727-7003.

VIBATIV is a lipoglycopeptide antibacterial indicated for the treatment of adult patients with complicated skin and skin structure infections caused by susceptible Gram-positive bacteria.

For additional information, including the complete Indication and Boxed Warning please review the enclosed full Prescribing Information, and Medication Guide.

Sincerely,

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

/s/

SUMATHI NAMBIAR
07/27/2011