

INITIAL REMS APPROVAL: JULY 11, 2011

NDA 20-931 TIKOSYN (DOFETILIDE)

Antiarrhythmic

Pfizer, Inc.

235 East 42nd Street

New York, NY 10017

RISK EVALUATION AND MITIGATION STRATEGY (REMS) DOCUMENT

I. GOALS

To mitigate the risk of Tikosyn induced arrhythmia by:

- Ensuring that Tikosyn is prescribed only by certified prescribers, dispensed only by certified dispensers, and dispensed for use only with documentation of safe use conditions;
- Educating health care providers about the risks and the need to initiate and re-initiate therapy in a health care facility that can provide calculations of creatinine clearance, continuous electrocardiographic monitoring, and cardiac resuscitation;
- Informing patients about the serious risks associated with Tikosyn therapy.

II. REMS ELEMENTS

A. Medication Guide

A Medication Guide will be dispensed with each Tikosyn prescription in accordance with 21 CFR 208.24 and by Healthcare Providers (HCPs) as described below.

B. Elements to Assure Safe Use

1. Healthcare providers who prescribe Tikosyn will be specially certified

- a. Pfizer will ensure that healthcare providers who prescribe Tikosyn (Prescribers) are specially certified. To become certified, each prescriber will enroll in the Tikosyn Program by submitting to Pfizer a completed Prescriber Certification Form, and agreeing to the following:

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- i. I understand that patients initiated or re-initiated on Tikosyn should be admitted for a minimum of 3 days to a healthcare facility that can provide calculations of creatinine clearance, continuous electrocardiographic monitoring, and cardiac resuscitation;
 - ii. I understand that following the treatment initiation and dosing guidelines in the Tikosyn label will decrease the risk of Tikosyn induced arrhythmia;
 - iii. I will inform my patients that Tikosyn is associated with the risk of induced arrhythmias;
 - iv. I will inform my patients that their blood lab measures and ECG should be re-evaluated every 3 months;
 - v. I will provide the Tikosyn Medication Guide to each patient at the initiation and re-initiation of Tikosyn therapy. I will review the contents of the Medication Guide with each patient.
- b. Pfizer will require a one-time re-certification of all currently certified prescribers within 6 months after REMS approval.
 - c. Within 30 days of the initial approval of the Tikosyn REMS, Pfizer will send Dear Healthcare Provider Letters to all currently certified prescribers to notify them of the need to re-certify. The re-certification letter will reinforce the safety messages, safe use conditions, and REMS program elements. The letter will include a copy of the Tikosyn Full Prescribing Information, Medication Guide, Tikosyn Treatment Guidelines and Certification form, and will be available on the Tikosyn REMS program website for 6 months from the date of issuance of the letter.
 - d. Pfizer will assess the need for additional, future re-certification of prescribers based on the results of assessments and monitoring.
 - e. The Prescriber Certification Forms will be archived in the Pfizer National Tikosyn Database and a confirmation letter will be sent by Pfizer to the certified prescribers.
 - f. The following prescriber materials are part of the REMS and are appended:
 1. Dear Healthcare Provider Letter for re-certification
 2. Dear Healthcare Provider Letter for new enrollees
 3. Tikosyn Program Treatment Guidelines
 4. Prescriber Certification Form
 5. Tikosyn REMS Website

2. Tikosyn will only be dispensed by pharmacies and health care settings that are specially certified

- a. Pfizer will ensure that Tikosyn will be dispensed only by pharmacies and health care settings that are specially certified. To be certified to dispense Tikosyn, each pharmacy and healthcare setting will be enrolled in the Tikosyn program.

The enrollment process is comprised of the following steps that must be completed:

- i. Each health care setting where Tikosyn is dispensed for use will designate a representative. The designated representative will enroll in the Tikosyn Program by submitting to Pfizer a completed Institution Certification Form, and agreeing to the following:
 1. I attest that the healthcare facility where Tikosyn is initiated or re-initiated can provide calculations of creatinine clearance, continuous electrocardiographic monitoring, and cardiac resuscitation;
 2. I will ensure that all appropriate staff (including physicians, pharmacists, and telemetry nurses) are trained regarding the Tikosyn REMS program and will comply with all of the program requirements;
 3. I will establish or oversee the establishment of a system, order sets, protocols, or other measures to ensure appropriate dosing and monitoring;
 4. I will ensure that the pharmacy staff verifies that the prescribing healthcare provider is enrolled in the Tikosyn program prior to dispensing Tikosyn for inpatient use;
 5. I understand that, prior to patient discharge, the health care facility must either: provide a free 7-day (14-count) supply of Tikosyn and the Medication Guide to patients, or ensure the patient's take-home prescription is filled.
- ii. Each pharmacy where Tikosyn is dispensed will designate a representative. The designated representative will enroll in the Tikosyn Program by submitting to Pfizer a completed Tikosyn In Pharmacy Systems (T.I.P.S) Program Certification Form, agreeing to the following:
 1. I will ensure that all appropriate staff are trained and have read and understand the T.I.P.S. program materials.
 2. I will ensure that pharmacy staff will verify that the prescriber is certified in the Tikosyn program prior to dispensing each prescription, by accessing the system.
 3. I will ensure pharmacy staff stamp each prescription with the provided T.I.P.S. Stamp and initial and date the Tikosyn stamped prescription in the appropriate areas, verifying prescriber certification status.

4. I will ensure that the Medication Guide is provided by the pharmacy staff to the patient with each prescription.
 5. I will ensure a copy of the above attestations is posted or otherwise made available to pharmacy staff to ensure that the pharmacy staff understands these special conditions for use of Tikosyn.
- b. A Tikosyn Stamp will be provided to certified Retail/Mail-order Pharmacies in the T.I.P.S materials sent to pharmacies after certification so that they will be able to stamp the prescription.
 - c. Pfizer will require a one time re-certification of all currently certified health care facilities and pharmacies within 6 months after REMS approval.
 - d. Within 30 days of the initial approval of the Tikosyn REMS, Pfizer will send Dear Pharmacist letters to all currently certified health care settings and pharmacies to notify them of the need to re-certify. The re-certification letter will reinforce the safety messages, safe use conditions, and REMS program elements. The letter will include a copy of the Tikosyn Full Prescribing Information, Medication Guide, Tikosyn Treatment Guidelines and Certification form, and will be available on the Tikosyn REMS program website for 6 months from the date of issuance of the letter.
 - e. Pfizer will de-certify Tikosyn Program participant(s) for non-compliance, if warranted by assessments to evaluate compliance to Tikosyn Program requirements.
 - f. The following materials are part of the REMS and are appended:
 1. Dear Pharmacist Letter for re-certification (Institution and Retail/Mail-order Pharmacies, as applicable)
 2. Dear Pharmacist Letter for new enrollees (Institution and Retail/Mail-order Pharmacies, as applicable)
 3. Tikosyn Program Treatment Guidelines
 4. Pharmacy Certification Form (Institution and Retail/Mail-order Pharmacies, as applicable)
 5. T.I.P.S. Program Kit
 6. Tikosyn REMS Website

C. Implementation System

The Implementation System will include the following:

1. Pfizer will distribute Tikosyn only to certified prescribers, pharmacies, and health care settings.

2. Pfizer will maintain the Pfizer National Tikosyn Database, which includes the record of all enrolled and certified health care settings and pharmacies that dispense and prescribers who prescribe Tikosyn.
3. Pfizer will review distribution data to assess compliance with the requirements that Tikosyn only be dispensed by certified dispensers.
4. Pfizer will monitor compliance with the Tikosyn program to help ensure prescriptions are written by certified prescribers and that certified dispensers dispense Tikosyn in accordance with the program requirements, by conducting surveys of institutions and prescribers.
5. Based on the monitoring and evaluation of the implementation of the elements to assure safe use provided for under section B2, Pfizer will take reasonable steps to improve implementation of these elements and adherence to the REMS requirements to meet the goal of the REMS.

D. Timetable for Submission of Assessments

Pfizer will submit REMS Assessments to the FDA at 6 months and 1 year from the date of the approval of the REMS, and annually thereafter. 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. Pfizer will submit each assessment so that it will be received by the FDA on or before the due date.

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