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:

   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.

U.S. Pharmaceuticals
Pfizer Inc.
235 East 42nd Street
New York, NY 10017-5755

U.S. Pharmaceuticals

New FDA Requirement: Prescriber Certification Needed to Prescribe TIKOSYN® (dofetilide)

[Date]

Dear Dr [insert last name]:

Per FDA requirements, in order to prescribe TIKOSYN, new prescribers are required to complete a one-time certification. TIKOSYN is indicated for the conversion to and maintenance of normal sinus rhythm (delay in the time to recurrence of atrial fibrillation/atrial flutter) in highly symptomatic patients with atrial fibrillation/atrial flutter of greater than 1 week.

The TIKOSYN Education Distribution Program, currently known as the TIKOSYN Risk Evaluation and Mitigation Strategy (REMS), is required by the FDA to ensure safe use of TIKOSYN in order to mitigate the risk of 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.

In order to become certified you must review the enclosed materials and sign the certification form. The materials include the following:

- TIKOSYN Treatment Guidelines
- Prescribing Information
- Medication Guide
- Prescriber Certification Form

When you have reviewed all the materials, **please sign and mail or fax back the certification form.** The fax number is (800)-788-2637. After we have received your certification form, we will send a written confirmation of receipt.

In addition to your certification, **retail pharmacies** and **institutional pharmacies** must also be certified in order to dispense TIKOSYN. Before dispensing a prescription for TIKOSYN, the pharmacist must confirm that you are a health care professional who has been certified and is listed in the Pfizer National TIKOSYN Database.

I
avoid any disruptions in their treatment. Although patients must be provided with TIKOSYN upon discharge, it may take a few business days for the pharmacy to order TIKOSYN for subsequent prescriptions.

Should you have any questions regarding the certification program, please call
1-877-TIKOSYN or visit www.TIKOSYNREMS.com.

Regards,

Robert Wolkow, MD, FAAFP
Senior Medical Director/Team Leader
U.S. Brands
Established Products Business Unit

U.S. Pharmaceuticals
Pfizer Inc.
235 East 42nd Street
New York, NY 10017-5755

U.S. Pharmaceuticals

New FDA Requirement:
Prescriber Re-certification Required by November 2011 to Prescribe TIKOSYN® (dofetilide)

May 2011

Dear Dr [insert last name]:

You previously completed the TIKOSYN Certification Requirement, which acknowledged that you reviewed TIKOSYN education material. **Per FDA requirements, in order to continue to prescribe TIKOSYN, you are required to secure a one-time re-certification by November 2011**.

TIKOSYN is indicated for the conversion to and maintenance of normal sinus rhythm (delay in the time to recurrence of atrial fibrillation/atrial flutter) in highly symptomatic patients with atrial fibrillation/atrial flutter of greater than 1 week.

The TIKOSYN Education Distribution Program, currently known as the TIKOSYN Risk Evaluation and Mitigation Strategy (REMS), is required by the FDA to ensure safe use of TIKOSYN in order to mitigate the risk of 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.

In order to become recertified, you must review the enclosed materials and sign the certification form. The materials include the following:

- TIKOSYN Treatment Guidelines
- Prescribing Information
- Medication Guide
- Prescriber Certification Form

When you have reviewed all the materials, **please sign and mail or fax back the certification form.** The fax number is (800) 233-9141. After the certification form is received, you will receive written confirmation of receipt.

In addition to your re-certification, **retail pharmacies** and **institutional pharmacies** must also be certified. Before dispensing a prescription for TIKOSYN, the pharmacist must confirm that you are a health care professional who has been certified and is listed in the Pfizer National TIKOSYN Database.

It is important that you tell your patients to fill their TIKOSYN prescriptions as soon as possible after they are discharged to avoid any disruptions in their treatment. Although patients must be provided with TIKOSYN upon discharge, it may take a few business days for the pharmacy to order TIKOSYN for subsequent prescriptions.

Should you have any questions regarding the certification program, please call 866-249-7261 or visit www.TIKOSYNREMS.com.

Regards,

Robert Wolkow M.D.

Robert Wolkow, MD, FAAFP
Senior Medical Director/Team Leader

U.S. Pharmaceuticals
Pfizer Inc.
235 East 42nd Street
New York, NY 10017-5755

U.S. Pharmaceuticals

U.S. Brands
Established Products Business Unit

TIKOSYN® (dofetilide) TREATMENT GUIDELINES

These guidelines are part of the TIKOSYN Risk Evaluation and Mitigation Strategy (REMS) program. Prescribers and Pharmacists are required to read these guidelines and sign a Certification Form acknowledging they understand the potential risks of TIKOSYN in order to prescribe and dispense TIKOSYN.

Below, you will find detailed treatment guidelines for TIKOSYN® (dofetilide). Please call 1-877-TIKOSYN if you need additional information.

Table of Contents

Important Safety Information

TIKOSYN is indicated for the conversion and maintenance of normal sinus rhythm (delay in the time to recurrence of atrial fibrillation/atrial flutter) in highly symptomatic patients with atrial fibrillation/atrial flutter of greater than 1 week.

TIKOSYN is contraindicated with verapamil, with hydrochlorothiazide (alone or in combinations such as with triamterene), and with cation transport inhibitors such as cimetidine, ketoconazole, trimethoprim (alone or in combination with sulfamethoxazole), prochlorperazine, and megestrol. (Alternatives to cimetidine include Maalox®, Prilosec®, and Zantac®.)

Warnings/Interactions: Inhibitors of the CYP3A4, renal cation transports, drugs that prolong the QT interval, and other antiarrhythmics may increase the risk of proarrhythmia either by increasing dofetilide exposure or by adding to its QT-prolonging effect.

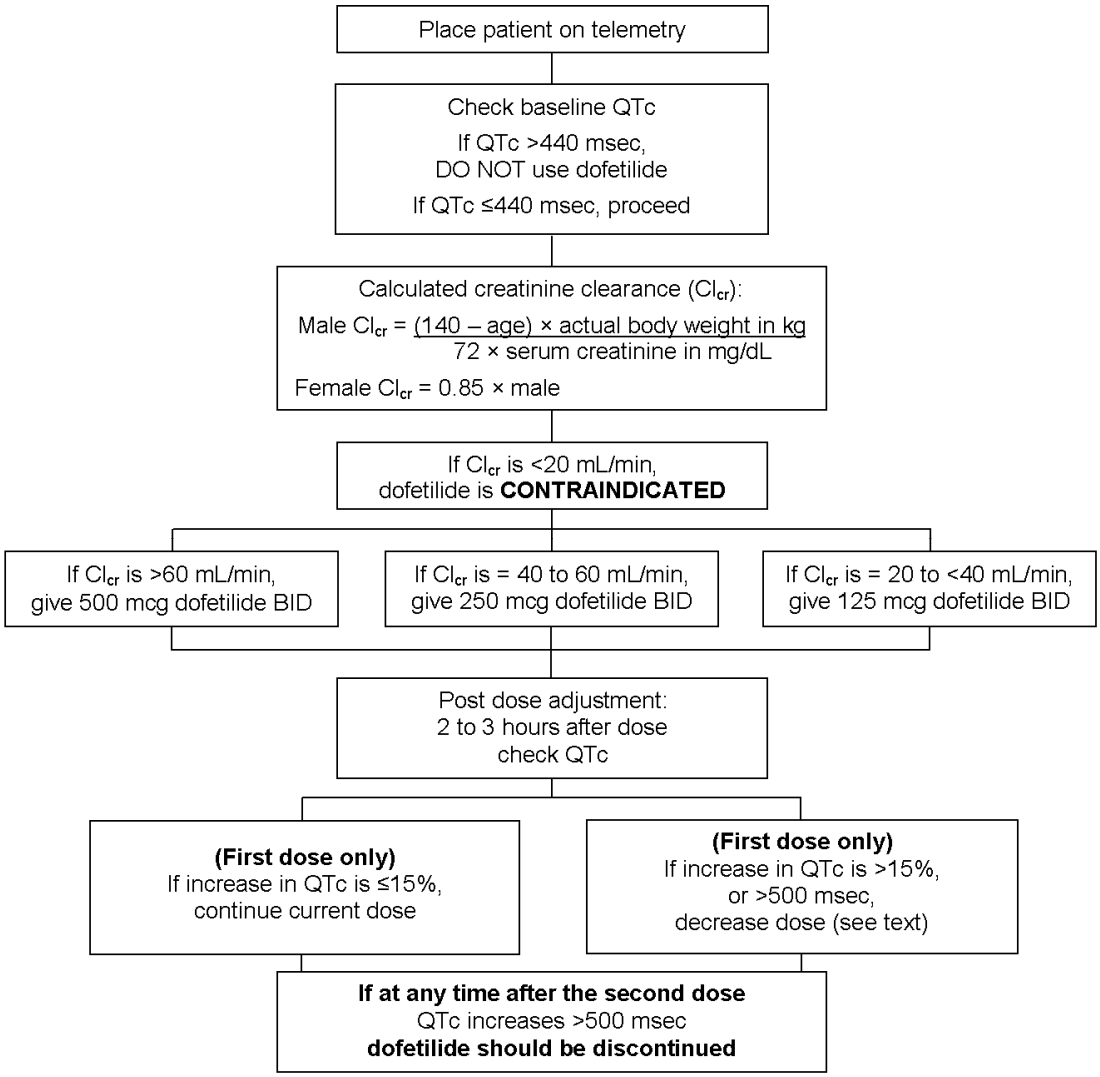
Precautions/Interactions: The following should be coadministered with care as they might increase dofetilide levels: macrolide antibiotics, azole antifungal agents, protease inhibitors, selective serotonin reuptake inhibitors, amiodarone, cannabinoids, diltiazem, nefazodone, zafirlukast, norfloxacin, quinine, triamterene, metformin, amiloride, and grapefruit juice.

To minimize the risk of induced arrhythmia, patients initiated or re-initiated on TIKOSYN should be placed for a minimum of 3 days in a facility that can provide calculations of creatinine clearance, continuous electrocardiographic monitoring, and cardiac resuscitation. TIKOSYN is available only to hospitals and prescribers who have received appropriate TIKOSYN dosing and treatment initiation education.

Dosing Overview

Please review this overview of dosing for TIKOSYN® (dofetilide).

Dosing Algorithm Used in the TIKOSYN Clinical Program



TIKOSYN [product information] New York, NY; Pfizer Inc.: 2004

Steps for Initiation and Dosing

The following are suggested guidelines for the initiation and dosing of TIKOSYN® (dofetilide).

PREDOSE STEPS

1. Before initiating TIKOSYN therapy, previous antiarrhythmic therapy should be withdrawn for a minimum of 3 plasma half-lives. TIKOSYN should not be initiated following amiodarone therapy until amiodarone plasma levels are below 0.3 mcg/mL or until amiodarone has been withdrawn for at least 3 months.

2. Patients with atrial fibrillation should be anticoagulated according to usual medical practice.

3. Admit patient to the telemetry unit; choose a telemetry lead with a visible QT interval. All measurements of the QT interval should be from this lead.

4. Telemetry monitoring should continue for a minimum of 3 days or for 12 hours after conversion to normal sinus rhythm, whichever is longer.

5. The concomitant use of verapamil, hydrochlorothiazide (alone or in combination, such as with triamterene), or the cation transport system inhibitors cimetidine, trimethoprim (alone or in combination with sulfamethoxazole), and ketoconazole with TIKOSYN is contraindicated, as each drug causes a substantial increase in dofetilide plasma concentration. In addition, other known inhibitors of the renal cation transport system, such as prochlorperazine and megestrol, should not be used in patients on TIKOSYN. Please see full prescribing information for TIKOSYN.

6. CAUTION should be used when coadministering TIKOSYN with macrolide antibiotics, azole antifungals, protease inhibitors, and SRIs, as these agents may increase blood levels of TIKOSYN.

7. Concomitant administration of TIKOSYN and digoxin is permitted. Carefully monitor patients for the signs and symptoms of digoxin toxicity. The concomitant administration of digoxin was associated with a higher occurrence of torsades de pointes. It is not clear whether this represents an interaction with TIKOSYN or the presence of more severe structural heart disease in patients taking digoxin.

8. If potassium (K+) is <4.0 mEq/L, replace K+ before administration of TIKOSYN.

9. Before administering the first dose of TIKOSYN on Day 1, measure the QTc interval (determine the QT if the heart rate is <60 bpm or >100 bpm).

- If baseline QTc is >440 msec (500 msec in patients with ventricular conduction abnormalities), TIKOSYN is **CONTRAINDICATED**; if ≤440 msec, you may proceed.
- Note time, date, and the telemetry lead on the strip.
- All measurements of the QTc interval should be from this lead.

10. Measure the QT interval (determine QTc) 2-3 hours after each dose of TIKOSYN until the patient is discharged.

11. Determine the patient's actual body weight in kg.

12. Measure patient's serum creatinine level as mg/dL.

13. Calculate patient's creatinine clearance using the following formula:

$$\text{Male creatinine clearance} = \frac{(140\text{-age}) \times \text{actual body weight in kg}}{72 \times \text{serum creatinine (mg/dL)}}$$

$$\text{Female creatinine clearance} = \frac{(140\text{-age}) \times \text{actual body weight in kg} \times 0.85}{72 \times \text{serum creatinine (mg/dL)}}$$

DOSING

14. The creatinine clearance results should be received by the pharmacy to dispense the first TIKOSYN® (dofetilide) dose.

15. If the calculated creatinine clearance is <20 mL/min, TIKOSYN is **CONTRAINDICATED.**

16. If the calculated creatinine clearance is >60 mL/min, the appropriate dose of TIKOSYN is 500 mcg BID.

- 2-3 hours after the **initial dose**, if QTc increases to >15% from baseline, then decrease TIKOSYN to 250 mcg BID.

17. If the calculated creatinine clearance is between 40 mL/min and 60 mL/min, the appropriate dose of TIKOSYN is 250 mcg BID.

- 2-3 hours after the **initial dose**, if QTc increases to >15% from baseline, then decrease TIKOSYN to 125 mcg BID.
- If QTc increases to >500 msec (550 msec in the presence of a ventricular conduction abnormality), TIKOSYN should be decreased to 125 mcg BID.

18. If the calculated creatinine clearance is 20 mL/min to <40 mL/min, the appropriate dose of TIKOSYN is 125 mcg BID.

- >2-3 hours after the **initial dose**, if QTc increases to >15% from baseline, then decrease TIKOSYN to 125 mcg QD.
- If QTc increases to >500 msec (550 msec in the presence of a ventricular conduction abnormality), then decrease TIKOSYN to 125 mcg QD.

POSTDOSE ADJUSTMENTS

19. The **second dose** of TIKOSYN should only be given after the QT has been determined. Only 1 down titration of TIKOSYN for QTc is suggested. If QTc is still excessively prolonged, DISCONTINUE TIKOSYN therapy.

20. During therapy initiation in the hospital, at 2-3 hours after each dose of TIKOSYN, determine the QTc to see if dose adjustment is necessary.

- Response to QT measurement after the **first dose**:
    - If QTc increases by >15% or is >500 msec (550 msec in the presence of a ventricular conduction abnormality), decrease the TIKOSYN® (dofetilide) dose as described above.
- Response to QT measurement after **subsequent doses**:
    - If after subsequent doses the QTc is >500 msec (550 msec in the presence of a ventricular conduction abnormality), TIKOSYN should be DISCONTINUED.

21. TIKOSYN should be given q12h (actual times may vary according to local hospital practice; the doses should be given at the same time each day, ie, 12 hours apart); QD TIKOSYN should be given at the same time every day. The risk of torsades de pointes is related to dose as well as to patient characteristics. Physicians may, therefore, in some cases, choose doses lower than determined by the algorithm. If at any time this lower dose is increased, the patient needs to be rehospitalized for 3 days. Previous toleration of higher doses does not eliminate the need for rehospitalization.

22. After the third TIKOSYN dose, discuss with patient the option of filling Rx with patient's mail-order or retail pharmacy. Both the mail-order and retail pharmacy must be enrolled in the T.I.P.S. program. The physician who orders a TIKOSYN prescription must be a confirmed participant of a TIKOSYN education program. You will need the patient's final dose of TIKOSYN, patient's full name (correct spelling), address, insurer, and physician's name. If the TIKOSYN dose is changed or discontinued after the prescription has been faxed, please notify the mail-order or retail pharmacy immediately.

The T.I.P.S.™ Program is designed to allow retail pharmacies to stock and dispense TIKOSYN once they have been enrolled. Please visit www.TIKOSYNREMS.com for T.I.P.S.™ enrollment information.

23. Contact your hospital pharmacy to order a TIKOSYN bottle with 14 capsules of the final dosage strength.* The patient should be discharged with this bottle to ensure a sufficient drug supply for uninterrupted dosing until the patient receives the first outpatient supply of medication. Patient will be directed to fill prescription as soon as possible, since pharmacy may not have TIKOSYN stocked and requires at least 24 hours to fill prescription.

*This bottle is supplied free of charge to hospitals.

ACTIONS PRIOR TO PATIENT DISCHARGE

24. Ensure the patient received the TIKOSYN discharge bottle with 14 capsules.

25. Review the Medication Guide with your patient.

26. Alert patients that blood work and ECG will be re-evaluated every 3 months by their doctor to check the renal function and the QTc.

- If QTc exceeds 500 msec (550 msec in patients with ventricular conduction abnormalities), TIKOSYN therapy should be discontinued and patients should be carefully monitored until QTc returns to baseline levels. If renal function deteriorates, adjust dose as described in steps 16-18 under "Dosing Overview."

27. Inform the patient's Healthcare Professional that the patient is now on TIKOSYN® (dofetilide). Important points to mention include:

- TIKOSYN is contraindicated with verapamil, hydrochlorothiazide (alone or in combination, such as with triamterene), and cation transport inhibitors such as cimetidine, ketoconazole, trimethoprim (alone or in combination with sulfamethoxazole), prochlorperazine, and megestrol.
- Renal function and QTc should be re-evaluated every 3 months or as medically warranted.
- TIKOSYN is available through a mail-order or retail pharmacy enrolled in the T.I.P.S. program. If the Healthcare Professional would like to write a refill for the patient, he or she must be a confirmed participant in a TIKOSYN REMS program before the mail-order or retail pharmacy can fill the prescription. The Healthcare Professional can learn how to do this by calling 1-877-TIKOSYN (845-6796). Alternatively, the Healthcare Professional can continue to see the patient in consultation with a physician who is a confirmed participant in a TIKOSYN REMS program.
- On receipt of patient information, the Healthcare Professional should read the enclosed package insert for more information. The most serious side effect of TIKOSYN is torsades de pointes. The most common side effects with TIKOSYN occurred at rates similar to placebo and included headache, chest pain, and dizziness.

Patient Counseling

28. Advise your patients to:

- Read the Medication Guide every time they receive their prescription, including refills
- Not take cimetidine, verapamil, ketoconazole, trimethoprim/sulfamethoxazole, hydroclorothiazide, prochlorperazine, or megestrol
- Tell you of all medications they are taking including prescription, non-prescription, natural/herbal remedies, and vitamins or dietary supplements
- Report symptoms associated with electrolyte imbalance, including excessive or prolonged diarrhea, sweating, vomiting, or loss of appetite or thirst
- Not miss doses or take extra doses of TIKOSYN
- Not start any other medications, including OTCs without first consulting their doctor
- Get prescriptions filled and refilled as soon as possible to avoid any disruptions in treatment
- Report any adverse events

TIKOSYN is indicated for the conversion to and maintenance of normal sinus rhythm (delay in the time to recurrence of atrial fibrillation/atrial flutter) in highly symptomatic patients with atrial fibrillation/atrial flutter of greater than 1 week.

To minimize the risk of induced arrhythmia, patients initiated or re-initiated on TIKOSYN should be placed for a minimum of 3 days in a facility that can provide calculations of creatinine clearance, continuous electrocardiographic monitoring, and cardiac resuscitation. TIKOSYN is available only to hospitals and prescribers who have received appropriate TIKOSYN dosing and treatment initiation education.

For full prescribing information, please visit www.TIKOSYNREMS.com.

TIKOSYN® (dofetilide)
Prescriber Certification Form

For Pfizer Internal Use Only
Document Number

PRIMARY OFFICE INFORMATION (Please print. All information required.)

Your Name			
Address 1			
Address 2			
City			
State	Zip	Professional Designation: ☐ MD ☐ DO ☐ PA ☐ NP	

YOUR WORK PHONE	YOUR OFFICE FAX NUMBER	YOUR EMAIL ADDRESS

PRIMARY DEA NUMBER		PRIMARY STATE LICENSE NUMBER
	If you do not have a DEA #, you must provide your state license #. If you have both, please provide both.	

PLEASE LIST ALL OTHER DEA NUMBERS (or additional state license numbers if you do not have a DEA #)

SECOND DEA NUMBER		STATE	Please print your secondary state license number and state in the space provided
THIRD DEA NUMBER	☐ If you have more than four DEA #s, please put a check in the box at the left	STATE	Please print your tertiary state license number and state in the space provided
FOURTH DEA NUMBER			

Hospital Affiliation Information

☐ In case you are affiliated with one or more hospitals, please fill in the information below, starting with your primary. If more than four affiliations, put a check in the box at the left.

PRIMARY		
Hospital Name		
Address Line 1		
Address Line 2		
City	State	Zip

SECOND		
Hospital Name		
Address Line 1		
Address Line 2		
City	State	Zip

THIRD		
Hospital Name		
Address Line 1		
Address Line 2		
City	State	Zip

FOURTH		
Hospital Name		
Address Line 1		
Address Line 2		
City	State	Zip

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

- 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.
- I understand that following the treatment initiation and dosing guidelines as per the TIKOSYN label will decrease the risk of TIKOSYN-induced arrhythmia.
- I will inform my patients that TIKOSYN is associated with the risk of induced arrhythmias.
- I will inform my patients that their blood lab measures and ECG should be reevaluated every 3 months.
- 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.

I confirm that the above information is correct. I confirm that I have read and understand the TIKOSYN educational materials. I understand this information will be used to enable Pfizer to identify prescribers who are eligible to initiate and/or prescribe TIKOSYN under this program. I understand Pfizer might share this information with others acting on its behalf and/or government agencies.

Prescriber Signature _____ Date _____

Please retain a copy of this form for your records.
For any questions please call **1-877-TIKOSYN** or visit **www.TIKOSYNREMS.com**.

Please mail or fax this document to:
TIKOSYN
PO Box 2147
Morrisville, PA 19067-0647
FAX (800) 233-9141

To minimize the risk of induced arrhythmia, patients initiated or re-initiated on TIKOSYN should be placed for a minimum of 3 days in a facility that can provide calculations of creatinine clearance, continuous electrocardiographic monitoring, and cardiac resuscitation. TIKOSYN is available only to hospitals and prescribers who have received appropriate TIKOSYN dosing and treatment initiation education.

TKU00129

Printed in USA/April 2011

U.S. Pharmaceuticals
Pfizer Inc.
235 East 42nd Street
New York, NY 10017-5755

U.S. Pharmaceuticals

New FDA Requirement:
Institution Certification Needed to Order, Stock, and Dispense TIKOSYN® (dofetilide)

[Date]

Dear Dr. [insert last name]:

Per FDA requirements, in order to order, stock, and dispense TIKOSYN, new pharmacies are required to secure a one-time certification. TIKOSYN is indicated for the conversion to and maintenance of normal sinus rhythm (delay in the time to recurrence of atrial fibrillation/atrial flutter) in highly symptomatic patients with atrial fibrillation/atrial flutter of greater than 1 week.

The TIKOSYN Education Distribution Program, currently known as the TIKOSYN Risk Evaluation and Mitigation Strategy (REMS), is required by the FDA to ensure safe use of TIKOSYN in order to mitigate the risk of 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.

To order, stock, and dispense TIKOSYN, you must review and follow the TIKOSYN certification procedures. This will acknowledge that you, along with the appropriate staff in the institution, have been trained regarding the TIKOSYN REMS program. In order to become certified, you must review the enclosed materials and sign the certification form. The materials include the following:

- TIKOSYN Treatment Guidelines
- Prescribing Information
- Medication Guide
- Institution Certification Form

Before dispensing TIKOSYN, the pharmacist is required to confirm that the prescriber has been certified. In addition, the institution must agree to stock and provide patients prior to discharge a free 7-day (14 count) supply of TIKOSYN and the Medication Guide. As a contingency, if the initiating/re-initiating institution does not have outpatient licensing privileges to dispense the free 7-day supply of TIKOSYN, the institution will ensure the patient's take home prescription is ordered and filled at a retail pharmacy prior to patient discharge.

When you have reviewed all the materials, **please sign and mail or fax back the certification form.** The fax number is 800-788-2637. After the certification form is received, you will receive written confirmation of receipt. In addition, before dispensing TIKOSYN, you are required to confirm that the prescriber has been certified.

Should you have any questions regarding the certification program, please call 1-877-TIKOSYN or visit www.TIKOSYNREMS.com.

Regards,

Robert Wolkow M.D.

Robert Wolkow, MD, FAAFP
Senior Medical Director/Team Leader
U.S. Brands

U.S. Pharmaceuticals
Pfizer Inc.
235 East 42nd Street
New York, NY 10017-5755

U.S. Pharmaceuticals

Established Products Business Unit

U.S. Pharmaceuticals
Pfizer Inc.
235 East 42nd Street
New York, NY 10017-5755

U.S. Pharmaceuticals

New FDA Requirement:
Institution Re-certification by November 2011 Needed to Order, Stock and Dispense TIKOSYN® (dofetilide)

May 2011

Dear Dr. [insert last name]:

You previously completed the TIKOSYN Certification Requirement, which acknowledged that you reviewed the TIKOSYN education materials and that the appropriate staff in the institution had been trained regarding the TIKOSYN REMS program. **Per FDA requirements, in order to continue to order, stock, and dispense TIKOSYN you are required to secure a one-time re-certification by November 2011**.

TIKOSYN is indicated for the conversion to and maintenance of normal sinus rhythm (delay in the time to recurrence of atrial fibrillation/atrial flutter) in highly symptomatic patients with atrial fibrillation/atrial flutter of greater than 1 week.

The TIKOSYN Education Distribution currently known as the TIKOSYN Risk Evaluation and Mitigation Strategy (REMS), is required by the FDA to ensure safe use of TIKOSYN in order to mitigate the risk of 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.

In order to become recertified, you must review the enclosed materials and sign the certification form. The materials include the following:

- TIKOSYN Treatment Guidelines
- Prescribing Information
- Medication Guide
- Institution Certification Form

Before dispensing TIKOSYN, the pharmacist is required to confirm that the prescriber has been certified. In addition, the institution must agree to stock and provide patients prior to discharge a free 7-day (14 count) supply of TIKOSYN and the Medication Guide. As a contingency, if the initiating/re-initiating institution does not have outpatient licensing privileges to dispense the free 7-day supply of TIKOSYN, the institution will ensure the patient's take home prescription is ordered and filled at a retail pharmacy prior to patient discharge.

When you have reviewed all the materials **please sign and mail or fax back the certification form.** The fax number is (800) 233-9141. After the certification form is received, you will receive written confirmation of receipt. In addition, before dispensing TIKOSYN, you are required to confirm that the prescriber has been certified.

Should you have any questions regarding the certification program, please call (866) 249-7261 or visit www.TIKOSYNREMS.com.

Regards,

Robert Wolkow, MD, FAAFP
Senior Medical Director/Team Leader
U.S. Brands

U.S. Pharmaceuticals
Pfizer Inc.
235 East 42nd Street
New York, NY 10017-5755

U.S. Pharmaceuticals

Established Products Business Unit

TIKOSYN® (dofetilide)
Institution Certification Form

A designated representative must complete and sign this form as part of the TIKOSYN REMS requirements.

For Pfizer Internal Use Only
Document Number

PRIMARY INSTITUTION INFORMATION (Please print. All information required.)

Designated Representative Name	
Title/Position	
Institution Name	
Address 1	
Address 2	
City	
State	Zip

YOUR WORK PHONE	YOUR OFFICE FAX NUMBER	YOUR EMAIL ADDRESS

I DESIGNATE THE FOLLOWING AFFILIATED IN-HOSPITAL PHARMACIES, IDENTIFIED BY DEA NUMBER(S) UNDER THIS AUTHORIZATION

PLEASE LIST THE DEA #(S) COVERED BY THIS AGREEMENT

DEA NUMBER(S)

Each healthcare 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:

- 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.
- 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.
- I will establish or oversee the establishment of a system, order sets, protocols, or other measures to ensure appropriate dosing and monitoring.
- 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.
- I understand that, prior to patient discharge, the healthcare 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.

I confirm that the above information about this Institution is correct. I confirm I have read and understand the TIKOSYN educational materials. I understand the information will be used to enable Pfizer to identify Institutions that are eligible to dispense TIKOSYN under this program. I understand Pfizer might share this information with others acting on its behalf and/or government agencies.

Designated Representative Signature _____ Date _____

Please mail or fax this document to:
TIKOSYN
PO Box 2147
Morrisville, PA 19067-0647
FAX (800) 233-9141

Please retain a copy of this form for your records.
For any questions please call **1-877-TIKOSYN** or visit **www.TIKOSYNREMS.com**.

To minimize the risk of induced arrhythmia, patients initiated or re-initiated on TIKOSYN should be placed for a minimum of 3 days in a facility that can provide calculations of creatinine clearance, continuous electrocardiographic monitoring, and cardiac resuscitation. TIKOSYN is available only to hospitals and prescribers who have received appropriate TIKOSYN dosing and treatment initiation education.

T.I.P.S. PROCEDURES BOOKLET

Welcome to the T.I.P.S.™ (TIKOSYN In Pharmacy System) program

TIKOSYN® (dofetilide)
Available in
Retail Pharmacy

To minimize the risk of induced arrhythmia, patients initiated or re-initiated on TIKOSYN should be placed for a minimum of 3 days in a facility that can provide calculations of creatinine clearance, continuous electrocardiographic monitoring, and cardiac resuscitation. TIKOSYN is available only to hospitals and prescribers who have received appropriate TIKOSYN dosing and treatment initiation education.

TIKOSYN® (dofetilide) 500 250 125 mcg capsules

TIKOSYN® (dofetilide)
AVAILABLE IN RETAIL PHARMACY

The T.I.P.S. procedures booklet will guide you through the program's 3 steps: Enroll, Order, and Dispense TIKOSYN.

If you have any questions about TIKOSYN or any of the T.I.P.S. program procedures, or if you need additional program supplies, please call 1-877-TIKOSYN (1-877-845-6796) or visit www.TIKOSYNREMS.com.

1-877-TIKOSYN (1-877-845-6796)

TIKOSYN® (dofetilide) PRESCRIBING INFORMATION

TIKOSYN® is indicated for the conversion to and maintenance of normal sinus rhythm (delay in the time to recurrence of atrial fibrillation/atrial flutter) in highly symptomatic patients with atrial fibrillation/atrial flutter of greater than 1 week. As described in the TIKOSYN official US prescribing package insert (enclosed), to minimize the risk of induced arrhythmia, patients initiated or re-initiated on TIKOSYN should be placed for a minimum of 3 days in a facility that can provide calculations of creatinine clearance, continuous electrocardiographic monitoring, and cardiac resuscitation. TIKOSYN is available only to hospitals and prescribers who have received appropriate TIKOSYN dosing and treatment initiation education.

For full prescribing information, see enclosed US prescribing package insert.

ENROLLING IN T.I.P.S.

You must enroll in the T.I.P.S. program to order and dispense TIKOSYN® (dofetilide).

TO ENROLL IN THE T.I.P.S. PROGRAM

- Complete the enclosed TIKOSYN Pharmacy Certification Form
- Sign and fax the form to 1-800-788-2637
- After 1 to 2 business days, confirm your enrollment by calling 1-877-TIKOSYN (1-877-845-6796) or visiting www.tikosynlist.com. You will need to enter your pharmacy DEA number
- Your signature on the enclosed TIKOSYN certification form acknowledges that the appropriate staff members in your pharmacy are aware of the procedures for dispensing TIKOSYN
- Please post the enclosed magnetic reference piece in your pharmacy as a reference for the T.I.P.S. program procedures and TIKOSYN Important Safety Information

ORDERING TIKOSYN® (dofetilide)

Enrollment in the T.I.P.S. program must be completed before you place an order for TIKOSYN.

TO ORDER

- Order TIKOSYN through your wholesaler
- TIKOSYN is available only in bottles of 60 capsules in 3 dosage strengths: 125, 250, and 500 mcg
- All TIKOSYN orders will be drop-shipped directly to your pharmacy

DISPENSING TIKOSYN® (dofetilide)

Prescriber must be a confirmed registrant in the TIKOSYN Risk Evaluation and Mitigation Strategy (REMS) program before TIKOSYN is dispensed.

Before dispensing a prescription for TIKOSYN, you must confirm that the prescriber is a healthcare professional who has registered for the TIKOSYN REMS program and is listed in the TIKOSYN confirmed registrant database.

To verify that a prescriber is a registrant in the program, access the program database by calling the IVR (Interactive Voice Response) at 1-800-788-7353 or visiting www.tikosynlist.com and entering your pharmacy DEA number.

- At the prompt, enter the prescriber's DEA or medical license number
- The message will state, "The DEA number belongs to a prescriber who is a confirmed participant in a TIKOSYN REMS program"

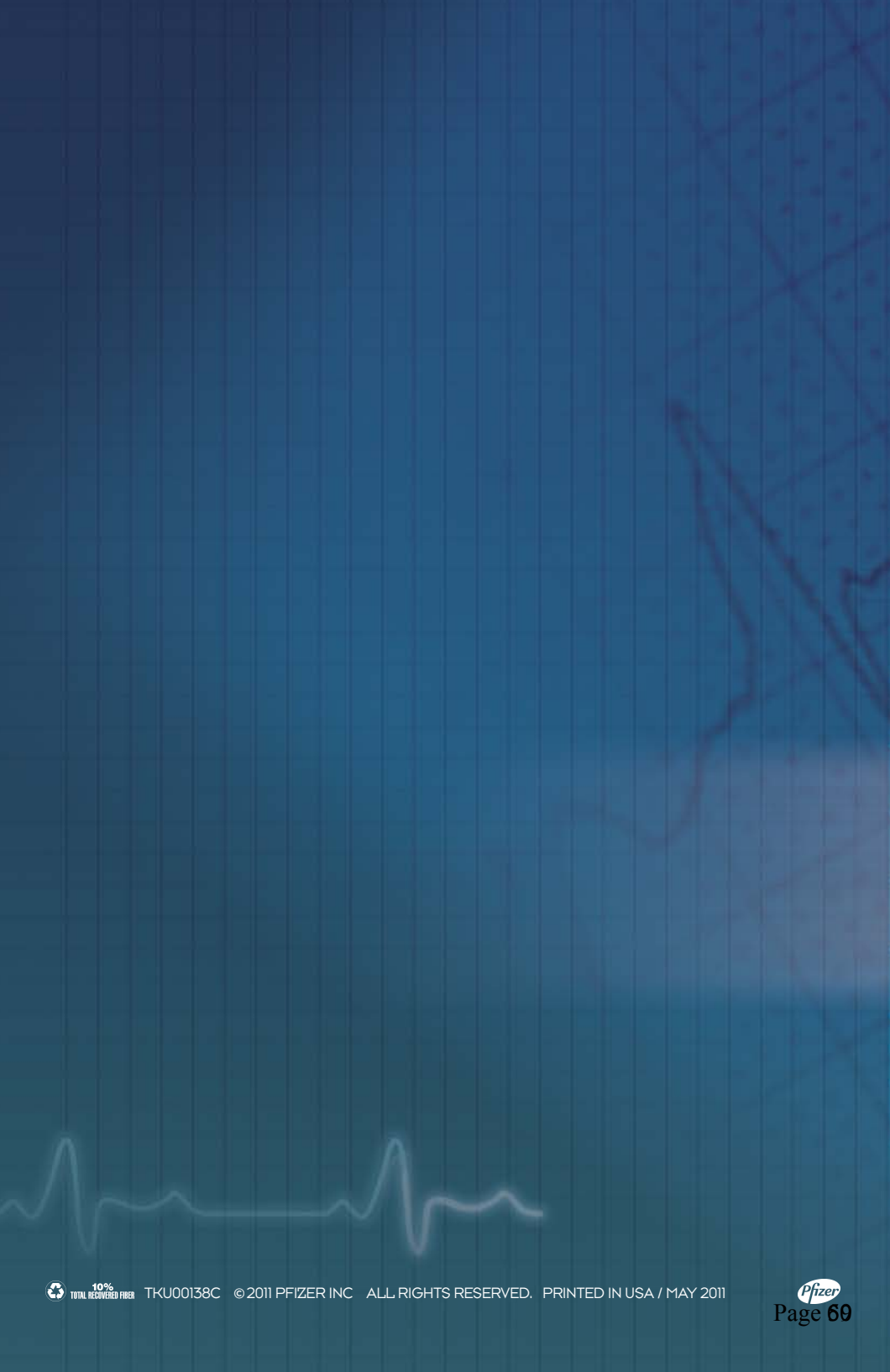
- DO NOT dispense TIKOSYN if prescriber participation in the TIKOSYN REMS program cannot be verified. Refer these prescribers to I-877-TIKOSYN (I-877-845-6796) to speak to a TIKOSYN Customer Representative

- After verifying the prescriber is a confirmed registrant, stamp the back of the prescription with the TIKOSYN stamp and put your initials and the date in the space provided

- Dispense TIKOSYN as prescribed in accordance with standard pharmacy practice (TIKOSYN must be ordered directly from Pfizer per individual prescription)

- Prescriptions filed according to standard pharmacy practice are subject to standard periodic review processes to ensure compliance with these conditions

We thank you for your interest in Pfizer and hope this information is helpful. If you would like additional information about TIKOSYN or the T.I.P.S. program, please call I-877-TIKOSYN (I-877-845-6796) or visit www.TIKOSYNREMS.com.



TIKOSYN® (dofetilide)

Follow the 3 steps in the T.I.P.S.™ (TIKOSYN In Pharmacy System) program

1. ENROLL

- Your pharmacy must be enrolled in the T.I.P.S. program to order and dispense TIKOSYN
- To confirm your enrollment, call 1 877 TIKOSYN (1 877 845 6796) or visit www.tikosynlist.com

2. ORDER

- Order TIKOSYN through your wholesaler
- TIKOSYN orders faxed by your wholesaler are processed during normal Pfizer Customer Service business hours Monday through Friday 7:00 AM to 6:00 PM Central Standard Time

Pfizer will verify pharmacy enrollment and drop-ship TIKOSYN to the pharmacy.

3. DISPENSE

- On receipt of a prescription, confirm that the prescriber is a participant in the TIKOSYN Risk Evaluation and Mitigation Strategy (REMS) program by calling the IVR (Interactive Voice Response) at 1-800-788-7353 or visiting www.tikosynlist.com
- After verification, stamp the back of the prescription with the T.I.P.S. stamp and write in your initials and the date
- File the prescription
- If you cannot verify that the prescriber has registered in the TIKOSYN REMS program, call 1-877 TIKOSYN (1-877-845-6796) to speak with a TIKOSYN Customer Representative

See T.I.P.S. program procedures booklet for complete guidelines. If you have questions about TIKOSYN or T.I.P.S. program procedures, please call 1-877 TIKOSYN (1-877-845-6796) or visit www.TIKOSYNREMS.com

TIKOSYN® is indicated for the conversion to and maintenance of normal sinus rhythm (delay in the time to recurrence of atrial fibrillation/atrial flutter) in highly symptomatic patients with atrial fibrillation/atrial flutter of greater than 1 week.

To minimize the risk of induced arrhythmia, patients initiated or re initiated on TIKOSYN should be placed for a minimum of 3 days in a facility that can provide calculations of creatinine clearance, continuous electrocardiographic monitoring and cardiac resuscitation TIKOSYN is available only to hospitals and prescribers who have received appropriate TIKOSYN dosing and treatment initiation education.

Please see full prescribing information and patient information for TIKOSYN® (dofetilide) capsules in T.I.P.S. Kit.

TIKOSYN® (dofetilide) 500 250 125 mcg capsules

TIKOSYN® (dofetilide)
IMPORTANT SAFETY INFORMATION

TIKOSYN is indicated for the maintenance of normal sinus rhythm (delay in time to recurrence of atrial fibrillation/atrial flutter [AF/AFl]) in patients with atrial fibrillation/atrial flutter of greater than one week duration who have been converted to normal sinus rhythm. Because TIKOSYN can cause life-threatening ventricular arrhythmias, it should be reserved for patients in whom atrial fibrillation/atrial flutter is highly symptomatic. In general, antiarrhythmic therapy for atrial fibrillation/atrial flutter aims to prolong the time in normal sinus rhythm. Recurrence is expected in some patients.

TIKOSYN is indicated for the conversion of atrial fibrillation and atrial flutter to normal sinus rhythm.

TIKOSYN has not been shown to be effective in patients with paroxysmal atrial fibrillation.

TIKOSYN is contraindicated in patients with congenital or acquired long QT syndromes, a baseline QT interval or QTc >440 msec (500 msec in patients with ventricular conduction abnormalities), severe renal impairment (calculated creatinine clearance <20 mL/min), or known hypersensitivity to TIKOSYN.

TIKOSYN is also contraindicated with verapamil, hydrochlorothiazide (alone or in combination, such as with triamterene), and cation transport system inhibitors such as cimetidine, ketoconazole, trimethoprim (alone or in combination with sulfamethoxazole), prochlorperazine, and megestrol because these drugs may cause an increase in dofetilide plasma concentration.

TIKOSYN can cause serious ventricular arrhythmias, primarily torsade de pointes type ventricular tachycardia, a polymorphic ventricular tachycardia associated with QT interval prolongation. QT interval prolongation is directly related to dofetilide plasma concentrations. Factors such as reduced creatinine clearance or certain dofetilide drug interactions will increase dofetilide plasma concentration. The risk of TdP can be reduced by controlling the plasma concentration through adjustment of the initial dofetilide dose according to creatinine clearance and by monitoring the ECG for excessive increases in the QT interval. Calculation of creatinine clearance and QTc for all patients must precede administration of the first dose of TIKOSYN. Renal function and QTc should be re-evaluated every 3 months or as medically warranted.

The most common adverse events reported were headache, chest pain, dizziness, respiratory tract infection, dyspnea, and nausea.

Please see full prescribing information and patient information for TIKOSYN® (dofetilide) capsules in T.I.P.S. Kit.

TIKOSYN® 500 250 125 mcg capsules
(dofetilide)

Pfizer

U.S. Pharmaceuticals
Pfizer Inc.
235 East 42nd Street
New York, NY 10017-5755

U.S. Pharmaceuticals

New FDA Requirement:
Pharmacy Certification Needed to Order and Dispense TIKOSYN® (dofetilide)

[Date]

Dear Dr. [insert last name]:

Per FDA requirements, to order and dispense TIKOSYN, retail pharmacies are required to secure a one-time certification. TIKOSYN is indicated for the conversion to and maintenance of normal sinus rhythm (delay in the time to recurrence of atrial fibrillation/atrial flutter) in highly symptomatic patients with atrial fibrillation/atrial flutter of greater than 1 week.

The TIKOSYN Education Distribution Program, currently known as the TIKOSYN Risk Evaluation and Mitigation Strategy (REMS) is required by the FDA to ensure safe use of TIKOSYN in order to mitigate the risk of 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.

To order and dispense TIKOSYN, you must review and follow the TIKOSYN In Pharmacy System (T.I.P.S.™) certification procedures below and enroll in the T.I.P.S. program.

- Complete the enclosed TIKOSYN Pharmacy Certification Form
- Sign and fax the form to 1-800-788-2637
- After 1 to 2 business days, confirm your certification by calling 1-877-TIKOSYN (1-877-845-6796) or visit www.tikosynlist.com. You will need to enter your pharmacy DEA number
- Your signature on the enclosed TIKOSYN certification form acknowledges that the appropriate staff members in your pharmacy are aware of the procedures for dispensing TIKOSYN
- Please post the enclosed magnetic reference piece as a reference of the T.I.P.S. program procedures and TIKOSYN contraindications in your pharmacy

Upon receipt of your certification form, a written confirmation will be sent to you. A TIKOSYN stamp will also be sent to you after certification so that you may stamp prescriptions.

Through pharmacy certification the pharmacy acknowledges that:

- The pharmacist will verify that a prescriber has participated in the TIKOSYN REMS and is confirmed in the Pfizer National TIKOSYN Database before dispensing.
- The pharmacist will stamp each prescription for distribution with the T.I.P.S. stamp, verifying that the prescriber is a confirmed participant in the TIKOSYN REMS. The pharmacist will then initial and date the TIKOSYN stamped prescription in the appropriate areas.
- The pharmacist will dispense a Medication Guide with each prescription.

Should you have any questions regarding the certification program, please call 1-877-TIKOSYN or visit www.TIKOSYNREMS.com.

Regards,

U.S. Pharmaceuticals
Pfizer Inc.
235 East 42nd Street
New York, NY 10017-5755

U.S. Pharmaceuticals

Robert Wolkow, MD, FAAFP
Senior Medical Director/Team Leader
U.S. Brands
Established Products Business Unit

U.S. Pharmaceuticals
Pfizer Inc.
235 East 42nd Street
New York, NY 10017-5755

U.S. Pharmaceuticals

New FDA Requirement:
Pharmacy Re-certification by November 2011 Needed to Order and Dispense TIKOSYN® (dofetilide)

May 2011

Dear Dr. [insert last name]:

You previously completed the TIKOSYN In Pharmacy System (T.I.P.S.™) certification procedure and enrolled in the T.I.P.S. program, which acknowledged that you reviewed TIKOSYN materials. **Per FDA requirements, in order to continue to order and dispense TIKOSYN you are required to secure a one-time re-certification by November 2011**.

TIKOSYN is indicated for the conversion to and maintenance of normal sinus rhythm (delay in the time to recurrence of atrial fibrillation/atrial flutter) in highly symptomatic patients with atrial fibrillation/atrial flutter of greater than 1 week.

The TIKOSYN Education Distribution Program, currently known as the TIKOSYN Risk Evaluation and Mitigation Strategy (REMS) is required by the FDA to ensure safe use of TIKOSYN in order to mitigate the risk of 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.

In order to continue to order and dispense TIKOSYN, you must review and follow the T.I.P.S. certification procedures below and enroll in the T.I.P.S. program.

- Complete the enclosed TIKOSYN Pharmacy Certification Form
- Sign and fax the form to 1-800-233-9141
- After 1 to 2 business days, confirm your certification by calling 1-877-TIKOSYN (1-877-845-6796) or visit www.tikosynlist.com. You will need to enter your pharmacy DEA number
- Your signature on the enclosed TIKOSYN Pharmacy Certification Form acknowledges that the appropriate staff members in your pharmacy are aware of the procedures for dispensing TIKOSYN
- Please post the enclosed magnetic reference piece as a reference of the T.I.P.S. program procedures and TIKOSYN contraindications in your pharmacy

Upon receipt of your certification form, a written confirmation will be sent to you. A TIKOSYN stamp will also be sent to you after re-certification so that you may stamp prescriptions.

Through pharmacy certification the pharmacy acknowledges that:

- The pharmacist will verify that a prescriber has participated in the TIKOSYN REMS and is confirmed in the Pfizer National TIKOSYN Database before dispensing.
- The pharmacist will stamp each prescription for distribution with the T.I.P.S. stamp, verifying that the prescriber is a confirmed participant in the TIKOSYN REMS. The pharmacist will then initial and date the TIKOSYN stamped prescription in the appropriate areas.
- The pharmacist will dispense a Medication Guide with each prescription.

Should you have any questions regarding the certification program, please call (866) 249-7261 or visit www.TIKOSYNREMS.com.

Regards,

U.S. Pharmaceuticals
Pfizer Inc.
235 East 42nd Street
New York, NY 10017-5755

U.S. Pharmaceuticals

Robert Wolkow, MD, FAAFP
Senior Medical Director/Team Leader
U.S. Brands
Established Products Business Unit

TIKOSYN® (dofetilide)

T.I.P.S.™ (TIKOSYN in Pharmacy System)

Pharmacy Certification Form

For Pfizer Internal Use Only
Document Number

An authorized pharmacist must complete and sign this form as part of the TIKOSYN REMS requirements.

PHARMACY INFORMATION* (Please print. All information required.)		
Name of Pharmacy		
Authorized Pharmacist Name		
Address 1		
Address 2		
City		
State		Zip Code
TELEPHONE NUMBER	If you do not have a DEA number, you must provide your NABP number.	FAX NUMBER
DEA NUMBER		NABP NUMBER

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 System (T.I.P.S.) program Enrollment Form and agreeing to the following:

- I will ensure that all appropriate staff are trained and have read and understand the T.I.P.S. program materials.
- 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.
- 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.
- I will ensure that the Medication Guide is provided by the pharmacy staff to the patient with each prescription.
- 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.

Note that the purpose of the TIKOSYN stamp is to document that the pharmacist has verified the certification status of the prescriber prior to dispensing TIKOSYN. The purpose of the pharmacy's standard periodic review process, in reference to the stamp, is to verify that TIKOSYN Program procedures, to which the pharmacy has attested, are being carried out.

I confirm that the above information about this pharmacy is correct. I confirm that I have read and understand the TIKOSYN educational materials. I understand the information will be used to enable Pfizer to identify Pharmacies that are eligible to dispense TIKOSYN under this program. I understand Pfizer might share this information with others acting on its behalf and/or government agencies.

Authorized Pharmacist Signature _____ Date _____

Please retain a copy of this form for your records.
For any questions please call **1-877-TIKOSYN** or visit **www.TIKOSYNREMS.com**.

Please mail or fax this document to:
TIKOSYN
PO Box 2147
Morrisville, PA 19067-0647
FAX (800) 233-9141

*For corporate pharmacy enrollment, check here ☐. For corporate pharmacy enrollment, a list of pharmacy sites that have been trained should be provided with this enrollment form. Please email the following information to TIKOSYNREMS@medimedia.com. This list should include the required **Pharmacy Information** detailed above for each pharmacy site.

To minimize the risk of induced arrhythmia, patients initiated or re-initiated on TIKOSYN should be placed for a minimum of 3 days in a facility that can provide calculations of creatinine clearance, continuous electrocardiographic monitoring, and cardiac resuscitation. TIKOSYN is available only to hospitals and prescribers who have received appropriate TIKOSYN dosing and treatment initiation education.

Please fax this document to TIKOSYN Risk Evaluation and Mitigation Strategy (REMS) Database Manager at (800) 233-9141.

TIKOSYN® (dofetilide)

Risk Evaluation and Mitigation Strategy (REMS)

A Risk Evaluation and Mitigation Strategy (REMS) is a strategy to manage known or potential serious risks associated with a drug product and is required by the Food and Drug Administration (FDA) to ensure that the benefits of the drug outweigh its risks.

Please read the following materials:

- Prescribing Information
- Medication Guide
- TIKOSYN Treatment Guidelines

To verify your certification status please click here

Risks associated with TIKOSYN

In order for Pfizer to communicate certain risks about TIKOSYN, Pfizer has worked with the FDA to develop materials to communicate the risk of induced arrhythmia.

The goals of the REMS for TIKOSYN are 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 keratinize clearance, continuous electrocardiographic monitoring, and cardiac resuscitation;
- Informing patients about the serious risks associated with TIKOSYN therapy.

Please click if you are a(n): Prescriber | Pharmacy | Institution Pharmacy

TIKOSYN is indicated for the conversion to and maintenance of normal sinus rhythm (delay in the time to recurrence of atrial fibrillation/atrial flutter) in highly symptomatic patients with atrial fibrillation/atrial flutter of greater than 1 week.

To minimize the risk of induced arrhythmia, patients initiated or re-initiated on TIKOSYN should be placed for a minimum of 3 days in a facility that can provide calculations of creatinine clearance, continuous electrocardiographic monitoring, and cardiac resuscitation (for detailed instructions regarding dose selection, see DOSAGE AND ADMINISTRATION). TIKOSYN is available only to hospitals and prescribers who have received appropriate TIKOSYN dosing and treatment initiation education (see DOSAGE AND ADMINISTRATION). For full Prescribing information, please click here.

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

/s/

MARY R SOUTHWORTH
07/11/2011