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**NDA 20-931**

**TIKOSYN (dofetilide) and Authorized Generic (Dofetilide Capsules)**

Antiarrhythmic

Pfizer, Inc.

235 East 42<sup>nd</sup> Street

New York, NY 10017

**RISK EVALUATION AND MITIGATION STRATEGY (REMS) DOCUMENT**

## **I. GOALS**

To mitigate the risk of Tikosyn and its authorized generic induced arrhythmia by:

- Ensuring that Tikosyn and its authorized generic are prescribed only by certified prescribers, and dispensed only by certified dispensers;
- Educating Health Care Providers (HCPs) 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 and its authorized generic therapy

## **II. REMS ELEMENTS**

### **A. Medication Guide**

A Medication Guide for Tikosyn or its authorized generic will be dispensed with each prescription in accordance with 21 CFR 208.24 and by HCPs as described below.

### **B. Elements to Assure Safe Use**

#### **1. Health Care Providers who prescribe Tikosyn or its authorized generic will be specially certified**

- a. Pfizer will ensure that HCPs who prescribe Tikosyn or its authorized generic, are specially certified. To become certified, each prescriber will enroll in the Tikosyn and its Authorized Generic REMS Program by submitting to Pfizer a completed Tikosyn and its Authorized Generic Prescriber Certification Form, and agreeing to the following:
  - I understand that patients initiated or re-initiated on Tikosyn or its authorized generic should be admitted for a minimum of 3 days to a health care facility that can provide calculations of creatinine clearance, continuous electrocardiographic monitoring, and cardiac resuscitation;
  - I understand that following the treatment initiation and dosing guidelines in the Tikosyn or its authorized generic label will decrease the risk of Tikosyn and its authorized generic induced arrhythmia;
  - I will inform my patients that Tikosyn and its authorized generic are associated with the risk of induced arrhythmias;
  - I will inform my patients that their blood lab measures and electrocardiogram (ECG) should be re-evaluated every 3 months;
  - I will provide the Medication Guide for Tikosyn or its authorized generic to each patient at the initiation and re-initiation of Tikosyn or its authorized generic 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 initial Tikosyn REMS approval.
- c. Within 30 days of the initial approval of the Tikosyn REMS, Pfizer will send Dear Health Care 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, 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 Tikosyn and its Authorized Generic Prescriber Certification Forms will be archived in the National Tikosyn and its Authorized Generic 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:
  - Dear HCP Letter for re-certification
  - Dear HCP Letter for new enrollees
  - Tikosyn and its Authorized Generic Program Treatment Guidelines
  - Tikosyn and its Authorized Generic Prescriber Certification Form
  - Tikosyn and its Authorized Generic REMS Website screenshots

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

- a. Pfizer will ensure that Tikosyn and its authorized generic will be dispensed only by pharmacies and health care settings that are specially certified. To be certified to dispense Tikosyn and its authorized generic, each pharmacy and health care setting will be enrolled in the Tikosyn and its Authorized Generic REMS Program

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

1. Each health care setting (institution) where Tikosyn or its authorized generic are dispensed for use will designate a representative. The designated representative will enroll in the Tikosyn and its Authorized Generic REMS Program by submitting to Pfizer a completed Tikosyn and its Authorized Generic Institution Certification Form, and agreeing to the following:

- I attest that the health care facility where Tikosyn or its authorized generic are 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 and its Authorized Generic 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 HCP is enrolled in the Tikosyn and its Authorized Generic REMS Program prior to dispensing Tikosyn or its authorized generic for inpatient use;
  - I understand that, prior to patient discharge; the health care facility must either: provide a free 7-day (14-count) supply of Tikosyn or its authorized generic and the Medication Guide to patients, or ensure the patient's take-home prescription is filled.
2. Each pharmacy where Tikosyn or its authorized generic are dispensed will designate a representative. The designated representative will enroll in the Tikosyn and its Authorized Generic REMS Program by submitting to Pfizer a completed Tikosyn and its Authorized Generic Pharmacy Certification Form, agreeing to the following:
- I will ensure that all appropriate staff are trained and have read and understand the Tikosyn and its Authorized Generic REMS Program materials.
  - I will ensure that pharmacy staff will verify that the prescriber is certified in the Tikosyn and its Authorized Generic REMS Program prior to dispensing each prescription, by accessing the system.
  - 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 and its authorized generic.
- b. Pfizer will require a one-time re-certification of all currently certified health care facilities and pharmacies within 6 months after initial Tikosyn REMS approval.
- c. 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, 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 de-certify Tikosyn and its Authorized Generic REMS Program participant(s) for non-compliance, if warranted by assessments to evaluate compliance to Tikosyn and its Authorized Generic REMS Program requirements.
- e. The following materials are part of the REMS and are appended:
  - Dear Pharmacist Letter for re-certification (institution and retail/mail-order pharmacies, as applicable)
  - Dear Pharmacist Letter for new enrollees (institution and retail/mail-order pharmacies, as applicable)
  - Tikosyn and its Authorized Generic Program Treatment Guidelines
  - Tikosyn and its Authorized Generic Pharmacy Certification Form
  - Tikosyn and its Authorized Generic Institution Certification Form
  - Tikosyn and its Authorized Generic In Pharmacy Systems (T.I.P.S™) Program Brochure describing the steps needed for retail pharmacies to enroll, order and dispense Tikosyn and its authorized generic
  - Tikosyn and Authorized Generic REMS Website screenshots

### **C. Implementation System**

The Implementation System will include the following:

1. Pfizer will distribute Tikosyn and its authorized generic only to certified prescribers, pharmacies, and health care settings.
2. Pfizer will maintain the National Tikosyn and Authorized Generic Database, which includes the record of all enrolled and certified health care settings and pharmacies that dispense and prescribers who prescribe Tikosyn or its authorized generic.
3. Pfizer will review distribution and prescription data to assess compliance with the requirements that Tikosyn and its authorized generic may only be prescribed by certified prescribers, and dispensed by certified dispensers.
4. Based on the monitoring and evaluation of the implementation of the elements to assure safe use provided for under [Section B.2.](#), 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 Food and Drug Administration (FDA) at 6 months and annually from the date of the initial approval of the REMS. 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.

## MEDICATION GUIDE

### Dofetilide Capsules

Read the Medication Guide before you start taking dofetilide and each time you get a refill. This information does not take the place of talking with your doctor about your condition or treatment.

#### **What is the most important information I should know about dofetilide?**

Dofetilide can cause serious side effects, including a type of abnormal heartbeat called Torsade de Pointes, which can lead to death.

To establish the right dose of dofetilide capsules, treatment with dofetilide must be started in a hospital where your heart rate and kidney function will be checked for the first 3 days of treatment. It is important that when you go home, you take the exact dose of dofetilide that your doctor prescribed for you.

While you take dofetilide, always watch for signs of abnormal heartbeat.

Call your doctor and go to the hospital right away if you:

- feel faint
- become dizzy, or
- have a fast heartbeat

#### **What is dofetilide?**

Dofetilide is a prescription medicine that is used to treat an irregular heartbeat (atrial fibrillation or atrial flutter).

It is not known if dofetilide is safe and effective in children under 18 years of age.

#### **Who should not take dofetilide?**

Do not take dofetilide if you:

- have an irregular heartbeat called long QT syndrome
- have kidney problems or are on kidney dialysis
- take any of these medicines:
  - cimetidine (TAGAMET, TAGAMET HB)\*
  - verapamil (CALAN, CALAN SR, COVERA-HS, ISOPTIN, ISOPTIN SR, VERELAN, VERELAN PM, TARKA)\*
  - ketoconazole (NIZORAL, XOLEGEL, EXTINA)\*
  - trimethoprim alone (PROLOPRIM, TRIMPEX)\* or the combination of trimethoprim and sulfamethoxazole (BACTRIM, SEPTRA SULFATRIM)\*
  - prochlorperazine (COMPAZINE, COMPO)\*
  - megestrol (MEGACE)\*
  - dolutegravir (TIVICAY)\*
  - hydrochlorothiazide alone or in combination with other medicines (such as ESIDRIX, EZIDE, HYDRODIURIL, HYDRO-PAR, MICROZIDE, or ORETIC)\*

Ask your doctor if you are not sure if any of your medicines are the kind listed above.

- are allergic to dofetilide. See the end of this leaflet for a complete list of ingredients in dofetilide capsules.

### **What should I tell my doctor before taking dofetilide?**

Before taking dofetilide, tell your doctor about all of your medical conditions including if you:

- have heart problems
- have kidney or liver problems
- are pregnant or plan to become pregnant. It is not known if dofetilide will harm your unborn baby.
- are breast-feeding or plan to breast-feed. It is not known if dofetilide passes into your breast milk. You and your doctor should decide if you will take dofetilide or breast-feed. You should not do both.

Especially tell your doctor if you take medicines to treat:

- heart problems
- high blood pressure
- depression or other mental problems
- asthma
- allergies, or hay fever
- skin problems
- infections

Ask your doctor if you are not sure about the medicines you take. Tell your doctor about all prescription and non-prescription medicines, vitamins, dietary supplements, and any natural or herbal remedies. Dofetilide and other medicines may affect each other, causing serious side effects. If you take dofetilide with certain medicines, you will be more likely to have a different type of abnormal heartbeat. See “Who should not take dofetilide?”

Know the medicines you take. Keep a list of your medicines and show it to your doctor and pharmacist when you get a new medicine.

### **How should I take dofetilide?**

- Take dofetilide exactly as your doctor tells you.
- Do not change your dofetilide dose unless your doctor tells you to.
- Your doctor will do tests before you start and while you take dofetilide.
- Do not stop taking dofetilide until your doctor tells you to stop. If you miss a dose, just take the next dose at your regular time. **Do not take 2 doses of dofetilide at the same time.**
- Dofetilide can be taken with or without food.
- If you take too much dofetilide, call your doctor or go to the nearest hospital emergency room right away. Take your dofetilide capsules with you to show to the doctor.

### **What are the possible side effects of dofetilide?**

Dofetilide can cause serious side effects, including a type of abnormal heartbeat called Torsade de Pointes, which can lead to death. See “What is the most important information I should know about dofetilide?”

The most common side effects of dofetilide include:

- headache
- chest pain
- dizziness

Call your doctor right away if you have signs of electrolyte imbalance:

- severe diarrhea
- unusual sweating
- vomiting
- not hungry (loss of appetite)
- increased thirst (drinking more than normal)

Tell your doctor if you have any side effects that bother you or do not go away.

These are not all the possible side effects of dofetilide. For more information, ask your doctor or pharmacist. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

### **How should I store dofetilide?**

- Store dofetilide between 59° to 86°F (15° to 30°C).
- Keep dofetilide away from moisture and humidity.
- Keep dofetilide in a tightly closed container.
- Keep dofetilide and all medicines out of the reach of children.

### **General information about dofetilide**

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use dofetilide for a condition for which it was not prescribed. Do not give dofetilide to other people, even if they have the same symptoms you have. It may harm them.

This Medication Guide summarizes the most important information about dofetilide. If you would like more information, talk with your doctor. You can ask your doctor or pharmacist for information about dofetilide that is written for health professionals.

For more about dofetilide, you can visit [www.greenstonellc.com](http://www.greenstonellc.com) or call 1-800-438-1985.

### **What are the ingredients in dofetilide capsules?**

**Active ingredient:** dofetilide

**Inactive ingredients:**

**Capsule fill:** microcrystalline cellulose, corn starch, colloidal silicon dioxide, and magnesium stearate

**Capsule shell:** gelatin, titanium dioxide, and FD&C Yellow 6

**Imprinting ink:** iron oxide black, shellac, n-butyl alcohol, isopropyl alcohol, propylene glycol, and ammonium hydroxide

\* Listed trademarks are the property of their respective owners.



**GREENSTONE® BRAND**

*Distributed by:*

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**Greenstone LLC**  
Peapack, NJ 07977

LAB-0741-1.0

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This Medication Guide has been approved by the U.S. Food and Drug Administration.

## **TREATMENT GUIDELINES**

## **TIKOSYN (dofetilide) and Authorized Generic (Dofetilide Capsules)**

### **TREATMENT GUIDELINES**

These guidelines are part of the TIKOSYN and Authorized Generic Risk Evaluation and Mitigation Strategy (REMS) Program for Tikosyn and its authorized generic, Dofetilide Capsules. Prescribers and Pharmacists are required to read these guidelines and sign a Certification Form acknowledging they understand the potential risks of TIKOSYN and its authorized generic in order to prescribe and dispense TIKOSYN and its authorized generic.

Note: The page numbering reflects pagination for this individual document.

The product information in this document is intended for residents of the United States only.

Below, you will find detailed treatment guidelines for TIKOSYN® and its authorized generic. Please call 1-877-TIKOSYN if you need additional information for Tikosyn and 1-800-447-3360 for Dofetilide Capsules.

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## Important Safety Information

TIKOSYN and its authorized generic are 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 and its authorized generic are contraindicated:

- In patients with a known hypersensitivity to the drug
- In patients with congenital or acquired long QT syndromes (baseline QT interval or corrected QT [QTc] interval greater than 440 msec or 500 msec in patients with ventricular conduction abnormalities)
- In patients with severe renal impairment (calculated creatinine clearance <20 mL/min)
- With verapamil
- With hydrochlorothiazide (alone or in combination such as with triamterene)
- With cation transport inhibitors such as cimetidine\*, ketoconazole, trimethoprim (alone or in combination with sulfamethoxazole), prochlorperazine, megestrol, and dolutegravir

\*Alternatives to cimetidine include Maalox<sup>®</sup>, Prilosec<sup>®</sup>, and Zantac<sup>®</sup>

Warnings/Interactions: Inhibitors of CYP3A4 or renal cation transport, 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.

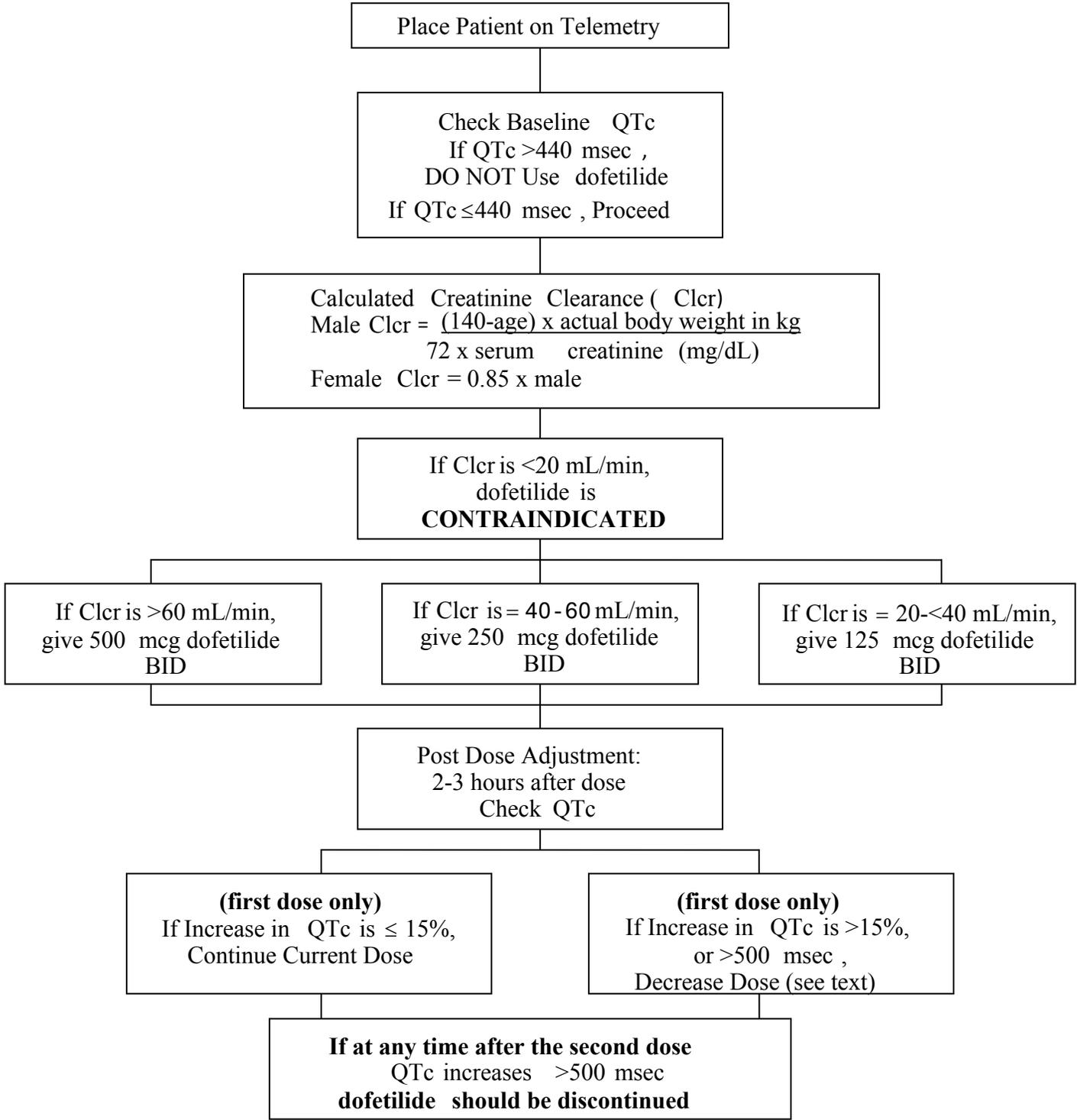
To minimize the risk of induced arrhythmia, patients initiated or re-initiated on TIKOSYN and its authorized generic should be placed for a minimum of 3 days in a facility that can provide calculations of creatinine clearance, continuous electrocardiographic monitoring, and cardiac resuscitation. TIKOSYN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

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## Dosing Overview

Please review this overview of dosing for TIKOSYN<sup>®</sup> and its authorized generic.

Dosing Algorithm Used in the TIKOSYN and its Authorized Generic Clinical Program



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## Steps for Initiation and Dosing

The following are suggested guidelines for the initiation and dosing of TIKOSYN<sup>®</sup> and its authorized generic:

### **PREDOSE STEPS**

1. Before initiating TIKOSYN or its authorized generic therapy, previous antiarrhythmic therapy should be withdrawn for a minimum of 3 plasma half-lives. TIKOSYN and its authorized generic 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 and its authorized generic 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, dolutegravir and megestrol, should not be used in patients on TIKOSYN or its authorized generic. Please see full prescribing information for TIKOSYN and its authorized generic
6. **CAUTION should be used when coadministering TIKOSYN or its authorized generic with macrolide antibiotics, azole antifungals, protease inhibitors, SRIs, amiodarone, cannabinoids, diltiazem, nefazodone, norfloxacin, quinine, zafirlukast, triamterene, metformin, amiloride, and grapefruit juice, as these agents may increase blood levels of TIKOSYN and its authorized generic**
7. Concomitant administration of TIKOSYN or its authorized generic 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 Torsade de Pointes. It is not clear whether this represents an interaction with TIKOSYN and its authorized generic or the presence of more severe structural heart disease in patients taking digoxin
8. If potassium (K<sup>+</sup>) is <4.0 mEq/L, replace K<sup>+</sup> before administration of TIKOSYN or its authorized generic.

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9. Before administering the first dose of TIKOSYN or its authorized generic on Day 1, measure the QTc interval (determine the QT if the heart rate is <60 bpm).
  - If baseline QTc is >440 msec (500 msec in patients with ventricular conduction abnormalities), TIKOSYN and its authorized generic are **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 and its authorized generic 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® or its authorized generic dose.
15. If the calculated creatinine clearance is <20 mL/min, TIKOSYN and its authorized generic is **CONTRAINDICATED**.
16. If the calculated creatinine clearance is >60 mL/min, the appropriate dose of TIKOSYN and its authorized generic is 500 mcg BID.
  - 2–3 hours after the **initial dose**, if QTc increases to >15% from baseline, then decrease TIKOSYN or its authorized generic to 250 mcg BID
17. If the calculated creatinine clearance is between 40 mL/min and 60 mL/min, the appropriate dose of TIKOSYN and its authorized generic is 250 mcg BID.
  - 2–3 hours after the **initial dose**, if QTc increases to >15% from baseline, then decrease TIKOSYN or its authorized generic to 125 mcg BID.

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

## POSTDOSE ADJUSTMENTS

19. The second dose of TIKOSYN or its authorized generic should only be given after the QT has been determined. Only 1 down titration of TIKOSYN or its authorized generic for QTc is suggested. If QTc is still excessively prolonged, DISCONTINUE TIKOSYN or its authorized generic therapy.
20. During therapy initiation in the hospital, at 2-3 hours after each dose of TIKOSYN or its authorized generic, 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<sup>®</sup> or its authorized generic 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 and its authorized generic should be DISCONTINUED
21. TIKOSYN and its authorized generic should be given q12h (actual times may vary according to local hospital practice; the doses should be given at the same time each day, i.e., 12 hours apart); QD TIKOSYN and its authorized generic should be given at the same time every day. The risk of Torsade 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 or its authorized generic 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 Tikosyn and Authorized Generic REMS Program. The physician who orders a TIKOSYN or its authorized generic prescription must be a
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confirmed participant of the TIKOSYN and Authorized Generic REMS Program. You will need the patient's final dose of TIKOSYN or its authorized generic, patient's full name (correct spelling), address, insurer, and physician's name. If the TIKOSYN or its authorized generic dose is changed or discontinued after the prescription has been faxed, please notify the mail-order or retail pharmacy immediately.

Tikosyn and Authorized Generic In Pharmacy Systems (T.I.P.S<sup>TM</sup>) Program Brochure describes the steps needed to enroll, order and dispense Tikosyn and its authorized generic for retail pharmacies. Please visit [www.TIKOSYNREMS.com](http://www.TIKOSYNREMS.com) for enrollment information.

23. Contact your hospital pharmacy to order a TIKOSYN or its authorized generic 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 or its authorized generic 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 or its authorized generic discharge bottle with 14 capsules.
25. Review the Medication Guide with your patient.
26. Alert patients that blood work and electrocardiogram (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 and its authorized generic 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<sup>®</sup> or its authorized generic. Important points to mention include:
  - TIKOSYN and its authorized generic are 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, megestrol and dolutegravir.
  - Renal function and QTc should be re-evaluated every 3 months or as medically warranted.

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- TIKOSYN and its authorized generic is available through a mail-order or retail pharmacy enrolled in the Tikosyn and Authorized Generic REMS Program. If the Healthcare Professional would like to write a refill for the patient, he or she must be a confirmed participant in the TIKOSYN and Authorized Generic REMS Program before the mail-order or retail pharmacy can fill the prescription. The Healthcare Professional can learn how to do this by calling 1-866-249-7261. Alternatively, the Healthcare Professional can continue to see the patient in consultation with a physician who is a confirmed participant in the TIKOSYN and Authorized Generic 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 and its authorized generic is Torsade de Pointes. The most common side effects with TIKOSYN and its authorized generic 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, hydrochlorothiazide, prochlorperazine, megestrol, or dolutegravir
- 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 or its authorized generic
- 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 and its authorized generic are 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 or its authorized generic should be placed for a minimum of 3 days in a

The product information in this document is intended for residents of the United States only.

facility that can provide calculations of creatinine clearance, continuous electrocardiographic monitoring, and cardiac resuscitation. TIKOSYN and its authorized generic are available only to hospitals and prescribers who have received appropriate TIKOSYN and its authorized generic dosing and treatment initiation education.

For full prescribing information, please visit [www.TIKOSYNREMS.com](http://www.TIKOSYNREMS.com).

The product information in this document is intended for residents of the United States only.

**PRESCRIBER CERTIFICATION LETTERS**



**FDA Requirement: Prescriber Certification Needed to Prescribe Tikosyn and its Authorized Generic**

[Date]

Dear Dr. [insert last name]:

**Per the Food and Drug Administration (FDA) requirements, in order to prescribe TIKOSYN or its authorized generic, new prescribers are required to complete a one-time certification.** TIKOSYN and its authorized generic are 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 and Authorized Generic Education Distribution Program, currently known as the TIKOSYN and Authorized Generic Risk Evaluation and Mitigation Strategy (REMS), is required by the FDA to ensure safe use of TIKOSYN and its authorized generic in order to mitigate the risk of induced arrhythmia by:

- Ensuring that TIKOSYN and its authorized generic are prescribed only by certified prescribers, and dispensed only by certified dispensers;
- 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 and its authorized generic therapy.

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

- TIKOSYN and Authorized Generic Treatment Guidelines
- Prescribing Information
- Medication Guide
- Tikosyn and Authorized Generic 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 and its authorized generic. Before dispensing a prescription for TIKOSYN or its authorized generic, the pharmacist must confirm that you



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235 East 42nd Street  
New York, NY 10017-5755

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are a health care professional who has been certified and is listed in the Pfizer National TIKOSYN and Authorized Generic Database.

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

Should you have any questions regarding the certification program, please call 1-866-249-7261 or visit [www.TIKOSYNREMS.com](http://www.TIKOSYNREMS.com).

Regards,

A handwritten signature in black ink that reads "Pol Vandebroucke". The signature is written in a cursive style with a large initial "P".

Pol Vandebroucke, MD, MSc, MBA, FFPM  
Regional Medical Affairs Lead, North America  
Global Established Pharma, Pfizer Inc.



**New FDA Requirement:**  
**Prescriber Re-Certification Required by November 2011 to Prescribe Tikosyn®**  
**(dofetilide)**

May 2011

**This letter ceased being distributed in February 2012**

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



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235 East 42nd Street  
New York, NY 10017-5755

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**U.S. Pharmaceuticals**

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](http://www.TIKOSYNREMS.com).

Regards,

A handwritten signature in black ink that reads "Robert Wolkow M.D." in a cursive style.

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

**PRESCRIBER CERTIFICATION FORM**

**TIKOSYN<sup>®</sup> AND AUTHORIZED GENERIC  
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: <input type="checkbox"/> MD <input type="checkbox"/> DO <input type="checkbox"/> PA <input type="checkbox"/> NP	

<b>YOUR WORK PHONE</b>	<b>YOUR OFFICE FAX NUMBER</b>	<b>YOUR EMAIL ADDRESS</b>
<b>PRIMARY DEA NUMBER</b>	If you do not have a DEA #, you must provide your state license # If you have both, please provide both.	<b>PRIMARY STATE LICENSE NUMBER</b>

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

<b>SECOND DEA NUMBER</b>	<input type="checkbox"/> If you have more than four DEA #s, please put a check in the box at the left	<b>STATE</b>	Please print your secondary state license number and state in the space provided
<b>THIRD DEA NUMBER</b>		<b>STATE</b>	Please print your tertiary state license number and state in the space provided
<b>FOURTH DEA NUMBER</b>			

**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			SECOND		
Hospital Name			Hospital Name		
Address Line 1			Address Line 1		
Address Line 2			Address Line 2		
City	State	Zip	City	State	Zip
THIRD			FOURTH		
Hospital Name			Hospital Name		
Address Line 1			Address Line 1		
Address Line 2			Address Line 2		
City	State	Zip	City	State	Zip

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

- i. I understand that patients initiated or re-initiated on dofetilide 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 and its authorized generic label will decrease the risk of Tikosyn and its authorized generic -induced arrhythmia;
- iii. I will inform my patients that Tikosyn and its authorized generic are associated with the risk of induced arrhythmias;
- iv. I will inform my patients that their blood lab measures and ECG should be reevaluated every 3 months;
- v. I will provide the Tikosyn or Authorized Generic Medication Guide to each patient at the initiation and re-initiation of Tikosyn or its authorized generic 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 and its authorized generic educational materials. I understand this information will be used to enable Pfizer to identify prescribers who are eligible to initiate and/or prescribe TIKOSYN and its authorized generic under this program. I understand Pfizer might share this information with others acting on its behalf and/or government agencies.*

\_\_\_\_\_  
 Prescriber Signature \_\_\_\_\_  
 Date  
 Please mail or fax this document to:  
 TIKOSYN  
 200 Pinecrest Plaza  
 Morgantown, WV 26505  
 FAX (800) 788-2637

Please retain a copy of this form for your records.  
For any questions please call 1-866-249-7261 or visit [www.TIKOSYNREMS.com](http://www.TIKOSYNREMS.com).

To minimize the risk of induced arrhythmia, patients initiated or re-initiated on TIKOSYN or its authorized generic 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 and its authorized generic are available only to hospitals and prescribers who have received appropriate TIKOSYN and its authorized generic dosing and treatment initiation education.



**INSTITUTION CERTIFICATION LETTERS**



**FDA Requirement:**  
**Institution Certification Needed to Order, Stock, and Dispense Tikosyn and Authorized Generic**

[Date]

Dear Dr. [insert last name]:

**Per FDA requirements, in order to order, stock, and dispense TIKOSYN or its authorized generic, new pharmacies are required to secure a one-time certification.** TIKOSYN and its authorized generic are 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 and Authorized Generic Education Distribution Program, currently known as the TIKOSYN and Authorized Generic Risk Evaluation and Mitigation Strategy (REMS) Program, is required by the FDA to ensure safe use of TIKOSYN and its authorized generic in order to mitigate the risk of induced arrhythmia by:

- Ensuring that TIKOSYN and its authorized generic are prescribed only by certified prescribers, and dispensed only by certified dispensers;
- 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 and its authorized generic therapy.

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

- TIKOSYN and Authorized Generic Treatment Guidelines
- Prescribing Information
- Medication Guide
- Institution Certification Form

Before dispensing TIKOSYN or its authorized generic, the pharmacist is required to confirm that the prescriber has been certified. In addition, the institution must agree to stock and



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provide patients prior to discharge a free 7-day (14 count) supply of TIKOSYN or its authorized generic 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 or its authorized generic, 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 and its authorized generic, you are required to confirm that the prescriber has been certified.

Should you have any questions regarding the certification program, please call 1-866-249-7261 or visit [www.TIKOSYNREMS.com](http://www.TIKOSYNREMS.com).

Regards,

A handwritten signature in black ink, appearing to read "Pol Vandebroucke".

Pol Vandebroucke, MD, MSc, MBA, FFPM  
Regional Medical Affairs Lead, North America  
Global Established Pharma, Pfizer Inc.



**New FDA Requirement:**  
**Institution Re-Certification by November 2011 Needed to Order, Stock and Dispense**  
**Tikosyn<sup>®</sup> (dofetilide)**

**This letter ceased being distributed in February 2012**

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



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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](http://www.TIKOSYNREMS.com).

Regards,

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

## **INSTITUTION CERTIFICATION FORM**

# TIKOSYN<sup>®</sup> AND AUTHORIZED GENERIC Institution Certification Form

For Pfizer Internal Use Only

Document Number

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

## 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 health care setting where Tikosyn and its authorized generic are dispensed for use will designate a representative. The designated representative will enroll in the Tikosyn and Authorized Generic REMS Program by submitting to Pfizer a completed Tikosyn and Authorized Generic Institution Certification Form, and agreeing to the following:

- i. I attest that the healthcare facility where Tikosyn and its authorized generic are initiated or re-initiated can provide calculations of creatinine clearance, continuous electrocardiographic monitoring, and cardiac resuscitation;
- ii. I will ensure that all appropriate staff (including physicians, pharmacists, and telemetry nurses) are trained regarding the Tikosyn and Authorized Generic REMS Program and will comply with all of the program requirements;
- iii. I will establish or oversee the establishment of a system, order sets, protocols, or other measures to ensure appropriate dosing and monitoring;
- iv. I will ensure that the pharmacy staff verifies that the prescribing healthcare provider is enrolled in the Tikosyn and Authorized Generic REMS Program prior to dispensing Tikosyn or its authorized generic for inpatient use;
- v. I understand that, prior to patient discharge, the health care facility must either: provide a free 7-day (14-count) supply of Tikosyn or its authorized generic 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 and Authorized Generic educational materials. I understand the information will be used to enable Pfizer to identify Institutions that are eligible to dispense TIKOSYN and its authorized generic 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  
200 Pinecrest Plaza  
Morgantown, WV 26505  
FAX (800) 788-2637

Please retain a copy of this form for your records.  
For any questions please call 1-866-249-7261 or  
visit [www.TIKOSYNREMS.com](http://www.TIKOSYNREMS.com).

To minimize the risk of induced arrhythmia, patients initiated or re-initiated on TIKOSYN or its authorized generic 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 and its authorized generic are available only to hospitals and prescribers who have received appropriate TIKOSYN and its authorized generic dosing and treatment initiation education.

**PHARMACY CERTIFICATION LETTERS**



**FDA Requirement:**  
**Pharmacy Certification Needed to Order and Dispense Tikosyn and its Authorized Generic**

[Date]

Dear Dr. [insert last name]:

**Per the Food and Drug Administration (FDA) requirements, to order and dispense TIKOSYN or its authorized generic, retail pharmacies are required to secure a one-time certification.** TIKOSYN and its authorized generic are 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 and Authorized Generic Education Distribution Program, currently known as the TIKOSYN and Authorized Generic Risk Evaluation and Mitigation Strategy (REMS) Program is required by the FDA to ensure safe use of TIKOSYN and its authorized generic in order to mitigate the risk of induced arrhythmia by:

- Ensuring that TIKOSYN and its authorized generic are prescribed only by certified prescribers, and dispensed only by certified dispensers;
- 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 and its authorized generic therapy

To order and dispense TIKOSYN and its authorized generic, you must review and follow the TIKOSYN and Authorized Generic in Pharmacy System (T.I.P.S.<sup>TM</sup>) REMS certification procedures below and enroll in the Tikosyn and Authorized Generic REMS Program:

- Complete the enclosed TIKOSYN and Authorized Generic Pharmacy Certification Form
- Sign and fax the form to 1-800-788-2637
- After 1 to 2 business days, confirm your certification by calling 1-866-249-7261 or visit [www.tikosynlist.com](http://www.tikosynlist.com). You will need to enter your pharmacy DEA number
- Your signature on the enclosed TIKOSYN and Authorized Generic REMS certification form acknowledges that the appropriate staff members in your pharmacy are aware of the procedures for dispensing TIKOSYN and its authorized generic.



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Upon receipt of your certification form, a written confirmation will be sent to you and the Tikosyn and Authorized Generic In Pharmacy Systems (T.I.P.S<sup>TM</sup>) Program Brochure describing the steps needed to enroll, order and dispense Tikosyn and its authorized generic.

Through pharmacy certification the pharmacy acknowledges that:

- The pharmacist will verify that a prescriber has participated in the TIKOSYN and Authorized Generic REMS Program and is confirmed in the Pfizer National TIKOSYN and Authorized Generic Database available at [www.tikosynlist.com](http://www.tikosynlist.com) before dispensing
- The pharmacist will dispense a Medication Guide with each prescription

Should you have any questions regarding the certification program, please call 1-866-249-7261 or visit [www.TIKOSYNREMS.com](http://www.TIKOSYNREMS.com).

Regards,

Pol Vandembroucke, MD, MSc, MBA, FFPM  
Regional Medical Affairs Lead, North America  
Global Established Pharma, Pfizer Inc.



**New FDA Requirement:**  
**Pharmacy Re-Certification by November 2011 Needed to Order and Dispense Tikosyn®**  
**(dofetilide)**

May 2011

**This letter ceased being distributed in February 2012**

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](http://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



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**U.S. Pharmaceuticals**

- 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](http://www.TIKOSYNREMS.com).

Regards,

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

**PHARMACY CERTIFICATION FORM**



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## 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.

### Risks associated with Tikosyn and its authorized generic

In order for Pfizer to communicate certain risks about Tikosyn and its authorized generic, Pfizer has worked with the FDA to develop materials to communicate the risk of induced arrhythmia.

Tikosyn and its authorized generic are prescription medicines that contain dofetilide.

You must enroll in the Tikosyn and Authorized Generic REMS program to prescribe or dispense Tikosyn® or its authorized generic.

### The goals of the REMS for Tikosyn and its authorized generic are to mitigate the risk of Tikosyn and its authorized generic induced arrhythmia by:

- Ensuring that Tikosyn and its authorized generic are prescribed only by certified prescribers, and dispensed only by certified dispensers;
- 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 and its authorized generic therapy.

Please read the following materials:

[Prescribing Information](#)

[Medication Guide](#)

[TIKOSYN and its authorized generic Treatment Guidelines](#)

Pharmacists: to verify a prescriber's certification status, [click here](#)

If you are a prescriber and want to check your certification status, please call 866-249-7261

Please click if you are a(n):

[Prescriber](#)

[Pharmacy](#)

[Institution Pharmacy](#)

Tikosyn and its authorized generic are 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 or its authorized generic 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 and its authorized generic are available only to hospitals and prescribers who have received appropriate Tikosyn and its authorized generic dosing and treatment initiation education (see [DOSAGE AND ADMINISTRATION](#)). For full Prescribing information, please [click here](#).



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GREENSTONE  
DELIVERING TRUSTED GENERICS™



## Prescribers

Per FDA requirements, in order to prescribe Tikosyn or its authorized generic new prescribers are required to complete a one-time certification. Even if you have been certified **prior to 2011**, you are required to secure a one-time recertification. You must enroll in the Tikosyn and Authorized Generic REMS program to prescribe or dispense Tikosyn® or its authorized generic. To become (re)certified you must review the following materials:

[Tikosyn and Authorized Generic Treatment Guidelines](#)

[Prescribing Information](#)

[Medication Guide](#)

When you have reviewed all the materials, please print, sign, and mail or fax the [Tikosyn and Authorized Generic Prescriber Certification Form](#).

The fax number is 1-800-788-2637. 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 and its authorized generic. Before dispensing a prescription for Tikosyn or its authorized generic, the pharmacist must confirm that you are a health care professional who has been certified and is listed in the National Tikosyn and Authorized Generic Database.

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

## Contact us

Should you have any questions regarding the certification program, please call 1-866-249-7261.

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Tikosyn and its authorized generic are 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 or its authorized generic 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 and its authorized generic are available only to hospitals and prescribers who have received appropriate Tikosyn and its authorized generic dosing and treatment initiation education (see [DOSAGE AND ADMINISTRATION](#)). For full Prescribing information, please [click here](#).



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## Pharmacy

Per FDA requirements, to order and dispense Tikosyn and its authorized generic, retail pharmacies are required to secure a one-time certification. Even if you have been certified prior to 2011, you are required to secure a one-time recertification. You must enroll in the Tikosyn and Authorized Generic REMS program to prescribe or dispense Tikosyn® or its authorized generic.

To become (re)certified you must review and follow the TIKOSYN and Authorized Generic REMS Program certification procedures below and (re)enroll in the REMS Program:

- Review the [Prescribing Information](#), including the [Medication Guide](#) and [Treatment Guidelines](#)
- Complete the Tikosyn and Authorized Generic REMS [Pharmacy Certification Form](#)
- Sign and fax the form to 1-800-788-2637
- After 1 to 2 business days, confirm your certification by calling 1-866-249-7261 or visit [www.tikosynlist.com](http://www.tikosynlist.com). You will need to enter your pharmacy DEA number
- Your signature on the REMS certification form acknowledges that the appropriate staff members in your pharmacy are aware of the procedures for dispensing Tikosyn and its authorized generic
- The Tikosyn and Authorized Generic In Pharmacy Systems (T.I.P.S™) Program Brochure describing the steps needed for retail pharmacies to enroll, order and dispense Tikosyn and its Authorized Generic are available [here](#). Please post the T.I.P.S. program procedures, and dofetilide contraindications in your pharmacy.

### Corporate Pharmacy Enrollment (certifying multiple pharmacies)

For corporate pharmacy enrollment you must print out a copy of the blank

[Tikosyn and Authorized Generic Pharmacy Certification Form](#) and complete the required fields.

A list of pharmacy sites that have been trained should be included as a separate attachment: this list must include the same required Pharmacy Information detailed on the enrollment form for EACH pharmacy.

Both the completed form and the attached list of pharmacy site information should be emailed to

[TIKOSYNREMS@UBC.com](mailto:TIKOSYNREMS@UBC.com)

Through pharmacy certification the pharmacy acknowledges that:

- The pharmacist will verify that a prescriber has participated in the Tikosyn and Authorized Generic REMS Program and is confirmed in the National Tikosyn and Authorized Generic Database before dispensing.
- The pharmacist will dispense a Medication Guide with each prescription.

### Contact us

Should you have any questions regarding the certification program, please call 1-866-249-7261.

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**GREENSTONE**  
DELIVERING TRUSTED GENERICS™



## Institution Pharmacy

Per FDA requirements, in order to order, stock, and dispense Tikosyn and its authorized generic new pharmacies are required to secure a one-time certification. Even if your institution has been certified **prior to 2011**, you are required to secure a one-time recertification. You must enroll in the Tikosyn and Authorized Generic REMS program to prescribe or dispense Tikosyn® or its authorized generic. To become (re)certified you must review the following materials:

[Tikosyn and Authorized Generic Treatment Guidelines](#)

[Prescribing Information](#)

[Medication Guide](#)

And sign the Institution Certification Form:

NOTE: A designated representative must complete and sign this form as part of the Tikosyn and Authorized Generic REMS Program requirement.

[Tikosyn and Authorized Generic Institution Form](#)

When you have reviewed all the materials, please print, sign, and mail or fax back the Certification Form. The fax number is 1-800-788-2637. After the Certification Form is received, you will receive written confirmation of receipt. In addition, before dispensing Tikosyn or its authorized generic, you are required to confirm that the prescriber has been certified.

Before dispensing Tikosyn or its authorized generic, 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 or its authorized generic 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 or its authorized generic, the institution will ensure the patient's take home prescription is ordered and filled at a retail pharmacy prior to patient discharge.

### Contact us

Should you have any questions regarding the Tikosyn and Authorized Generic certification, please call 1-866-249-7261.

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Tikosyn and its authorized generic are 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 or its authorized generic 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 and its authorized generic are available only to hospitals and prescribers who have received appropriate Tikosyn and its authorized generic dosing and treatment initiation education (see [DOSAGE AND ADMINISTRATION](#)). For full Prescribing information, please [click here](#).



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This Web site allows pharmacies that have completed the TIKOSYN and Authorized Generic Risk Evaluation and Mitigation Strategy (REMS) Program to verify the status of TIKOSYN and its authorized generic prescribers affiliated with your hospital.

## PHARMACY DEA/NABP LOOKUP

To access this system, please enter your **Pharmacy** DEA or NABP number.

### Important Safety Information

To minimize the risk of induced arrhythmia, patients initiated or re-initiated on dofetilide 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 and Dofetilide Capsules is available only to hospitals and prescribers who have received appropriate Tikosyn and Dofetilide Capsules dosing and treatment initiation education.

Dofetilide 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 dofetilide.

Dofetilide 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, dolutegravir and megestrol because these drugs may cause an increase in dofetilide plasma concentration.

Dofetilide 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 dofetilide. 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.

### Indication

Dofetilide 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 dofetilide 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.

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

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

**TIKOSYN**<sup>®</sup>  
(dofetilide)  
500  
250  
125  
mcg  
capsules

**Dofetilide  
Capsules**  
500  
250  
125  
mg

- DO NOT order or dispense TIKOSYN<sup>®</sup> or its authorized generic if prescriber participation in the TIKOSYN and Authorized Generic REMS Program cannot be verified. Refer these prescribers to **1-866-249-7261** to speak to a REMS Customer Service Representative
- Dispense TIKOSYN or its authorized generic as prescribed in accordance with standard pharmacy practice
- Prescriptions filled 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. Please call **1-877-865-6136** if you need additional information for TIKOSYN and **1-800-447-3360** for Dofetilide Capsules. If you want more information about the T.I.P.S. certification procedures or the REMS program, please call **1-866-249-7261** or visit [www.TIKOSYNREMS.com](http://www.TIKOSYNREMS.com)

### Indication

TIKOSYN<sup>®</sup> and its authorized generic are 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 and its authorized generic can cause life-threatening ventricular arrhythmias, they 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 and its authorized generic are indicated for the conversion of atrial fibrillation and atrial flutter to normal sinus rhythm.

TIKOSYN and its authorized generic have not been shown to be effective in patients with paroxysmal atrial fibrillation.

### Important Safety Information

**To minimize the risk of induced arrhythmia, patients initiated or re-initiated on TIKOSYN or its authorized generic 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 and its authorized generic are available only to hospitals and prescribers who have received appropriate TIKOSYN and its authorized generic dosing and treatment initiation education.**

TIKOSYN and its authorized generic are contraindicated in patients with congenital or acquired long QT syndromes, a baseline QT interval or QTc >440 msec (500 msec in patients

**TIKOSYN**<sup>®</sup>  
(dofetilide)  
500  
250  
125  
mcg  
capsules

**Dofetilide  
Capsules**  
500  
250  
125  
mg

with ventricular conduction abnormalities), severe renal impairment (calculated creatinine clearance <20 mL/min), or known hypersensitivity to TIKOSYN and its authorized generic.

TIKOSYN and its authorized generic are 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, megestrol, and dolutegravir because these drugs may cause an increase in dofetilide plasma concentration.

TIKOSYN and its authorized generic 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 TIKOSYN or its authorized generic 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 or its authorized generic. 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 accompanying full Prescribing Information, including Boxed Warning, and Medication Guide.**



Available in  
Retail Pharmacy

**TIKOSYN**<sup>®</sup>  
(dofetilide)  
500  
250  
125  
mcg  
capsules

**Dofetilide  
Capsules**  
500  
250  
125  
mg

## T.I.P.S.<sup>™</sup> Procedures Booklet

### Welcome to the TIKOSYN<sup>®</sup> and Authorized Generic In Pharmacy System (T.I.P.S.) Program

TIKOSYN and its authorized generic are prescription medicines that contain dofetilide. Dofetilide Capsules are the Authorized Generic of TIKOSYN (by Pfizer Inc) distributed by Greenstone LLC, a subsidiary of Pfizer Inc.

### Boxed Warning

**To minimize the risk of induced arrhythmia, patients initiated or re-initiated on TIKOSYN or its authorized generic 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 and its authorized generic are available only to hospitals and prescribers who have received appropriate TIKOSYN and its authorized generic dosing and treatment initiation education.**

**Please see accompanying full Prescribing Information, including Boxed Warning, and Medication Guide.**

## Available in Retail Pharmacy

TIKOSYN® and its authorized generic are prescription medicines that contain dofetilide.

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

The T.I.P.S. procedures booklet will guide you through the REMS program's 3 steps: Enroll, Order, and Dispense TIKOSYN or its authorized generic. If you have any questions about TIKOSYN or its authorized generic or any of the T.I.P.S. program procedures, or if you need additional program supplies, please call **1-866-249-7261** or visit [www.TIKOSYNREMS.com](http://www.TIKOSYNREMS.com).

**1-866-249-7261**

### Boxed Warning

**To minimize the risk of induced arrhythmia, patients initiated or re-initiated on TIKOSYN or its authorized generic 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 and its authorized generic are available only to hospitals and prescribers who have received appropriate TIKOSYN and its authorized generic dosing and treatment initiation education.**