



NDA 020931/S-003

SUPPLEMENT APPROVAL

Pfizer Global Research & Development
Attention: Tricia Douglas
Manager, Worldwide Regulatory Strategy
235 East 42nd Street
New York, NY 10017

Dear Ms. Douglas:

Please refer to your supplemental New Drug Application (sNDA) dated September 12, 2008, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Tikosyn (dofetilide) Capsules.

We acknowledge receipt of your amendments dated April 3, October 23, 2009, December 3, 2010, April 21, and June 16, and 24, 2011.

This prior approval supplemental new drug application provides for a proposed risk evaluation and mitigation strategy (REMS) for Tikosyn (dofetilide) and was submitted in accordance with section 909(b)(1) of the Food and Drug Administration Amendments Act of 2007 (FDAAA). Under section 909(b)(1) of FDAAA, we identified Tikosyn (dofetilide) as a product deemed to have in effect an approved REMS because there were in effect on the effective date of FDAAA, March 25, 2008, elements to assure safe use.

In accordance with section 505-1 of the FDCA, we have determined that a REMS is necessary for Tikosyn (dofetilide) to ensure the benefits of the drug outweigh the risk of ventricular arrhythmias. Your proposed REMS, as amended and appended to this letter, is approved. The REMS consists of a Medication Guide, elements to assure safe use, an implementation system, and a timetable for submission of assessments of the REMS.

The elements to assure safe use will ensure that the drug is prescribed only by healthcare providers who have been educated about the safe use (inpatient initiation, creatinine monitoring) of Tikosyn.

We remind you that section 505-1(f)(8) of FDCA prohibits holders of an approved covered application with elements to assure safe use from using any element to block or delay approval of an application under section 505(b)(2) or (j). A violation of this provision in 505-1(f) could result in enforcement action.

The REMS assessment plan should include, but is not limited to, the following:

1. Results of surveys conducted of prescribers' and institutions' understanding and knowledge of the serious risks of Tikosyn induced arrhythmia and their adherence to the key REMS requirements.
2. Results of surveys conducted of patients' understanding and knowledge of the serious risks of Tikosyn induced arrhythmia.
3. A report on the number of Dear Healthcare Professional letters for re-certification that are mailed (prescriber and pharmacy), when the letters were mailed, what information was included in the mailings, and number of returned mailings.
4. An assessment of data on certification of Prescribers, Institutions, and Pharmacies:
 - a. The number of Prescribers certified (and re-certified, reported separately) in the Tikosyn Program (during the reporting period, and cumulatively).
 - b. The number of new Prescribers certified in the Tikosyn Program during the reporting period.
 - c. The number of Institutions certified (and re-certified, reported separately) in the Tikosyn Program (during the reporting period, and cumulatively).
 - d. The number of new Institutions certified in the Tikosyn Program during the reporting period.
 - e. The number of Retail/Mail-Order Pharmacies certified (and re-certified, reported separately) in the Tikosyn Program (during the reporting period, and cumulatively).
 - f. The number of new Retail/Mail-Order Pharmacies certified in the Tikosyn Program during the reporting period.
 - g. The number of Prescribers, Institutions, and Retail/Mail-Order Pharmacies de-certified in the Tikosyn Program during the reporting period.
 - h. The number of Prescribers who have ordered/prescribed Tikosyn who were not enrolled (during the reporting period and cumulative).
 - i. The total number of institutions that stocked Tikosyn prior to the REMS approval, and the number of those institutions that did not certify within 6 months of REMS approval and were required to return Tikosyn inventory.
5. An assessment of data on Tikosyn ordering:
 - a. The number of Institutions ordering Tikosyn (during the reporting period and cumulatively).

- b. The number of Retail/Mail-Order Pharmacies ordering Tikosyn (during the reporting period and cumulatively).
 - c. The number of Institutions that attempted to order Tikosyn although they were not certified in the Tikosyn Program (during the reporting period, and cumulatively).
 - d. The number of Retail/Mail-Order Pharmacies that attempted to order Tikosyn although they were not certified in the Tikosyn program (during the reporting period and cumulatively).
 - e. The number of Prescribers who attempted to order Tikosyn through the PAP Program who are not certified (during the reporting period, and cumulatively).
6. An assessment of data on Tikosyn distribution:
- a. The number of Institutions to which Tikosyn was shipped (during the reporting period and cumulatively).
 - b. The number of Retail/Mail-Order Pharmacies to which Tikosyn was shipped (during the reporting period and cumulatively).
 - c. The number of Prescribers to whom Tikosyn was shipped through the PAP Program (during the reporting period and cumulatively).
 - d. The number (if any) of Institutions to which Tikosyn was shipped although they were not certified in the Tikosyn Program (during the reporting period, and cumulatively).
 - e. The number (if any) of Retail/Mail-Order Pharmacies to which Tikosyn was shipped although they were not certified in the Tikosyn Program (during the reporting period and cumulatively).
 - f. The number (if any) of Prescribers to whom Tikosyn was shipped through the PAP Program, although they were not certified in the Tikosyn Program (during the reporting period and cumulatively).
7. An assessment of data on Tikosyn shipment denials and de-certification:
- a. The total number of Tikosyn orders requested, shipped, and denied (Institutions, Retail/Mail-Order Pharmacies and Prescribers reported separately) (during the reporting period and cumulatively).
 - b. The total number of Tikosyn orders requested, shipped, and denied to uncertified Institutions/Prescribers/Pharmacies (during the reporting period and cumulatively).

- c. The total number of Tikosyn orders requested, shipped, and denied to de-certified Institutions/Prescribers/Pharmacies (during the reporting period and cumulatively).
8. Based on the information reported, an assessment of and conclusion of whether the REMS is meeting its goals to mitigate a specific serious risk listed in the labeling of the drug, and whether modifications to the REMS are needed.
9. Information on the status of any post-approval study or clinical trial required under section 505(o) or otherwise undertaken to investigate a safety issue. With respect to any such post-approval study, you must include the status of such study, including whether any difficulties completing the study have been encountered. With respect to any such post-approval clinical trial, you must include the status of such clinical trial, including whether enrollment has begun, the number of participants enrolled, the expected completion date, whether any difficulties completing the clinical trial have been encountered, and registration information with respect to requirements under subsections (i) and (j) of section 402 of the Public Health Service Act. You can satisfy these requirements in your REMS assessments by referring to relevant information included in the most recent annual report required under section 506B and 21 CFR 314.81(b)(2)(vii) and including any material or significant updates to the status information since the annual report was prepared. Failure to comply with the REMS assessments provisions in section 505-1(g) could result in enforcement action.

In addition to the assessments submitted according to the timetable included in the approved REMS, you must submit a REMS assessment and may propose a modification to the approved REMS when you submit a supplemental application for a new indication for use as described in section 505-1(g)(2)(A) of FDCA.

If you currently distribute or plan to distribute an authorized generic product under this NDA, you must submit a complete proposed REMS that relates only to the authorized generic product. Submit a proposed REMS, REMS supporting document, and any required appended documents as a prior approval supplement. Approval of the proposed REMS is required before you may market your authorized generic product.

Prominently identify the submission containing the REMS assessments or proposed modifications of the REMS with the following wording in bold capital letters at the top of the first page of the submission as appropriate:

NDA 020931 REMS ASSESSMENT

**NEW SUPPLEMENT FOR NDA 020931
PROPOSED REMS MODIFICATION
REMS ASSESSMENT**

**NEW SUPPLEMENT (NEW INDICATION FOR USE)
FOR NDA 020931**

**REMS ASSESSMENT
PROPOSED REMS MODIFICATION (if included)**

If you do not submit electronically, please send 5 copies of REMS-related submissions.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>. Content of labeling must be identical to the enclosed labeling, with the addition of any labeling changes in pending “Changes Being Effected” (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.

Information on submitting SPL files using eLIST may be found in the guidance for industry titled “SPL Standard for Content of Labeling Technical Qs and As” at <http://www.fda.gov/downloads/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf>.

The SPL will be accessible from publicly available labeling repositories.

We request that the labeling approved today be available on your website within 10 days of receipt of this letter.

Under 21 CFR 208.24(d), you are responsible for ensuring that the label of each container or package includes a prominent and conspicuous instruction to authorized dispensers to provide a Medication Guide to each patient to whom the drug is dispensed, and states how the Medication Guide is provided. You should submit marked up carton and container labels of all strengths and formulations with the required statement alerting the dispenser to provide the Medication Guide. We recommend that you use one of the following two statements depending upon whether the Medication Guide accompanies the product or is enclosed in the carton (for example, unit of use):

- “Dispense the enclosed Medication Guide to each patient.” or
- “Dispense the accompanying Medication Guide to each patient.”

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit the following, in triplicate, (1) a cover letter requesting advisory comments, (2) the proposed materials in draft or mock-up form with annotated references, and (3) the package insert(s) to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications

5901-B Ammendale Road
Beltsville, MD 20705-1266

You must submit final promotional materials and package insert(s), accompanied by a Form FDA 2253, at the time of initial dissemination or publication [21 CFR 314.81(b)(3)(i)]. Form FDA 2253 is available at <http://www.fda.gov/opacom/morechoices/fdaforms/cder.html>; instructions are provided on page 2 of the form. For more information about submission of promotional materials to the Division of Drug Marketing, Advertising, and Communications (DDMAC), see <http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm>.

All promotional materials that include representations about your drug product must be promptly revised to be consistent with the labeling changes approved in this supplement, including any new safety information [21 CFR 314.70(a)(4)]. The revisions in your promotional materials should include prominent disclosure of the important new safety information that appears in the revised package labeling. Within 7 days of receipt of this letter, submit your statement of intent to comply with 21 CFR 314.70(a)(4) to the address above or by fax to 301-847-8444.

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, please call Russell Fortney, Regulatory Project Manager, at (301) 796-1068.

Sincerely,

{See appended electronic signature page}

Mary Ross Southworth, Pharm.D.
Deputy Director for Safety
Division of Cardiovascular and Renal
Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

Enclosures: REMS Document
REMS Materials

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