



NDA 22425/S-004

**SUPPLEMENT APPROVAL**

sanofi-aventis U.S., LLC  
Attention: Marsha Miller, Ph.D.  
Assistant Director, Regulatory Development  
9 Great Valley Parkway  
P.O. Box 3026  
Malvern, PA 19355

Dear Dr. Miller:

Please refer to your Supplemental New Drug Application (sNDA) dated October 26, 2010, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Multaq (dronedarone hydrochloride) Tablets 400 mg.

This “Prior Approval” supplemental new drug application provides for labeling revised as follows:

1. Under Drug Interactions, the “Digoxin and P-glycoprotein substrates” section has been revised from:

*Digoxin and P-glycoprotein substrates*

Dronedarone increased digoxin exposure by 2.5-fold by inhibiting the P-gP transporter [*see Drug Interactions (7.1)*]. Other P-gP substrates are expected to have increased exposure when co-administered with dronedarone.

To:

*P-glycoprotein substrates*

*Digoxin*

Dronedarone increased digoxin exposure by 2.5-fold by inhibiting the P-gP transporter [*see Drug Interactions (7.1)*].

*Dabigatran*

Exposure to dabigatran is higher when it is administered with dronedarone than when it is administered alone (1.7- to 2-fold).

Other P-gP substrates are expected to have increased exposure when co-administered with dronedarone.

We have completed our review of this supplemental application. It is approved, effective on the date of this letter, for use as recommended in the enclosed, agreed-upon labeling text.

**CONTENT OF LABELING**

As soon as possible, but no later than 14 days from the date of this letter, submit, using the FDA automated drug registration and listing system (eLIST), the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format, as described at <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>, that is identical to the enclosed labeling (text for the package insert, Medication Guide) and include the labeling changes proposed in any pending “Changes Being Effected” (CBE) supplements and any 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.

Also within 14 days, amend all pending supplemental applications for this NDA, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in MS Word format that includes the changes approved in this supplemental application.

**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>.

**LETTERS TO HEALTH CARE PROFESSIONALS**

If you decide to issue a letter communicating important safety-related information about this drug product (i.e., a “Dear Health Care Professional” letter), we request that you submit, at least 24 hours prior to issuing the letter, an electronic copy of the letter to this NDA to the following address:

MedWatch Program  
Office of Special Health Issues  
Food and Drug Administration

10903 New Hampshire Ave  
Building 32, Mail Stop 5353  
Silver Spring, MD 20993

**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

Enclosure: Content of Labeling

-----  
**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  
01/31/2011