



NDA 20-850/S-033

SUPPLEMENT APPROVAL

Boehringer Ingelheim Pharmaceuticals, Inc.
Attention: Ms. Heidi C. Reidies
900 Ridgebury Road, PO Box 368
Ridgefield, CT 06877

Dear Ms. Reidies:

Please refer to your Supplemental New Drug Application (sNDA) dated August 29, 2011, received August 29, 2011 submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Micardis (telmisartan) 20, 40, and 80 mg Tablets.

We acknowledge receipt of your amendments dated February 8, 2012 and September 10, 2012.

This “Prior Approval” supplemental new drug application provides for revisions to the **HIGHLIGHTS** and **FULL PRESCRIBING INFORMATION** in the **INDICATIONS AND USAGE** and **CLINICAL STUDIES** sections of the labeling in accordance with the Guidance for Industry, *Hypertension Indication: Drug Labeling for Cardiovascular Outcome Claims*, March 2011.

These changes have been made as follows (additions are shown as underlined text and deletions are shown as ~~strike-through text~~):

In **HIGHLIGHTS OF PRESCRIBING INFORMATION**

1. Under **RECENT MAJOR CHANGES**, the following changes were made:

<u>-----RECENT MAJOR CHANGES-----</u>	
<u>Boxed Warning</u>	<u>1/2012</u>
<u>Indications and Usage</u>	
<u>Hypertension (1.1)</u>	<u>9/2012</u>
<u>Contraindications (4)</u>	<u>1/2012</u>
<u>Warnings and Precautions</u>	
<u>Fetal Toxicity (5.1)</u>	<u>1/2012</u>

Note: The “Boxed Warning” and “Warnings and Precautions, Fetal Toxicity (5.1)” listings were inadvertently omitted from the **RECENT MAJOR CHANGES** in the last approved labeling supplement (S-035, approved January 19, 2012) and are being included in this supplement approval. The “Indications and Usage, Hypertension (1.1)” and “Contraindications (4)” listings reflect the changes approved in this supplement, S-033.

2. Under **INDICATIONS AND USAGE**, the following changes were made to the first bullet:

MICARDIS is an angiotensin II receptor blocker (ARB) indicated for:

- Treatment of hypertension, to lower blood pressure. Lowering blood pressure reduces the risk of fatal and nonfatal cardiovascular events, primarily strokes and myocardial infarctions. (1.1)

3. Under **DRUG INTERACTIONS**, the following changes were made:

- NSAIDs: use may lead to iIncreased risk of renal impairment and loss of anti-hypertensive effect (7)

In **FULL PRESCRIBING INFORMATION**

4. Under **INDICATIONS AND USAGE**, the following changes were made:

1.1 Hypertension

MICARDIS is indicated for the treatment of hypertension, to lower blood pressure. Lowering blood pressure reduces the risk of fatal and nonfatal cardiovascular events, primarily strokes and myocardial infarctions. These benefits have been seen in controlled trials of antihypertensive drugs from a wide variety of pharmacologic classes including the class to which this drug principally belongs.

Control of high blood pressure should be part of comprehensive cardiovascular risk management, including, as appropriate, lipid control, diabetes management, antithrombotic therapy, smoking cessation, exercise, and limited sodium intake. Many patients will require more than one drug to achieve blood pressure goals. For specific advice on goals and management, see published guidelines, such as those of the National High Blood Pressure Education Program's Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC).

Numerous antihypertensive drugs, from a variety of pharmacologic classes and with different mechanisms of action, have been shown in randomized controlled trials to reduce cardiovascular morbidity and mortality, and it can be concluded that it is blood pressure reduction, and not some other pharmacologic property of the drugs, that is largely responsible for those benefits. The largest and most consistent cardiovascular outcome benefit has been a reduction in the risk of stroke, but reductions in myocardial infarction and cardiovascular mortality also have been seen regularly.

Elevated systolic or diastolic pressure causes increased cardiovascular risk, and the absolute risk increase per mmHg is greater at higher blood pressures, so that even modest reductions of severe hypertension can provide substantial benefit. Relative risk reduction from blood pressure reduction is similar across populations with varying absolute risk, so the absolute benefit is greater in patients who are at higher risk independent of their hypertension (for example, patients with diabetes or hyperlipidemia), and such patients would be expected to benefit from more aggressive treatment to a lower blood pressure goal.

Some antihypertensive drugs have smaller blood pressure effects (as monotherapy) in black patients, and many antihypertensive drugs have additional approved indications and effects (e.g., on angina, heart failure, or diabetic kidney disease). These considerations may guide selection of therapy.

5. Under **1.2 Cardiovascular Risk Reduction**, the 1st sentence in the 3rd paragraph was changed as follows:

Studies of telmisartan in this setting do not exclude the possibility that ~~telmisartan~~ may not preserve a meaningful fraction of the effect of the ACE inhibitor to which it was compared.

6. Under **14 CLINICAL STUDIES**, at the end of the **14.1 Hypertension** subsection, the following sentence was added:

There are no trials of MICARDIS demonstrating reductions in cardiovascular risk in patients with hypertension, but at least one pharmacologically similar drug has demonstrated such benefits.

7. Under **14.2 Cardiovascular Risk Reduction**, the following changes were made:

- a) In the 2nd paragraph, the following sentence was added as the 4th sentence: “Mean blood pressure at randomization was 134/77 mmHg.”
- b) In the 3rd paragraph, the following sentence was added as the 5th sentence: “Mean blood pressure at randomization was 135/78 mmHg.”

In Patient Information

8. Under the “**What is High Blood Pressure (Hypertension)?**” section, the following changes were made:

Blood pressure is the force in your blood vessels when your heart beats and when your heart rests. You have high blood pressure when the force is too much. MICARDIS tablets can help your blood vessels relax so your blood pressure is lower. Medicines that lower your blood pressure lower your chance of having a stroke or heart attack.

High blood pressure makes the heart work harder to pump blood throughout the body and causes damage to the blood vessels. If high blood pressure is not treated, it can lead to stroke, heart attack, heart failure, kidney failure, and vision problems.

Minor editorial changes

9. Vertical margin marks were added to the text under **Warnings and Precautions, Fetal Toxicity (5.1)** in the **FULL PRESCRIBING INFORMATION** to correspond to the **RECENT MAJOR CHANGES** listing in **HIGHLIGHTS**.

Note: These vertical margin marks were inadvertently omitted in the last approved labeling supplement (S-035, approved January 19, 2012) and are being included in this supplement approval.

10. Minor editorial corrections were made.
11. The label number and revision dates have been updated.

We have completed our review of this supplemental application, as amended. 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 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 (text for the package insert, text for the patient package insert), with the addition of any labeling changes in pending “Changes Being Effectuated” (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.

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, as well as annual reportable changes and annotate each change. To facilitate review of your submission, provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

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 contact:

Quynh Nguyen, Pharm.D., RAC
Regulatory Health Project Manager
(301) 796-0510

Sincerely,

{See appended electronic signature page}

Norman Stockbridge, M.D., Ph.D.
Director
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/

NORMAN L STOCKBRIDGE
09/20/2012