DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

NDA 012911/S-026

SUPPLEMENT APPROVAL

Novartis Pharmaceuticals
Attention: Jonelle Chapman
Drug Brand Regional Manager, Drug Regulatory Affairs
One Health Plaza
East Hanover, NJ 07936-1080

Dear Ms. Chapman:

Please refer to your Supplemental New Drug Application (sNDA) dated October 6, 2009, received October 6, 2009, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Metopirone (metyrapone USP) 250 mg, Capsules.

We acknowledge receipt of your amendment dated July 19, 2010, and revised labeling dated October 12, 2010 (email).

The July 19, 2010, submission constituted a complete response to our April 27, 2010, action letter.

This Prior Approval supplemental new drug application provides for the following labeling revisions to the package insert.

(1) Addition of "*Cardiovascular system:* Hypotension" to the **ADVERSE REACTIONS** section and

(2) Revisions to the **PRECAUTIONS** section:

Carcinogenesis, Mutagenesis, Impairment of Fertility

Long-term carcinogenicity and reproduction studies in animals have not been conducted. Metopirone was not mutagenic with or without metabolic activation in three strains of bacteria.

Pregnancy Category C

A subnormal response to Metopirone may occur in pregnant women. Animal reproduction studies have not been conducted with Metopirone. The Metopirone test was administered to 20 pregnant women in their second and third trimester of pregnancy and evidence was found that the fetal pituitary responded to the enzymatic block.

It is not known if Metopirone can affect reproduction capacity. Metopirone should be given to a pregnant woman only if clearly needed.

Animal reproduction studies adequate to evaluate teratogenicity and postnatal development have not been conducted with Metopirone.

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.

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) and include the labeling changes proposed in any pending "Changes Being Effected" (CBE) supplements. 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 pending "Changes Being Effected" (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.

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 Ms. Jena Weber, Regulatory Project Manager, at 301-796-1306.

Sincerely,

{See appended electronic signature page}

Mary H. Parks, M.D.
Director
Division of Metabolism & Endocrinology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

Enclosure: package insert

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

/s/

MARY H PARKS
11/04/2010