NDA 19-758/SLR-045

Novartis Pharmaceuticals Corporation
Attention: James Rawls, Pharm.D.
Assistant Director, Drug Regulatory Affairs
59 Route 10
East Hanover, NJ 07936-1080

Dear Dr. Rawls:

Please refer to your supplemental new drug application dated September 24, 2001, received October 15, 2001, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Clozaril (clozapine) tablets.

We acknowledge receipt of your submissions of November 1, December 14 and December 21, 2001.

This supplemental new drug application provides for labeling changes as follows:

- The previously existing BOXED WARNING has been relocated to the beginning of the PI and revised to advise health care providers of the association of myocarditis with clozapine therapy.
- A subsection has been added to the WARNINGS section entitled “Myocarditis” to provide data and clozapine treatment guidelines related to this issue.

This supplement also provides the text for the “Dear Health Care Professional” letter that will be issued to convey the information listed above.

We have completed the review of this supplemental application, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the agreed upon attached labeling text. Accordingly, the supplemental application is approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the attached labeling (text for the package insert and “Dear Health Care Professional” letter).

Please submit the copies of final printed labeling (FPL) electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA* (January 1999). Alternatively, you may submit 20 paper copies of the FPL as soon as it is available but no more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FPL for approved supplement NDA 19-758/SLR-045." Approval of this submission by FDA is not required before the labeling is used.

Since a letter communicating this important information about Clozaril (i.e., a "Dear Health Care Professional" letter) is being issued to physicians and others responsible for patient care, we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20857

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, call Steven D. Hardeman, R.Ph., Senior Regulatory Project Manager, at (301) 594-5525.

Sincerely,

{See appended electronic signature page}

Russell Katz, M.D.
Director
Division of Neuropharmacological Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

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

/s/

Russell Katz
1/14/02 10:40:25 AM