



NDA 19-758 / SLR-054

Novartis Pharmaceuticals Corporation
Attention: James Rawls, Pharm.D.
One Health Plaza
East Hanover, NJ 07936-1080

Dear Dr. Rawls:

Please refer to your supplemental new drug application dated March 4, 2005, received March 8, 2005, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Clozaril (clozapine) Tablets.

We acknowledge receipt of your submissions of April 8, 2005 and May 2, 2005.

This supplemental new drug application provides for several changes to the agranulocytosis Warning statements, most notably for a decrease of the blood-monitoring schedule to every four weeks after a patient has maintained a normal White Blood Cell (WBC) count and Absolute Neutrophil Count (ANC) during weekly monitoring for six months followed by monitoring every two weeks for an additional six months.

We completed our review of this application, as amended. This application is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text (email of 5/11/05 from James Rawls, Pharm.D.).

Given the decreased frequency of WBC cell and ANC monitoring after the first year of Clozaril therapy, there is the possibility that the agranulocytosis rate may increase. We request that you propose a plan for tracking the agranulocytosis rate in the Clozaril National Registry following the institution of the approved changes to the WBC cell and ANC monitoring schedule.

The final printed labeling (FPL) must be identical to the enclosed agreed-upon labeling (text for the package insert).

Please submit an electronic version of the FPL according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA*. 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. Individually mount 15 of the copies on heavy-weight paper or similar material. For administrative purposes, designate this submission "**FPL for approved supplement NDA 19-758 / S-054.**" Approval of this submission by FDA is not required before the labeling is used.

All applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred. We are waiving the pediatric study requirement for this application.

We note that you have included a draft “Dear Health Care Professional” (DHP) letter, communicating the changes to the monitoring schedule, for our review. Once we reach agreement on your draft DHP, please submit a copy to your NDA and a copy to the following address:

MEDWATCH, HFD-410
FDA
5600 Fishers Lane
Rockville, MD 20857

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, 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
Center for Drug Evaluation and Research
Office of New Drug Evaluation I

Enclosure (labeling)

**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
5/12/05 10:40:39 AM