DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 17-473/SLR-038

Teva Pharmaceuticals
Attention: Tu Tu
1090 Horsham Rd.
P.O Box 1090
North Wales, PA 19454-1090

Dear Mr. Tu:

Please refer to your supplemental new drug application submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Orap (pimozide) tablets.

We acknowledge receipt of your amendment dated June 21, 2002, which was a complete response to our approvable letter dated March 25, 2002.

This supplemental application provides for the following revisions to your approved labeling:

1. Changing CYP 3A to CYP 3A4 wherever it appears in labeling.

2. The addition of the phrase, "or patients with known hypokalemia or hypomagnesemia (see also PRECAUTIONS-Drug Interactions)" under item 3 in contraindications.

3. The paragraph under Drug Interactions concerning other drugs that prolong the QT interval has been revised. The revised paragraph reads as follows: "Because ORAP prolongs the QT interval of the electrocardiogram, an additive effect on QT interval would be anticipated if administered with other drugs, such as phenothiazines, tricyclic antidepressants or antiarrhythmic agents, which prolong the QT interval. Accordingly, pimozide should not be given with dofetilide, sotalol, quinidine, other Class Ia and III anti-arrhythmics, mesoridazine, thioridazine, chlorpromazine, droperidol, pimozide, sparfloxacin, gatifloxacin, moxifloxacin, halofantrine, mefloquine, pentamidine, arsenic trioxide, levomethadyl acetate, dolasetron mesylate, probucol, tacrolimus, ziprasidone, or other drugs that have demonstrated QT prolongation as one of their pharmacodynamic effects. Also, the use of macrolide antibiotics in patients with prolonged QT intervals has been rarely associated with ventricular arrhythmias. Such concomitant administration should not be undertaken (see CONTRAINDICATIONS)."

4. "A single case report" has been changed to "rare case reports" in the sentence "Rare case reports have suggested possible additive effects of pimozide and fluoxetine leading to bradycardia" under the Drug Interactions section of labeling.

5. Fluvoxamine has been added to the list of contraindicated drugs, as follows: "Other drugs that are relatively less potent inhibitors of CYP 3A4 should also be avoided, in view of the risks e.g. zileuton, fluvoxamine."

We have completed the review of this application and it is approved effective the date of this letter.

The final printed labeling (FPL) must be identical to the June 21, 2002 submitted labeling text (identified Rev. K 6/02).

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 Melina Griffis, R.Ph., Senior Regulatory Project Manager, at (301) 594-5526.

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

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