DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-479

VALEANT Pharmaceuticals International
Attention: William L. Schary, PhD
Vice President, Regulatory Affairs
3300 Hyland Avenue
Costa Mesa, CA 92626

Dear Dr. Schary:

Please refer to your new drug application (NDA) dated March 29, 2002, received April 8, 2002, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Zelapar (selegiline hydrochloride) Orally Disintegrating Tablets, 1.25 mg.

We also acknowledge receipt of your submissions dated:

December 13, 2005	December 16, 2005	February 22, 2006
May 4, 2006	May 23, 2006.	

The December 13, 2005 submission constituted a complete response to our September 30, 2005 action letter.

This new drug application provides for the use of Zelapar (selegiline hydrochloride) Orally Disintegrating Tablets.

We have completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text.

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the package insert). Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

CARTON AND CONTAINER LABELING REQUESTS

We agree with your proposal to use Campaign 1 packaging at the initial launch of Zelapar. We note your commitment, as agreed to in a telephone conversation between members of your staff and staff of this division on June 13, 2006, to introduce Campaign 2 packaging no later than 6 months after the date of this approval letter. You have also agreed to incorporate the following additional changes into Campaign 2 carton and container labeling prior to their use:

A. BLISTER LABEL

1. The dosage form description "Orally Disintegrating Tablet" should follow the established name.
2. The dosage form description should be followed by the strength, in bolded type, with a space between the numeral "1.25" and the unit designation "mg."
3. The "Rx Only" statement should follow the strength designation and should be in unbolded type. For example:

(Selegiline HCl) Orally Disintegrating Tablet **1.25 mg** Rx Only

B. POUCH LABELING

1. Increase the prominence of the strength so that it has equal prominence to the proprietary name.
2. Increase the prominence of the established name, dosage form designation and strength relative to the trade name. Make the established name at least ½ the height of the brand name, without otherwise decreasing the prominence of the established name.

C. CARTON LABELING

1. Increase the prominence of the established name, dosage form designation and strength relative to the trade name. Make the established name at least ½ the height of the brand name, without otherwise decreasing the prominence of the established name.
2. Include a sticker stating "New Packaging" for no more than 6 months.

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 submissions "**FPL for approved NDA 21-479**" 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 remind you of your postmarketing study commitments. These commitments are listed below.

1. Perform a Phase 1 Clinical Pharmacology study to evaluate the effect of hepatic insufficiency on the PK of zydis selegiline.

Final Report Submission Date with Severe Patients: June 1, 2008

Final Report Submission Date with Mild & Moderate Patients: December 1, 2007

2. Perform a Phase 1 Clinical Pharmacology study to evaluate the effect of renal insufficiency on the PK of zydis selegiline.

Final Report Submission Date: June 1, 2007

3. Perform an *in vitro* study to evaluate the induction potential of selegiline.

Final Report Submission Date: June 1, 2007

4. You have committed to conduct a reproductive toxicity study in rats to assess the potential effects of selegiline on fertility and early embryonic development pursuant to guidelines set forth in ICH S5A (1994) and S5B (1996).

Final Report Submission Date: December 1, 2007

5. You have committed to conduct a reproductive toxicity study in rats to assess the potential effects of selegiline on embryo-fetal development in accordance with guidelines set forth in ICH S5A (1994).

Final Report Submission Date: December 1, 2007

6. You have committed to conduct a reproductive toxicity study in rabbits to assess the potential effects of selegiline on embryo-fetal development in accordance with guidelines set forth in ICH S5A (1994).

Final Report Submission Date: December 1, 2007

7. You have committed to conduct a reproductive toxicity study in rats to assess the potential effects of selegiline on prenatal and postnatal development including maternal function in accordance with guidelines set forth in ICH S5A (1994).

Final Report Submission Date: December 1, 2007

8. You have committed to conduct a full battery of genotoxicity studies to assess the genotoxic potential of selegiline in accordance with guidelines set forth in ICH S2A (1996) and S2B (1997):

(i) A test for gene mutation in bacteria.

Final Report Submission Date: January 1, 2007

(ii) An in vitro test with cytogenetic evaluation of chromosomal damage with mammalian cells *or* an in vitro mouse lymphoma tk assay (with colony sizing).

Final Report Submission Date: January 1, 2007

(iii) An in vivo test for chromosomal damage using rodent hematopoietic cells.

Final Report Submission Date: January 1, 2007

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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