DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20-648/S-008

Valeant Pharmaceuticals International
Attention: Arthur L. Rosenthal, R.A.C.
Director, Corporate Regulatory Affairs
3300 Hyland Avenue
Costa Mesa, CA 92626

Dear Mr. Rosenthal:

Please refer to your supplemental new drug application dated November 4, 2004, received November 5, 2004, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Diastat® AcuDial™ (diazepam rectal gel) Rectal Delivery System 10 mg and 20 mg.

We acknowledge receipt of your submissions dated May 13, 2005, July 14, 2005, July 18, 2005, August 25, 2005, and September 9, 2005. Your submission of May 13, 2005 constituted a complete response to our March 2, 2005 action letter.

This supplemental new drug application provides for a second generation drug delivery system for Diastat® (diazepam rectal gel) Rectal Delivery System. Specifically, this new system consists of pre-filled unit-dose syringes (two configurations) that can deliver varying quantities of diazepam 5 mg/mL: a 10 mg syringe with a 4.4 cm tip (that can deliver doses of 5, 7.5, and 10 mg) and a 20 mg syringe with a 6.0 cm tip (that can deliver doses of 10, 12.5, 15, 17.5, and 20 mg).

We have 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.

Final Printed Labeling

The final printed labeling (FPL) must be identical to the submitted labeling (package insert submitted August 25, 2005, patient package insert submitted August 25, 2005, immediate container and carton labels submitted July 14, 2005 and August 25, 2005).

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 20-648/S-008**." Approval of this submission by FDA is not required before the labeling is used.

As agreed during a September 15, 2005 phone conversation between you and Division representatives, we note that, at your next printing of the physician package insert and patient package insert, you will delete the following sentence, "It is important to note that if a dose greater than 10 mg is to be administered to a pediatric patient, two prescriptions must be written for 2 different twin packs, one for the 10 mg dose and one for the additional dose (SEE HOW SUPPLIED SECTION)".

Post-marketing Study Commitments

We remind you of your postmarketing study commitments described in your submission dated September 9, 2005. These commitments are listed below.

1. Development of a voluntary registry of 150 caregiver/patients and assessment of medication errors via questionnaires sent every six months in the first year and yearly thereafter for 3 years.

Protocol Submission:	by December 2005
Study Start:	by March 2006
Final Report Submission:	by September 2008

2. Revision of the 20 mg Diastat® AcuDial™ syringe configuration such that the 12.5 mg dose (not the 10 mg dose) is the minimum achievable dose with the 20 mg syringe.

Completion:	by March 2007

Submit clinical protocols to your IND for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all study final reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii), you should include a status summary of each commitment in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies, number of patients entered into each study. All submissions, including supplements, relating to these postmarketing study commitments must be prominently labeled "**Postmarketing Study Commitment Protocol**", "**Postmarketing Study Commitment Final Report**", or "**Postmarketing Study Commitment Correspondence**."

Dear Healthcare Professional Letters

We note that you have designed a risk management program (RMP) to minimize medication errors that may result from incorrect Diastat® AcuDial™ dosing due to failure to accurately dial and lock-in the prescribed dose in the delivery system and to ensure proper disposal of the unused diazepam gel after administration of the dose. A component of your RMP includes the mailing of several "Dear Pharmacist" and "Dear Doctor" letters. When these letters issue, we request that you submit a copy of each letter to this NDA and send a copy to the following address:

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

Other Comments and Recommendations

We have the following additional recommendations regarding this supplemental application:

- Adding a reference to the tip length (4.4 cm. vs. 6 cm.) to the external packaging.
- Increasing the size of the dose window and the font of the dose appearing in the dose window of the Diastat AcuDial syringes.

While agreement on the above changes is not required prior to this action, we ask that you consider them post-approval and continue discussions with us regarding their implementation.

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 Jacqueline H. Ware, Pharm.D., Senior Regulatory Project Manager, at (301) 594-2850.

Sincerely,

{See appended electronic signature page}

Russell Katz, M.D.
Director
Division of Neurology 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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