



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration  
Rockville, MD 20857

NDA 21-400

Bayer Corporation  
Attention: Mary Taylor, M.P.H.  
Vice President, Regulatory Affairs  
400 Morgan Lane  
West Haven, CT 06516-4175

Dear Ms. Taylor:

Please refer to your new drug application (NDA) dated September 24, 2001, received September 24, 2001, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Levitra® (vardenafil hydrochloride) tablets.

We acknowledge receipt of your submissions dated February 17, April 1 and 29, and May 1, 13 and 16, and August 14 and 19, 2003. The February 17, 2003 submission constituted a complete response to our July 23, 2002 action letter.

This new drug application provides for the use of Levitra® (vardenafil hydrochloride) tablets for the treatment of erectile dysfunction in men.

We 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, text for the patient package insert). Marketing the product with FPL that is not identical to the approved labeling text may render the product a misbranded and unapproved new drug.

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 NDA 21-400.**" Approval of this submission by FDA is not required before the labeling is used.

We remind you of the postmarketing study commitments you made in a teleconference held on August 19, 2003. The commitments are listed below:

1. To conduct a study to evaluate the impact on QT interval prolongation of combining LEVITRA with another drug with a similar QT effect size.

The timeline is as follows:

Protocol Submission	within six months of the date of this letter
Study Initiation	within 12 months of the date of this letter
Final Report Submission	within 20 months of the date of this letter

2. To conduct study(ies) to evaluate the pharmacokinetic/pharmacodynamic drug-drug interaction between LEVITRA 2.5mg and alpha-blockers used for BPH.

The timeline is as follows:

Protocol Submission	within six months of the date of this letter
Study Initiation	within 12 months of the date of this letter
Final Report Submission	within 20 months of the date of this letter

3. To conduct a study to evaluate the pharmacokinetic/pharmacodynamic drug-drug interaction between LEVITRA and the alpha-blocker alfuzosin.

The timeline is as follows:

Protocol Submission	within six months of the date of this letter
Study Initiation	within 12 months of the date of this letter
Final Report Submission	within 20 months of the date of this letter

4. To conduct a study to provide data to support labeling for the quantitative effects of LEVITRA on retinal function following repeat dosing of LEVITRA.

The timeline is as follows:

Protocol Submission	within six months of the date of this letter
Study Initiation	within 12 months of the date of this letter
Final Report Submission	within 20 months of the date of this letter

In addition, we request that you consider sharing the data from your QT studies, including Trial # 10929, with other sponsors who are either marketing or developing drugs in the phosphodiesterase type 5 inhibitor class.

Submit clinical protocols to your IND for this product 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 the 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 number of patients entered into each study. All submissions, including supplements, relating to this postmarketing study commitment must be prominently labeled **“Postmarketing Study Protocol”, “Postmarketing Study Final Report”, or “Postmarketing Study Correspondence.”**

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In addition, submit three copies of the introductory promotional materials that you propose to use for this product. Submit all proposed materials in draft or mock-up form, not final print. Send one copy to this division and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising,  
and Communications, HFD-42  
Food and Drug Administration  
5600 Fishers Lane  
Rockville, MD 20857

If you have any questions, please call Eufrecina DeGuia, Regulatory Health Project Manager at (301) 827-4260.

Sincerely,

*{See appended electronic signature page}*

Florence Houn, M.D., M.P.H.  
Director  
Office of Drug Evaluation III  
Center for Drug Evaluation and Research

Enclosure:  
Physician Insert  
Patient Package Insert

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**This is a representation of an electronic record that was signed electronically and  
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/s/

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Julie Beitz  
8/19/03 07:19:35 PM  
Signing for Florence Houn, MD