

**CENTER FOR DRUG EVALUATION AND RESEARCH**

**APPROVAL PACKAGE FOR:**

**APPLICATION NUMBER**

**21-487**

**Correspondence**



NDA 21-487

**DISCIPLINE REVIEW LETTER**

Forest Laboratories  
Attention: Doreen Morgan, Pharm. D  
Harborside Financial Center  
Plaza 3, Suite 602  
Jersey City, NJ 07311

Dear Dr. Morgan:

Please refer to your December 19, 2003 New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for memantine.

Our reviews of the Chemistry, Manufacturing and Controls sections of your submission and Nomenclature proposal are complete, and we have identified the following deficiencies:

1. The Division of Medication Errors and Technical Support (DMETS) does not recommend the use of the proposed name,           . However, DMETS and the Division have no objections to the use of the proposed name "Namenda". The following are additional recommendations from DMETS:
  - a) We note on all the labels and labeling an equivalency statement appears with the strength. The statement says "Equivalent to XX mg Memantine Hydrochloride". However, the established name is expressed in terms of the salt. Therefore, the equivalency statement is not necessary. If the salt were removed from the established name then the equivalency statement would be necessary. Revise accordingly.
  - b) For the Blister carton labeling (5 mg, 10 mg, 15 mg, 20 mg) please revise the dosage form statement to read "Tablet" rather than "Tablets". Additionally, when comparing the blister tablets side-by-side they look identical. We recommend revising the labels so that each strength is differentiated by contrasting color, boxing, or some other means.
  - c) For the Blister carton labeling (Titration Pack) we note that you propose to market the product in a titration pack that includes 5 mg and 10 mg tablets constituting a four week supply of medication. We do not recommend packaging the            together, as this increases the potential for medication errors. Additionally you should revise AM and PM to read "Morning" and "Evening". This wording will prevent the medication from being taken at 11:30 am and 12:30 pm. The principal display panel should prominently include the following:

This titration pack contains:  
4 week supply of Memantine Hydrochloride tablets  
5 mg and 10 mg

- Week 1 – seven 5 mg tablets
- Week 2 – fourteen 5 mg tablets
- Week 3 – seven 5 mg tablets and seven 10 mg tablets
- Week 4 – fourteen 10 mg tablets.

d) For container label (5 mg, 10 mg, 15 mg, 20 mg) please include the dosage form with the established name rather than in conjunction with the product strength. For example:

Namenda  
(Memantine Hydrochloride Tablets)  
5 mg

Also the net quantity should appear away from the product strength and you should include a "Usual Dosage" statement on the label per 21 CFR 201.55 and ensure the 60 count unit-of-use bottle has a child-resistant closure (CRC) cap.

2. The molecular weight of — in the package insert is in disagreement with the Statement of Nonproprietary Name adopted by the USAN Council. The correct molecular weight should be 215.76.
3. Please revise the size of the trade name to be no larger than 50% of the generic name.

Based on the above recommendations please submit revised carton and container labels (black & white are acceptable) and an updated package insert with the above recommendations.

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

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/s/

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Russell Katz  
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