CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-627

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

MEMORANDUM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: March 9, 2005

TO: Russell Katz, M.D., Director
Division of Neuropharmacological Drug Products
HFD-120

VIA: Melina Griffis, R.Ph., Senior Regulatory Project Manager
Division of Neuropharmacological Drug Products
HFD-120

FROM: Jeanine Best, M.S.N., R.N., P.N.P.
Patient Product Information Specialist
Division of Surveillance, Research, and Communication Support
HFD-410

THROUGH: Gerald Dal Pan, M.D., M.H.S., Director
Division of Surveillance, Research, and Communication Support
HFD-410

SUBJECT: DSRCS Review of Patient Instructions for Namenda Oral Solution, NDA 21-627

Background and Summary

The sponsor submitted draft *Patient Instructions for Namenda Oral Solution* for the Oral Solution dosing device on February 15, 2005. We have suggested minor revisions to these draft instructions (see attached).

Comments to the review division are bolded, underlined and italicized. We can provide a marked-up and clean copy of the revised document in Word if requested by the review division. Please call us if you have any questions.

PROPOSED PATIENT INSTRUCTIONS FOR* NAMENDA® *Oral Solution

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_____ § 552(b)(4) Trade Secret / Confidential

✓ § 552(b)(4) Draft Labeling

_____ § 552(b)(5) Deliberative Process

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/s/

Jeanine Best
3/9/05 10:04:19 AM
DRUG SAFETY OFFICE REVIEWER

Toni Piazza Hepp
3/11/05 04:58:51 PM
DRUG SAFETY OFFICE REVIEWER
for Gerald Dal Pan

CONSULTATION RESPONSE
Division of Medication Errors and Technical Support
Office of Drug Safety
(DMETS; HFD-420)

DATE RECEIVED: March 3, 2003	**DESIRED COMPLETION DATE:** May 5, 2003 **PDUFA DATE:** Oct. 20, 2003	**ODS CONSULT #:** 03-0094

TO: Russell Katz, MD
Director, Division of Neuropharmacological Drug Products
HFD-120

THROUGH: Melina Griffis
Project Manager
HFD-120

PRODUCT NAME: ——— (Primary name) **Namenda** (Alternate name) (Memantine Hydrochloride Tablets) 5 mg, 10 mg, 15 mg, and 20 mg and (Memantine Hydrochloride Oral Solution) 2 mg/mL and 4 mg/mL **NDA #'s: 21-487 and 21-627**	**SPONSOR**: Forest Laboratories, Inc.

SAFETY EVALUATOR: Tia M. Harper-Velazquez, Pharm.D.

SUMMARY: In response to a consult from the Division of Neuropharmacological Drug Products (HFD-120) for a review of the proposed proprietary names ——— and "Namenda" to determine the potential for confusion with approved proprietary and established names as well as pending names.

RECOMMENDATIONS:

1. DMETS does not recommend the use of the proposed name, " ——— ". However, DMETS has no objections to the use of the proposed name "Namenda". DMETS considers this a final review. If the approval of the application is delayed beyond 90 days from the signature date of this review, the name must be re-evaluated. A re-review of the name and its associated labels and labeling prior to NDA approval will rule out any objections based upon approvals of other proprietary or established names from this date forward.

2. DMETS recommends implementation of the labeling revisions as outlined in Section III of this review.

3. DDMAC finds the names ——— and "Namenda" acceptable from a promotional perspective.

Carol Holquist, R.Ph.
Deputy Director
Division of Medication Errors and Technical Support
Office of Drug Safety
Phone: (301) 827-3242 Fax: (301) 443-9664

Jerry Phillips, R.Ph.
Associate Director
Office of Drug Safety
Center for Drug Evaluation and Research
Food and Drug Administration

Division of Medication Errors and Technical Support
Office of Drug Safety
HFD-420; Parklawn Rm. 6-34
Center for Drug Evaluation and Research

PROPRIETARY NAME REVIEW

DATE OF REVIEW: July 15, 2003

NDA NUMBERS: 21-487 and 21-627

NAME OF DRUG: ——— (Primary name) and **Namenda** (Alternate name)
(Memantine Hydrochloride Tablets)
5 mg, 10 mg, 15 mg, and 20 mg
and
(Memantine Hydrochloride Oral Solution)
2 mg/mL and 4 mg/mL

NDA SPONSOR: Forest Laboratories, Inc.

I. INTRODUCTION

This consult was written in response to a request from the Division of Neuropharmacological Drug Products, for an assessment of the proprietary names ——— and "Namenda" regarding potential name confusion with other proprietary and/or established drug names. The draft blister container labels, carton and draft package insert labeling for ——— and Namenda were reviewed for possible interventions in minimizing medication errors.

PRODUCT INFORMATION

——— Namenda is the proposed proprietary name for memantine hydrochloride, an orally active N-methyl-D-aspartate (NMDA) receptor antagonist, indicated for the treatment of moderate to severe dementia of the Alzheimer's type. The recommended starting dose of ——— Namenda is 5 mg once daily. The recommended target dose is 20 mg per day. The dose should be increased in 5 mg increments to 10 mg/day (5 mg twice a day), 15 mg/day (5 mg and 10 mg as separate doses), and 20 mg/day (10 mg twice a day). The minimum recommended interval between dose increases is one week. ——— Namenda will be available as a tablet in strengths of 5 mg, 10 mg, 15 mg, and 20 mg in addition to an oral solution in strengths of 2 mg/mL and 4 mg/mL.

II. RISK ASSESSMENT

The medication error staff of DMETS conducted a search of several standard published drug product reference texts[i,ii] as well as several FDA databases[iii] for existing drug names which sound-alike or look-alike to ——— and Namenda to a degree where potential confusion between drug names

[i] MICROMEDEX Integrated Index, 2003, MICROMEDEX, Inc., 6200 South Syracuse Way, Suite 300, Englewood, Colorado 80111-4740, which includes all products/databases within ChemKnowledge, DrugKnowledge, and RegsKnowledge Systems.
[ii] Facts and Comparisons, online version, Facts and Comparisons, St. Louis, MO.
[iii] AMF Decision Support System [DSS], the Division of Medication Errors and Technical Support proprietary name consultation requests, New Drug Approvals 98-03, and the electronic online version of the FDA Orange Book.

could occur under the usual clinical practice settings. A search of the electronic online version of the U.S. Patent and Trademark Office's Text and Image Database[iv] and the data provided by Thomson & Thomson's SAEGIS™ Online Service[v] were also conducted. An expert panel discussion was conducted to review all findings from the searches. In addition, DMETS conducted three prescription analysis studies for each proposed name, consisting of two written prescription studies (inpatient and outpatient) and one verbal prescription study, involving health care practitioners within FDA. This exercise was conducted to simulate the prescription ordering process in order to evaluate potential errors in handwriting and verbal communication of the name.

A. EXPERT PANEL DISCUSSION

An Expert Panel discussion was held by DMETS to gather professional opinions on the safety of the proprietary names, [redacted] and Namenda. Potential concerns regarding drug marketing and promotion related to the proposed name was also discussed. This group is composed of DMETS Medication Errors Prevention Staff and representation from the Division of Drug Marketing, Advertising, and Communications (DDMAC). The group relies on their clinical and other professional experiences and a number of standard references when making a decision on the acceptability of a proprietary name.

1. The Expert Panel identified three medication names that have potential for confusion with [redacted] These products are listed in Table 1 (see page 4), along with the dosage forms available and usual FDA-approved dosage. The Expert Panel did not identify any names that were thought to have potential confusion with the proposed name, Namenda.

2. DDMAC did not have any concerns with [redacted] or Namenda with regard to promotional claims.

[iv] WWW location http://www.uspto.gov.

[v] Data provided by Thomson & Thomson's SAEGIS(tm) Online Service, available at www.thomson-thomson.com.

Table 1: Potential Sound-Alike/Look-Alike Names Identified by DMETS Expert Panel

Product Name	Dosage form(s), Established name	Usual adult dose*	Other**
—— or Namenda	**Memantine Hydrochloride** **Tablets: 5 mg, 10 mg, 15 mg, and 20 mg** **Oral Solution: 2 mg/mL and 4 mg/mL**	**The recommended starting dose of Nurvida is 5 mg once daily. The recommended target dose is 20 mg per day. The dose should be increased in 5 mg increments to 10 mg/day (5 mg twice a day), 15 mg/day (5 mg and 10 mg as separate doses), and 20 mg/day (10 mg twice a day). The minimum recommended interval between dose increases is one week.**	
Nuvaring (Rx)	Etonogestral and Ethinyl Estradiol Vaginal Ring 11.7 mg/2.7 mg	Insert one ring vaginally, prior to or on day five of cycle. Leave ring in place for three weeks, then remove for one ring-free week; repeat.	**S/A, L/A
Avita (Rx)	Tretinoin Cream; Gel 0.025%	Apply sparingly to cleansed and completely dry skin once daily at bedtime.	**S/A
Norvasc (Rx)	Amlodipine Tablets 2.5 mg, 5 mg, and 10 mg	Hypertension: 5 mg once daily, to a maximum dose of 10 mg once daily. Angina: 5 mg to 10 mg daily, using lower dose for elderly and patients with hepatic insufficiency.	**L/A

*Frequently used, not all-inclusive.
**L/A (look-alike), S/A (sound-alike)

B. PRESCRIPTION ANALYSIS STUDIES

1. Methodology:

Six separate studies were conducted within FDA for the proposed proprietary names to determine the degree of confusion of —— and Namenda with other U.S. drug names due to similarity in visual appearance with handwritten prescriptions or verbal pronunciation of the drug name. These studies employed a total of 105 health care professionals (pharmacists, physicians, and nurses) for each name. This exercise was conducted in an attempt to simulate the prescription ordering process. An inpatient order and outpatient prescriptions were written, each consisting of a combination of marketed and unapproved drug products and a prescription for —— and Namenda (see page 5). These prescriptions were optically scanned and one prescription was delivered to a random sample of the participating health professionals via e-mail. In addition, the outpatient orders were recorded on voice mail. The voice mail messages were then sent to a random sample of participating health professionals for their interpretations and review. After receiving either the written or verbal prescription orders, the participants sent their interpretations of the orders via e-mail to the medication error staff.

HANDWRITTEN PRESCRIPTION	VERBAL PRESCRIPTION
Outpatient RX:	
Inpatient RX:	

Namenda

HANDWRITTEN PRESCRIPTION	VERBAL PRESCRIPTION
Outpatient RX: Namenda 20mg Sig: 1 po qd #30	Namenda 20 mg, take one by mouth daily.
Inpatient RX: Namenda 20mg po QD	

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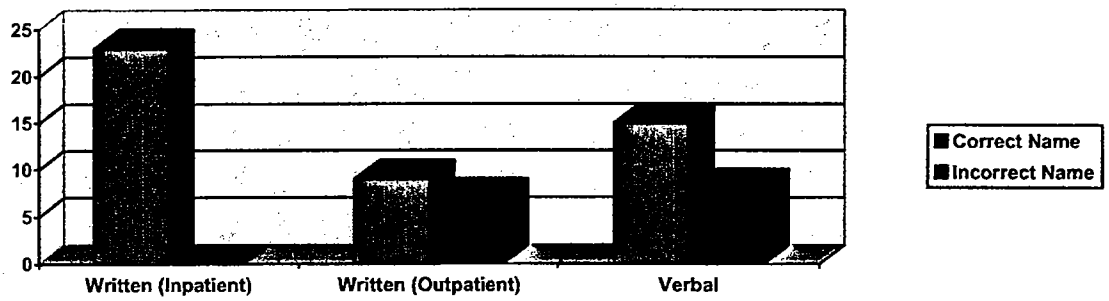
ii. The results for **Namenda** are summarized in Table 3.

Table 3

Study	# of Participants	# of Responses (%)	Correctly Interpreted (%)	Incorrectly Interpreted (%)
Written Inpatient	35	23 (66%)	23 (100%)	0 (0%)
Written Outpatient	31	16 (52%)	9 (56%)	7 (44%)
Verbal	39	23 (59%)	15 (65%)	8 (35%)
Total	105	62 (59%)	47 (76%)	15 (24%)



Among the verbal prescription study participants for Namenda, 8 of 23 (35%) of the participants interpreted the name incorrectly. The majority of the responses were misspelled variations of "Namenda". The incorrect responses were *Namedna (1), Naminda (6), and Naminemda (1).* None of the interpretations are similar to a marketed drug product.

Among the written inpatient prescription study participants for Namenda, none of the participants interpreted the name incorrectly.

Among the written outpatient prescription study participants for Namenda, 7 of 16 (44%) of the participants interpreted the name incorrectly. The majority of the responses were misspelled variations of "Namenda". The incorrect responses were *Mamenda (1), Namends (1), Namerda (1), Naminda (3), and Navenda (1).* None of the interpretations are similar to a marketed drug product

C. SAFETY EVALUATOR RISK ASSESSMENT

1.

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2. Namenda

In reviewing the proprietary name "Namenda", DMETS did not identify any proprietary names with a look-alike and/or sound-alike similarity to Namenda. We conducted prescription studies to simulate the prescription ordering process. Our studies did not confirm confusion between Namenda and currently marketed proprietary names.

III. COMMENTS TO THE SPONSOR

DMETS does not recommend the use of the proposed proprietary name, —— due to its potential to sound and look like —— However, DMETS has no objections to the use of the proprietary name Namenda.

Post-marketing reports have demonstrated that products with some sound-alike and look-alike similarities that also share an overlapping route of administration, dosage form, strength, and dosing regimen have been associated with an increased risk of error. For example, confusion and errors have been reported between Serzone and Seroquel, and Lamictal and Lamisil. Serzone and Seroquel share the same prefix ("Ser"), and have an overlapping dosage form (tablet), route of administration (oral), strengths (100 mg and 200 mg), and dosing regimen (twice daily). Lamictal and Lamisil share the same prefix ("Lam).

Additionally, Lamictal and Lamisil share an overlapping route of administration (oral), dosage form (tablet), dosing regimen (daily), and have similar numerals in their strengths (25 mg vs. 250 mg). Therefore, DMETS believes that the potential or confusion and error be considered for [redacted] given the post-marketing experience with Serzone and Seroquel, and Lamictal and Lamisil.

In addition, DMETS reviewed the blister labels, container labels, and carton and draft package insert labeling for [redacted] We have identified the following areas of possible improvement, which might minimize potential user error.

A. GENERAL COMMENT

[redacted]

B. BLISTER LABEL (5 mg, 10 mg, 15 mg, and 20 mg)

[redacted]

C. BLISTER CARTON LABELING (5 mg, 10 mg, 15 mg, and 20 mg)

[redacted]

D. BLISTER CARTON LABELING (Titration Pak)

[redacted]

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IV. RECOMMENDATIONS

1. DMETS does not recommend the use of the proprietary name ——— However, DMETS has no objection to the use of the proprietary name Namenda. DMETS considers this a final review. If the approval of the application is delayed beyond 90 days from the signature date of this review, the name and its associated labels and labeling must be re-evaluated. A re-review of the name prior to NDA approval will rule out any objections based upon approvals of other proprietary or established names from this date forward.

2. DMETS recommends implementation of the labeling revisions as outlined in Section III of this review.

3. DDMAC finds the names ——— and "Namenda" acceptable from a promotional perspective.

DMETS would appreciate feedback of the final outcome of this consult (e.g., copy of revised labels/labeling). We are willing to meet with the Division for further discussion as well. If you have any questions concerning this review, please contact Sammie Beam at 301-827-3242.

Tia M. Harper-Velazquez, Pharm.D.
Safety Evaluator
Division of Medication Errors and Technical Support
Office of Drug Safety

Concur:

Alina Mahmud, R.Ph.
Team Leader
Division of Medication Errors and Technical Support
Office of Drug Safety

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/s/

Tia Harper-Velazquez
8/22/03 11:13:02 AM
PHARMACIST

Alina Mahmud
8/22/03 11:14:47 AM
PHARMACIST

Carol Holquist
8/22/03 12:05:40 PM
PHARMACIST

Jerry Phillips
8/25/03 09:26:25 AM
DIRECTOR