

**CENTER FOR DRUG EVALUATION AND RESEARCH**

**APPLICATION NUMBER:**

**22-525**

**ADMINISTRATIVE and CORRESPONDENCE  
DOCUMENTS**

## EXCLUSIVITY SUMMARY

NDA # 22-525

SUPPL #

HFD # 120

Trade Name Namenda XR

Generic Name memantine hydrochloride

Applicant Name Forest Labs

Approval Date, If Known June 21, 2010

### PART I IS AN EXCLUSIVITY DETERMINATION NEEDED?

1. An exclusivity determination will be made for all original applications, and all efficacy supplements. Complete PARTS II and III of this Exclusivity Summary only if you answer "yes" to one or more of the following questions about the submission.

a) Is it a 505(b)(1), 505(b)(2) or efficacy supplement?

YES  NO

If yes, what type? Specify 505(b)(1), 505(b)(2), SE1, SE2, SE3, SE4, SE5, SE6, SE7, SE8

505(b)1

c) Did it require the review of clinical data other than to support a safety claim or change in labeling related to safety? (If it required review only of bioavailability or bioequivalence data, answer "no.")

YES  NO

If your answer is "no" because you believe the study is a bioavailability study and, therefore, not eligible for exclusivity, EXPLAIN why it is a bioavailability study, including your reasons for disagreeing with any arguments made by the applicant that the study was not simply a bioavailability study.

If it is a supplement requiring the review of clinical data but it is not an effectiveness supplement, describe the change or claim that is supported by the clinical data:

d) Did the applicant request exclusivity?

YES  NO

If the answer to (d) is "yes," how many years of exclusivity did the applicant request?

not stated

e) Has pediatric exclusivity been granted for this Active Moiety?

YES  NO

If the answer to the above question in YES, is this approval a result of the studies submitted in response to the Pediatric Written Request?

IF YOU HAVE ANSWERED "NO" TO ALL OF THE ABOVE QUESTIONS, GO DIRECTLY TO THE SIGNATURE BLOCKS AT THE END OF THIS DOCUMENT.

2. Is this drug product or indication a DESI upgrade?

YES  NO

IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8 (even if a study was required for the upgrade).

## **PART II FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES**

(Answer either #1 or #2 as appropriate)

1. Single active ingredient product.

Has FDA previously approved under section 505 of the Act any drug product containing the same active moiety as the drug under consideration? Answer "yes" if the active moiety (including other esterified forms, salts, complexes, chelates or clathrates) has been previously approved, but this particular form of the active moiety, e.g., this particular ester or salt (including salts with hydrogen or coordination bonding) or other non-covalent derivative (such as a complex, chelate, or clathrate) has not been approved. Answer "no" if the compound requires metabolic conversion (other than deesterification of an esterified form of the drug) to produce an already approved active moiety.

YES  NO

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).



summary for that investigation.

YES  NO

IF "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.

2. A clinical investigation is "essential to the approval" if the Agency could not have approved the application or supplement without relying on that investigation. Thus, the investigation is not essential to the approval if 1) no clinical investigation is necessary to support the supplement or application in light of previously approved applications (i.e., information other than clinical trials, such as bioavailability data, would be sufficient to provide a basis for approval as an ANDA or 505(b)(2) application because of what is already known about a previously approved product), or 2) there are published reports of studies (other than those conducted or sponsored by the applicant) or other publicly available data that independently would have been sufficient to support approval of the application, without reference to the clinical investigation submitted in the application.

(a) In light of previously approved applications, is a clinical investigation (either conducted by the applicant or available from some other source, including the published literature) necessary to support approval of the application or supplement?

YES  NO

If "no," state the basis for your conclusion that a clinical trial is not necessary for approval AND GO DIRECTLY TO SIGNATURE BLOCK ON PAGE 8:

(b) Did the applicant submit a list of published studies relevant to the safety and effectiveness of this drug product and a statement that the publicly available data would not independently support approval of the application?

YES  NO

(1) If the answer to 2(b) is "yes," do you personally know of any reason to disagree with the applicant's conclusion? If not applicable, answer NO.

YES  NO

If yes, explain:

(2) If the answer to 2(b) is "no," are you aware of published studies not conducted or sponsored by the applicant or other publicly available data that could independently demonstrate the safety and effectiveness of this drug product?

YES  NO

If yes, explain:

- (c) If the answers to (b)(1) and (b)(2) were both "no," identify the clinical investigations submitted in the application that are essential to the approval:

Efficacy study - MEM-MD-50

Studies comparing two products with the same ingredient(s) are considered to be bioavailability studies for the purpose of this section.

3. In addition to being essential, investigations must be "new" to support exclusivity. The agency interprets "new clinical investigation" to mean an investigation that 1) has not been relied on by the agency to demonstrate the effectiveness of a previously approved drug for any indication and 2) does not duplicate the results of another investigation that was relied on by the agency to demonstrate the effectiveness of a previously approved drug product, i.e., does not redemonstrate something the agency considers to have been demonstrated in an already approved application.

a) For each investigation identified as "essential to the approval," has the investigation been relied on by the agency to demonstrate the effectiveness of a previously approved drug product? (If the investigation was relied on only to support the safety of a previously approved drug, answer "no.")

Investigation #1 YES  NO

Investigation #2 YES  NO

If you have answered "yes" for one or more investigations, identify each such investigation and the NDA in which each was relied upon:

b) For each investigation identified as "essential to the approval", does the investigation duplicate the results of another investigation that was relied on by the agency to support the effectiveness of a previously approved drug product?

Investigation #1 YES  NO

Investigation #2 YES  NO



Investigation #1  
!  
!  
YES  ! NO   
Explain: ! Explain:

Investigation #2  
!  
!  
YES  ! NO   
Explain: ! Explain:

(c) Notwithstanding an answer of "yes" to (a) or (b), are there other reasons to believe that the applicant should not be credited with having "conducted or sponsored" the study? (Purchased studies may not be used as the basis for exclusivity. However, if all rights to the drug are purchased (not just studies on the drug), the applicant may be considered to have sponsored or conducted the studies sponsored or conducted by its predecessor in interest.)

YES  NO

If yes, explain:

---

Name of person completing form: Teresa Wheelous, R.Ph.  
Title: Sr. Regulatory Management Officer  
Date: 6/25/10

Name of Office/Division Director signing form: Russell Katz, M.D.  
Title: Director, Division of Neurology Products

Form OGD-011347; Revised 05/10/2004; formatted 2/15/05

**DEBARMENT CERTIFICATION**

Forest Laboratories, Inc hereby certifies that it did not and will not use in any capacity the services of any person debarred under section 306 of the Federal Food, Drug, and Cosmetic Act in connection with this application.



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Marco Taglietti, MD  
Corporate Vice President of Forest Laboratories, Inc  
and President of the Forest Research Institute

18 AUG 09

Date

"Confidential Information"

[http://darrts/images/fda\\_logo5.jpg](http://darrts/images/fda_logo5.jpg)

[http://darrts/images/dhhs\\_logo\\_thumb.gif](http://darrts/images/dhhs_logo_thumb.gif)

**Wheelous, Teresa A**

---

**From:** Niebo, Michael [Michael.Niebo@frx.com]  
**Sent:** Monday, June 21, 2010 10:03 AM  
**To:** Wheelous, Teresa A  
**Subject:** RE: Namenda XR Labeling

**Attachments:** draft-labeling-text-tracked 6.21.2010.doc; draft-labeling-text-clean 6.21.2010.doc; emfalert.txt



draft-labeling-te draft-labeling-te mfalert.txt (855  
xt-tracked 6.... xt-clean 6.21... B)

Teresa-

Here's the PI with the requested changes to Section 13.2 (except for the change of "MRHD" to "MIREd", since no one here at Forest understands that change). Please confirm that this is acceptable, and the files will be submitted to the eCTD immediately.

Thanks,

Michael P. Niebo, RAC

Asst. Director, Regulatory Affairs

Forest Research Institute

A Subsidiary of Forest Laboratories, Inc.

Harborside Financial Center

Plaza V, Suite 1900

Jersey City, NJ 07311

Office: 201-386-2046

Fax: 201-524-9711/9712

---

**From:** Wheelous, Teresa A [mailto:Teresa.Wheelous@fda.hhs.gov]  
**Sent:** Monday, June 21, 2010 8:58 AM  
**To:** Niebo, Michael  
**Subject:** RE: Namenda XR Labeling

Michael,

We received the carton / container labels. Will there be a revised package labeling (that contains the eALD changes that we discussed on Friday)?

I am currently out of the office, but will be in later this morning.

Thanks,

Teresa

---

**From:** Niebo, Michael [mailto:Michael.Niebo@frx.com]  
**Sent:** Monday, June 21, 2010 8:52 AM  
**To:** Wheelous, Teresa A  
**Subject:** RE: Namenda XR Labeling

Teresa-

The final revised labeling (PI and carton/container) was sent to the eCTD via the electronic gateway on Friday afternoon. Earlier in the afternoon I had also emailed you the same files. Please let me know if you have any questions or need any additional information. I'll be available all day today.

Thanks,

Michael P. Niebo, RAC

Asst. Director, Regulatory Affairs

Forest Research Institute

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Jersey City, NJ 07311

Office: 201-386-2046

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**From:** Wheelous, Teresa A [mailto:Teresa.Wheelous@fda.hhs.gov]  
**Sent:** Monday, June 21, 2010 8:49 AM  
**To:** Niebo, Michael  
**Subject:** Namenda XR Labeling

Michael,

I want to confirm that you will be sending me the Namenda XR labeling today.

Thanks,

Teresa

---

**Wheelous, Teresa A**

**From:** Niebo, Michael [Michael.Niebo@frx.com]  
**Sent:** Monday, June 21, 2010 9:17 AM  
**To:** Wheelous, Teresa A  
**Subject:** RE: Namenda XR Labeling

**Attachments:** emfalert.txt



emfalert.txt (855  
B)

Teresa-

The files that were submitted and emailed on Friday contained all of the changes discussed during the T-con on Friday morning, which included some of SEALD's comments as well as those discussed with Dr. Katz.

I have one clarification on the changes you emailed for Section 13.2: I noticed that the incidences of "MRHD" were changed to "MIREd" but those were not highlighted in red text. Is it supposed to be MRHD or MIREd? I know what MRHD stands for, but I'm not familiar with "MIREd"...

Thanks,

Michael P. Niebo, RAC

Asst. Director, Regulatory Affairs

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Michael P. Niebo, RAC

Asst. Director, Regulatory Affairs

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**Sent:** Monday, June 21, 2010 8:49 AM

**To:** Niebo, Michael

**Subject:** Namenda XR Labeling

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Thanks,

Teresa

## Wheelous, Teresa A

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**To:** Wheelous, Teresa A  
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**Attachments:** emfalert.txt



mfalert.txt (855  
B)

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Thanks,

Michael P. Niebo, RAC

Asst. Director, Regulatory Affairs

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**From:** Wheelous, Teresa A [mailto:Teresa.Wheelous@fda.hhs.gov]  
**Sent:** Monday, June 21, 2010 8:49 AM  
**To:** Niebo, Michael  
**Subject:** Namenda XR Labeling

Michael,

I want to confirm that you will be sending me the Namenda XR labeling today.

Thanks,

Teresa

## Wheelous, Teresa A

---

**From:** Freed, Lois M  
**Sent:** Friday, June 18, 2010 7:54 AM  
**To:** Yasuda, Sally; Hughes, Alice  
**Cc:** Hawver, David; Wheelous, Teresa A; Summers, Kelly  
**Subject:** RE: Namenda XR; ODE 1 - Tatiana; AP ltr w/ PMR

**Attachments:** Revised Namenda Approval with PMR 061110 JW lf.doc

Thanks to you both for checking on this. I have just a couple of minor suggestions (Sally, I didn't touch the PMR wording.) Unfortunately, you can't see my changes - all track changes are attributed to "author" for some reason.

Changes:

1. changed (b) (4) to "was", 2nd paragraph, 3rd line under Postmarketing Requirements.
2. italicized journal name in 4-5th lines of same paragraph.
3. incorporated that sentence in question into the previous paragraph, instead of having it as its own.



Revised  
nda Approval wi

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**From:** Yasuda, Sally  
**Sent:** Thursday, June 17, 2010 4:25 PM  
**To:** Hughes, Alice; Freed, Lois M  
**Cc:** Hawver, David; Wheelous, Teresa A; Summers, Kelly  
**Subject:** RE: Namenda XR; ODE 1 - Tatiana; AP ltr w/ PMR

Thanks, Alice.

---

**From:** Hughes, Alice  
**Sent:** Thursday, June 17, 2010 4:11 PM  
**To:** Yasuda, Sally; Freed, Lois M  
**Cc:** Hawver, David; Wheelous, Teresa A; Summers, Kelly  
**Subject:** RE: Namenda XR; ODE 1 - Tatiana; AP ltr w/ PMR

I have seen this sort of language in letters from other divisions' that I have reviewed during my SRT rotations. It is what SRT and SWAT are currently wanting in the letters.

The dates in the letter are definitely still firm legal requirements and are enforceable.

I think we should leave the language as is.

Thanks,  
Alice

---

**From:** Yasuda, Sally  
**Sent:** Thursday, June 17, 2010 12:56 PM  
**To:** Freed, Lois M; Hughes, Alice  
**Cc:** Hawver, David; Wheelous, Teresa A  
**Subject:** RE: Namenda XR; ODE 1 - Tatiana; AP ltr w/ PMR

I don't remember seeing that before either. Alice, please let us know what to do.

Thanks,

Sally

---

**From:** Freed, Lois M  
**Sent:** Thursday, June 17, 2010 12:55 PM  
**To:** Yasuda, Sally; Hughes, Alice  
**Cc:** Hawver, David  
**Subject:** RE: Namenda XR; ODE 1 - Tatiana; AP ltr w/ PMR

As Dave mentioned, I don't remember ever seeing the sentence they added about when the sponsor sent in the dates. I just checked the Sabril approval letter (which probably wins the contest for PMRs) and there is no such sentence. It just states the PMR and then lists the dates beneath it. Unless the rules have changed (which, of course, they may have), I'd suggest removing that sentence.

Lois

---

**From:** Yasuda, Sally  
**Sent:** Thursday, June 17, 2010 11:47 AM  
**To:** Hughes, Alice  
**Cc:** Freed, Lois M; Hawver, David  
**Subject:** FW: Namenda XR; ODE 1 - Tatiana; AP ltr w/ PMR

I am sending to Alice and Kelly so they will be in the loop about the letter. It looks like the language for the actual PMR is OK with you, so I will put that in the template and put the template in Darrrts.

Thanks,

Sally

---

**From:** Hawver, David  
**Sent:** Thursday, June 17, 2010 11:17 AM  
**To:** Yasuda, Sally  
**Subject:** RE: Namenda XR; ODE 1 - Tatiana; AP ltr w/ PMR

Sally,

Wait! Lois is uncertain why SLR has inserted the sentence referring to (b) (4), as this implies that it is their idea and not a firm legal requirement, which is what it is. She is going to research previous letters to see if anything like this has been included in past Approval letters with PMRs. I made a few other minor changes:

<< File: Revised Namenda Approval with PMR 061110 JW.doc >>

Thanks,

Dave

*David B. Hawver, Ph.D.*

Pharmacology/Toxicology Reviewer  
Division of Neurology Products  
Center for Drug Evaluation and Research  
Food and Drug Administration  
10903 New Hampshire Avenue, Building 22, Room 4333  
Silver Spring, MD 20993-0002  
301-796-1085 phone  
301-796-9842 fax  
david.hawver@fda.hhs.gov

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**From:** Yasuda, Sally  
**Sent:** Thursday, June 17, 2010 10:47 AM  
**To:** Freed, Lois M; Hawver, David  
**Subject:** FW: Namenda XR; ODE 1 - Tatiana; AP ltr w/ PMR

Here is the letter. Please see if you agree with SRT's changes to the PMR (changes are not in track changes in the PMR).

Sally

---

**From:** Safety Requirements Team  
**Sent:** Wednesday, June 16, 2010 11:31 AM  
**To:** Wheelous, Teresa A; Summers, Kelly; Yasuda, Sally; Hughes, Alice; Ware, Jacqueline H  
**Cc:** Honig, Susan L; Kashoki, Mwango; Lee, Cathryn; Oussova, Tatiana; Beitz, Julie G; Safety Requirements Team  
**Subject:** RE: Namenda XR; ODE 1 - Tatiana; AP ltr w/ PMR

Thanks Teresa. Your letter is cleared, with the revisions to the letter in the eRoom and attached.

[http://erom.fda.gov/eRoom/CDER/CDER-ONDIO/0\\_9f604](http://erom.fda.gov/eRoom/CDER/CDER-ONDIO/0_9f604)

Please copy me (Julie Marchick) in DARRTS when you issue the letter.

<< File: Namenda Approval with PMR 061110 JW.doc >>

Thanks,  
Julie

---

**From:** Wheelous, Teresa A  
**Sent:** Wednesday, June 16, 2010 11:09 AM  
**To:** Safety Requirements Team; Summers, Kelly; Yasuda, Sally; Hughes, Alice  
**Cc:** Honig, Susan L; Kashoki, Mwango; Lee, Cathryn; Oussova, Tatiana; Beitz, Julie G; Ware, Jacqueline H  
**Subject:** RE: Namenda XR; ODE 1 - Tatiana; AP ltr w/ PMR

SRT, Kelly, Sally, and Alice,

I checked with Lois Freed, the nonclinical supervisor, and the following is her response:

Yes, thanks. It's only one study. And the sponsor is aware that we are making our previous study request a PMR for the NDA.

Teresa

---

**From:** Wheelous, Teresa A  
**Sent:** Wednesday, June 16, 2010 10:44 AM  
**To:** Freed, Lois M  
**Subject:** FW: Namenda XR; ODE 1 - Tatiana; AP ltr w/ PMR

Lois,

You may be interested in this.

Teresa

---

**From:** Safety Requirements Team  
**Sent:** Wednesday, June 16, 2010 9:36 AM  
**To:** Summers, Kelly; Ware, Jacqueline H; Yasuda, Sally; Wheelous, Teresa A; Hughes, Alice  
**Cc:** Safety Requirements Team; Honig, Susan L; Kashoki, Mwango; Lee, Cathryn; Oussova, Tatiana; Beitz, Julie G  
**Subject:** Namenda XR; ODE 1 - Tatiana; AP ltr w/ PMR

Hi Kelly,

We have questions for you in the draft letter in the eRoom. Please respond to the questions and then we'll take another look at the letter.

Basically, our question is whether there is one study or two? Will there be one study for Namenda and one for Namenda XR, or will there only be one study? If there is only one study, we may decide to leave the letter as originally written.

[http://eroom.fda.gov/eRoom/CDER/CDER-ONDIO/0\\_9f604](http://eroom.fda.gov/eRoom/CDER/CDER-ONDIO/0_9f604)

Thanks,  
Julie

---

**From:** Summers, Kelly  
**Sent:** Monday, June 14, 2010 2:07 PM  
**To:** Safety Requirements Team  
**Cc:** Ware, Jacqueline H; Yasuda, Sally; Wheelous, Teresa A  
**Subject:** Namenda XR AP ltr w/ PMR

Please find attached the approval letter with a PMR for NDA 22525, Namenda XR.

PDUFA date is 6/21/10 though we'd love to be able to act on it by Friday.

Many thanks,  
Kelly

LT Kelly Summers, PharmD, USPHS  
Safety Project Manager  
Division of Neurology Products  
OND / CDER / FDA  
White Oak Bldg 22, Room 4321  
301-796-5264 (Office)  
301-796-9842 (Fax)

## **Wheelous, Teresa A**

---

**From:** Beitzell, Debra  
**Sent:** Thursday, June 17, 2010 5:32 PM  
**To:** Wheelous, Teresa A  
**Cc:** Burke, Laurie B  
**Subject:** SEALD Comments - NDA 22-525

**Attachments:** DBeitzellReview.06.17.10.doc

Teresa,

Here are SEALDs comments for NDA 22-525. I reviewed the labeling for conformance with PLR requirements and, except where otherwise noted, these comments are not optional and are required by the regulations and obligatory guidance.

Thanks,  
Debbie



.eitzellReview.  
06.17.10.doc (...)

**Wheelous, Teresa A**

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**From:** Niebo, Michael [Michael.Niebo@frx.com]  
**Sent:** Thursday, June 17, 2010 5:04 PM  
**To:** Wheelous, Teresa A  
**Subject:** RE: NDA 22525 Namenda XR; Carton & Container Labeling , Additional Labeling Edits  
**Attachments:** emfalert.txt; image001.gif

Great. Thanks again,

Michael P. Niebo, RAC

Asst. Director, Regulatory Affairs

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Jersey City, NJ 07311

Office: 201-386-2046

Fax: 201-524-9711/9712

---

**From:** Wheelous, Teresa A [mailto:Teresa.Wheelous@fda.hhs.gov]  
**Sent:** Thursday, June 17, 2010 5:03 PM  
**To:** Niebo, Michael  
**Subject:** RE: NDA 22525 Namenda XR; Carton & Container Labeling , Additional Labeling Edits

Michael,

A DMEPA representative will be participating.

Teresa

---

**From:** Niebo, Michael [mailto:Michael.Niebo@frx.com]  
**Sent:** Thursday, June 17, 2010 5:02 PM  
**To:** Wheelous, Teresa A  
**Subject:** RE: NDA 22525 Namenda XR; Carton & Container Labeling , Additional Labeling Edits

Teresa-

I do believe we would like to discuss some of the comments, so 9am is acceptable for us. Please use the following number: 201-427-8971, and please confirm if a DMEPA representative will also be on the call.

Thanks,

Michael P. Niebo, RAC  
Asst. Director, Regulatory Affairs  
Forest Research Institute  
A Subsidiary of Forest Laboratories, Inc.  
Harborside Financial Center  
Plaza V, Suite 1900  
Jersey City, NJ 07311  
Office: 201-386-2046  
Fax: 201-524-9711/9712

---

**From:** Wheelous, Teresa A [mailto:Teresa.Wheelous@fda.hhs.gov]  
**Sent:** Thursday, June 17, 2010 4:30 PM  
**To:** Niebo, Michael  
**Subject:** RE: NDA 22525 Namenda XR; Carton & Container Labeling , Additional Labeling Edits

Michael,

DMEPA has reviewed the information provided by email and has the following responses. I have also attached this document. Just in case we need to discuss this further, please try to be available around 9 AM on Friday.

Thanks

Teresa



mfalert.txt (855  
B)

**FOREST LABORATORIES, INC.**

**Harborside Financial Center**

**Plaza V, Suite 1900**

**Jersey City, New Jersey 07311**

**Direct Line: (201) 386-2046**

**Fax: (631) 858-7921**

6 Page(s) of Draft Labeling have been Withheld in Full as b4 (CCI/TS)  
immediately following this page

June 16, 2010

Russell G. Katz, MD, Director

Division of Neurology Products

Center for Drug Evaluation and Research

Food and Drug Administration

5901-B Ammendale Road

Beltsville, MD 20705-1266

**NDA: 22-525 - Namenda® (Memantine Hydrochloride) XR Extended Release Capsules**

The size of the electronic submission is approximately XX MB. The eCTD is provided through FDA's Electronic Submissions Gateway system. All files in this electronic submission have been verified to be virus free as of June 16, 2010 by the following antivirus program: McAfee VirusScan Enterprise 8.7.0.570.

If you have any questions about this submission, please do not hesitate to telephone me at (201) 386-2046 or, in my absence, James DeMartino, PhD, at (201) 386-2131.

Sincerely,

Michael P. Niebo

Assistant Director, Regulatory Affairs

[michael.niebo@frx.com](mailto:michael.niebo@frx.com)

---

**From:** Niebo, Michael [mailto:Michael.Niebo@frx.com]  
**Sent:** Thursday, June 17, 2010 8:25 AM  
**To:** Wheelous, Teresa A  
**Subject:** RE: NDA 22525 Namenda XR; Carton & Container Labeling , Additional Labeling Edits

Teresa-

Attached is the cover letter which will accompany the eCTD submission of the carton/container labeling. Please note that Forest has provided a detailed response to each request within the cover letter.

Thanks,

Michael P. Niebo, RAC

Asst. Director, Regulatory Affairs

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Thanks

---

**From:** Niebo, Michael [mailto:Michael.Niebo@frx.com]  
**Sent:** Wednesday, June 16, 2010 5:51 PM  
**To:** Wheelous, Teresa A  
**Subject:** RE: NDA 22525 Namenda XR; Carton & Container Labeling , Additional Labeling Edits

Teresa-

OK, I will send the container/carton labels tonight as soon as I receive them and they've been QC'd. Attached is the PI with the edits you've requested. This will be formally submitted to the eCTD tomorrow along with the container/carton labeling.

Thanks,

Michael P. Niebo, RAC  
Asst. Director, Regulatory Affairs  
Forest Research Institute  
A Subsidiary of Forest Laboratories, Inc.  
Harborside Financial Center  
Plaza V, Suite 1900  
Jersey City, NJ 07311  
Office: 201-386-2046  
Fax: 201-524-9711/9712

---

**From:** Wheelous, Teresa A [mailto:Teresa.Wheelous@fda.hhs.gov]  
**Sent:** Wednesday, June 16, 2010 5:37 PM  
**To:** Niebo, Michael  
**Subject:** NDA 22525 Namenda XR; Carton & Container Labeling , Additional Labeling Edits

Michael,

I received your voice message regarding the carton & container label proofs. If you have them ready this evening, then please email them to me.

Regarding the labeling, the following edits have been identified:

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In the legend to Figure 4, a period needs to be added at the end.

Regards,

Teresa

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**Sent:** Tuesday, June 15, 2010 4:33 PM  
**To:** Wheelous, Teresa A  
**Subject:** RE: NDA 22525 Namenda XR; Carton & Container Labeling , Follow-Up to Labeling Discussions

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Attached is the latest version of the PI label, with revisions as requested below. This label is being submitted via the electronic gateway this afternoon.

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Asst. Director, Regulatory Affairs

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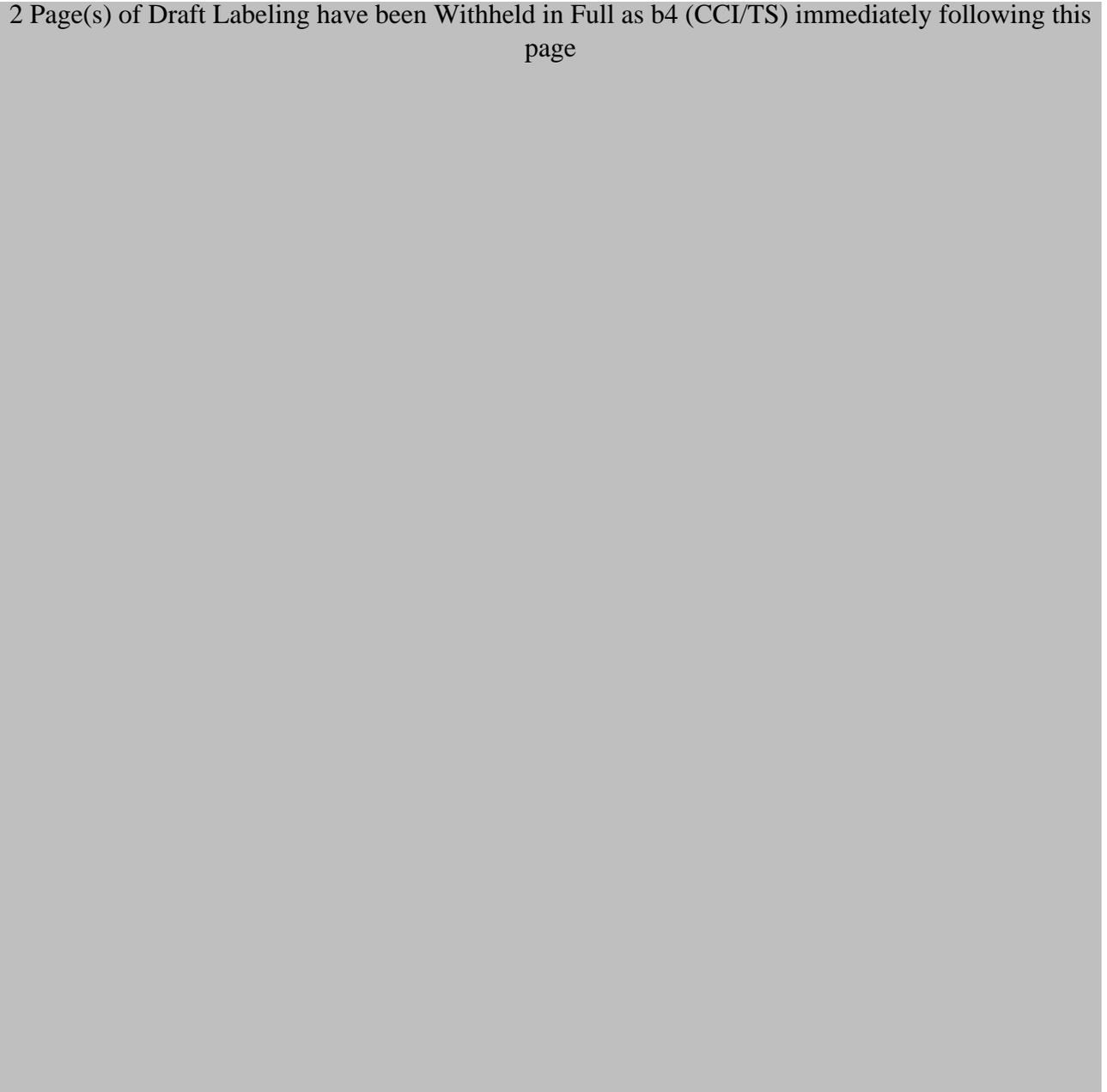
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The following are additional labeling revisions (that were not discussed this morning) and the Carton & Container labeling recommendations that were mentioned during our telecon:

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## Wheelous, Teresa A

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**Sent:** Thursday, June 17, 2010 5:02 PM  
**To:** Wheelous, Teresa A  
**Subject:** RE: NDA 22525 Namenda XR; Carton & Container Labeling , Additional Labeling Edits  
**Attachments:** emfalert.txt; image001.gif

Teresa-

I do believe we would like to discuss some of the comments, so 9am is acceptable for us. Please use the following number: 201-427-8971, and please confirm if a DMEPA representative will also be on the call.

Thanks,

Michael P. Niebo, RAC

Asst. Director, Regulatory Affairs

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1000 Broadview Avenue, Suite 1900

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If you have any questions about this submission, please do not hesitate to telephone me at (201) 386-2046 or, in my absence, James DeMartino, PhD, at (201) 386-2131.

Sincerely,

Michael P. Niebo

Assistant Director, Regulatory Affairs

[michael.niebo@frx.com](mailto:michael.niebo@frx.com)

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**Sent:** Thursday, June 17, 2010 8:25 AM

**To:** Wheelous, Teresa A

**Subject:** RE: NDA 22525 Namenda XR; Carton & Container Labeling , Additional Labeling Edits

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Thanks,

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## Wheelous, Teresa A

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**From:** Hawver, David  
**Sent:** Thursday, June 17, 2010 4:54 PM  
**To:** Wheelous, Teresa A  
**Cc:** Freed, Lois M; Mani, Ranjit B; Hughes, Alice; Yasuda, Sally; Ware, Jacqueline H  
**Subject:** NDA 22-525 Revised Namenda Approval Letter with PMR 061110 JW.doc

**Attachments:** Revised Namenda Approval with PMR 061110 JW.doc



Revised  
nda Approval wi

OK, here is the revised Approval letter for NDA 22-525 Namenda XR, with a few very minor adjustments made.

-Dave

## Wheelous, Teresa A

---

**From:** Wheelous, Teresa A  
**Sent:** Thursday, June 17, 2010 4:30 PM  
**To:** 'Niebo, Michael'  
**Subject:** RE: NDA 22525 Namenda XR; Carton & Container Labeling , Additional Labeling Edits

**Attachments:** attbd3a8.gif

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Thanks

Teresa



attbd3a8.gif (4  
KB)

**FOREST LABORATORIES, INC.**

**Harborside Financial Center**

**aza V, Suite 1900**

**Jersey City, New Jersey 07311**

**Direct Line: (201) 386-2046**

**FAX: (631) 858-7921**

June 16, 2010

Russell G. Katz, MD, Director

Division of Neurology Products

Center for Drug Evaluation and Research

Food and Drug Administration

5901-B Ammendale Road

Beltsville, MD 20705-1266

**NDA: 22-525 - Namenda® (Memantine Hydrochloride) XR Extended Release Capsules**

**Re: Labeling: Revisions to Container and Carton Labeling**

Dear Dr. Katz:

Reference is made to Forest's original New Drug Application, NDA 22-525 for Namenda® (Memantine Hydrochloride) XR Extended Release Capsules, dated August 21, 2009, the Agency's email communication dated June 11, 2010.

Forest is herewith providing the revised carton and container labeling as requested. The Agency's comments are provided below in bold italics, followed by Forest's response:

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Sincerely,

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Assistant Director, Regulatory Affairs

[michael.niebo@frx.com](mailto:michael.niebo@frx.com)

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Teresa

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**Wheelous, Teresa A**

---

**From:** Chan, Irene Z.  
**Sent:** Thursday, June 17, 2010 4:10 PM  
**To:** Wheelous, Teresa A  
**Cc:** Katz, Russell G; Griffis, Melina; Taylor, Kellie  
**Subject:** Namenda XR NDA 022525

**Attachments:** Namenda XR Cover Letter with FDA Responses 6 17 2010.doc

Hello Teresa,

Please see the attached document which contains our comments to the Applicant's proposed label and labeling revisions. These comments are based on the proposed labels and labeling e-mailed to us by the Applicant this morning. We request that the Applicant adopt our recommendations as written. We do not believe a teleconference with the Applicant is necessary at this time. Please ask the Applicant to submit revised labels to us. Please let me know if you have any questions. Thanks and have a great day!



Namenda XR  
Cover Letter with F

Sincerely,

Irene

Irene Z. Chan, Pharm.D., BCPS  
CDR, U.S. Public Health Service  
Drug Safety Evaluator  
Division of Medication Error Prevention and Analysis  
Office of Surveillance and Epidemiology  
Center for Drug Evaluation and Research  
Food and Drug Administration

The Federal Research Center at White Oak  
10903 New Hampshire Avenue  
Building 22, Rm. #4421 MS4447  
Silver Spring, Maryland 20993-0002  
[Irene.Chan2@fda.hhs.gov](mailto:Irene.Chan2@fda.hhs.gov)  
Office 301.796.3962  
Fax 301.796.9865

## **Wheelous, Teresa A**

---

**From:** Katz, Russell G  
**Sent:** Thursday, June 17, 2010 2:57 PM  
**To:** Wheelous, Teresa A  
**Subject:** Namenda XR carton/container labels

.resa-

I just spoke with Melina, Irene, and Kellie Taylor. Irene has looked at the carton/container labels and still has some relatively minor concerns. However, she also just learned that the sponsor submitted a second titration pack months ago that she had never seen. Apparently, it came in as a clinical submission, and she never saw it. She actually doesn't like this one, and isn't clear why the company needs two titration packs. So, she will have some minor concerns about the carton/container, and a question for the company about why they want two titration packs. She is going to e-mail these to you, and if you could get them to the sponsor as soon as you get them from her, that'd be great. Also, I think we need to reserve some time tomorrow to talk to the company if necessary; a half hour should be enough. With any luck, they'll make the changes Irene wants, and withdraw the second titration pack, and we will all live happily everafter. Also, could you please include Kellie Taylor on the meeting for tomorrow in addition to me and Irene.

Thanks a lot.  
Rusty

3 Page(s) has been Withheld in Full as b4 (CCI/TS) immediately following this page

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**Wheelous, Teresa A**

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**Attachments:** 1 2 Cover letter 6.17.2010.doc; emfalert.txt



1 2 Cover letter mfalert.txt (855  
6.17.2010.doc... B)

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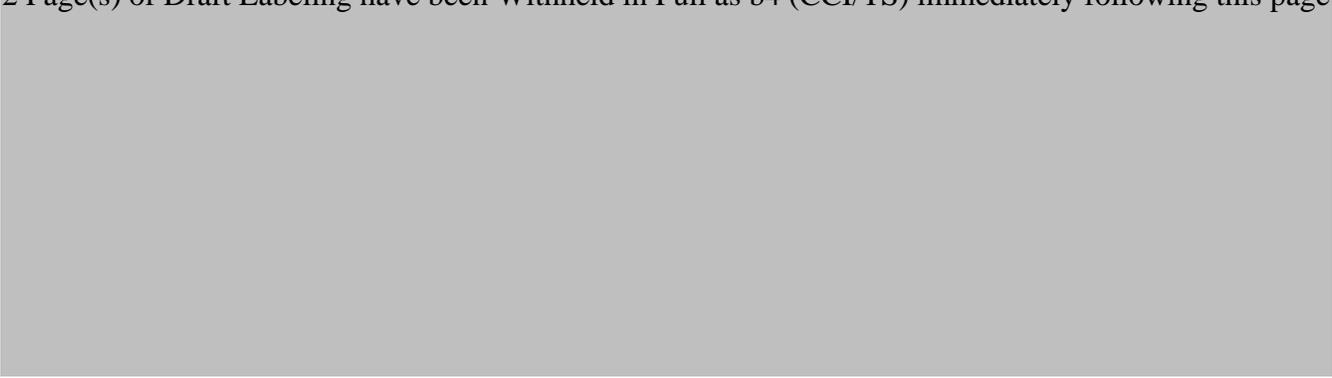
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**Sent:** Thursday, June 17, 2010 8:14 AM  
**To:** Wheelous, Teresa A  
**Subject:** FW: One additional file

**Attachments:** PSK\_Titration\_ (b) (4) logo\_step\_circle\_to Client\_6-16-10.pdf; emfalert.txt



PSK\_Titration\_or mfalert.txt (952  
nge logo\_step... B)

Teresa-

I got a delivery failure notice on this last file that I sent last night. Please let me know if you've received all of the labeling files now.

Thanks,

Michael P. Niebo, RAC

Asst. Director, Regulatory Affairs

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Michael P. Niebo, RAC

Asst. Director, Regulatory Affairs

Forest Research Institute

A Subsidiary of Forest Laboratories, Inc.

Harborside Financial Center

Plaza V, Suite 1900

Jersey City, NJ 07311

Office: 201-386-2046

Fax: 201-524-9711/9712

---

**From:** Wheelous, Teresa A [mailto:Teresa.Wheelous@fda.hhs.gov]

**Sent:** Friday, June 11, 2010 2:30 PM

**To:** Niebo, Michael

**Subject:** NDA 22525 Namenda XR; Carton & Container Labeling , Follow-Up to Labeling Discussions

Michael,

The following are additional labeling revisions (that were not discussed this morning) and the Carton & Container labeling recommendations that were mentioned during our telecon:

**ADDITIONAL LABELING REVISIONS**

2 Page(s) of Draft Labeling have been Withheld in Full as b4 (CCI/TS) immediately following this page

H. PROFESSIONAL SAMPLE PATIENT (b) (4) KIT

1. Delete the term 'starter' from professional samples in accordance with 64 FR 67720.
2. As there is no difference between the Kit and the Pack configurations, there is no need to differentiate the professional sample from the trade package with terminology other than "Professional Sample – Not for Sale". Delete the term "Patient Starter Kit" from the package and change the name to "Titration Pack".
3. See comment E above.
4. See comment F(3) above.

**Wheelous, Teresa A**

---

**From:** Wheelous, Teresa A  
**Sent:** Wednesday, June 16, 2010 5:37 PM  
**To:** 'Niebo, Michael'  
**Subject:** NDA 22525 Namenda XR; Carton & Container Labeling , Additional Labeling Edits

Michael,

I received your voice message regarding the carton & container label proofs. If you have them ready this evening, then please email them to me.

Regarding the labeling, the following edits have been identified:

Section 8.1

The last 2 sentences in this section, " There are no adequate and well-controlled studies of memantine in pregnant women....", have been inserted at the beginning of the section (as agreed). However, the sentences have not been deleted from the end of this section.

In Section 13.2, second paragraph, second to the last sentence, a comma after "(Cmax)," should be removed.

In Section 13.2, second paragraph, a period needs to be added to the last sentence.

In Section 7.7, a period needs to be added to the last sentence.

In the legend to Figure 2, a period needs to be added at the end.

In the legend to Figure 4, a period needs to be added at the end.

Regards,

Teresa

---

**From:** Niebo, Michael [mailto:Michael.Niebo@frx.com]  
**Sent:** Tuesday, June 15, 2010 4:33 PM  
**To:** Wheelous, Teresa A  
**Subject:** RE: NDA 22525 Namenda XR; Carton & Container Labeling , Follow-Up to Labeling Discussions

Teresa-

Attached is the latest version of the PI label, with revisions as requested below. This label is being submitted via the electronic gateway this afternoon.

Thanks,

Michael P. Niebo, RAC

Asst. Director, Regulatory Affairs

Forest Research Institute

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Jersey City, NJ 07311

Office: 201-386-2046

Fax: 201-524-9711/9712

---

**From:** Wheelous, Teresa A [mailto:Teresa.Wheelous@fda.hhs.gov]

**Sent:** Friday, June 11, 2010 2:30 PM

**To:** Niebo, Michael

**Subject:** NDA 22525 Namenda XR; Carton & Container Labeling , Follow-Up to Labeling Discussions

Michael,

The following are additional labeling revisions (that were not discussed this morning) and the Carton & Container labeling recommendations that were mentioned during our telecon:

**ADDITIONAL LABELING REVISIONS**

2 Page(s) of Draft Labeling have been Withheld in Full as b4 (CCI/TS) immediately following this page

H. PROFESSIONAL SAMPLE PATIENT (b) (4) KIT

1. Delete the term 'starter' from professional samples in accordance with 64 FR 67720.
2. As there is no difference between the Kit and the Pack configurations, there is no need to differentiate the professional sample from the trade package with terminology other than "Professional Sample – Not for Sale". Delete the term "Patient Starter Kit" from the package and change the name to "Titration Pack".
3. See comment E above.
4. See comment F(3) above.

**Wheelous, Teresa A**

---

**From:** Griffis, Melina  
**Sent:** Wednesday, June 16, 2010 12:50 PM  
**To:** Mani, Ranjit B; Chan, Irene Z.  
**Cc:** Wheelous, Teresa A; Kozauer, Nicholas; Katz, Russell G  
**Subject:** RE: NDA 22525; Namenda XR; Proposed Addition To "Highlights of Prescribing Information" Section

Ranjit,

Based on your rationale we are ok with not including it in the highlights

---

**From:** Mani, Ranjit B  
**Sent:** Wednesday, June 16, 2010 12:06 PM  
**To:** Griffis, Melina; Chan, Irene Z.  
**Cc:** Mani, Ranjit B; Wheelous, Teresa A; Kozauer, Nicholas; Katz, Russell G  
**Subject:** NDA 22525; Namenda XR; Proposed Addition To "Highlights of Prescribing Information" Section

Melina and Irene,

You will recall our discussion a short while ago about your suggestion that we consider adding the following (or a similar) statement to the "Highlights of Prescribing Information" section for Namenda XR.

(b) (4)

I am certainly willing to be persuaded otherwise regarding the above.

Ranjit

## Wheelous, Teresa A

---

**From:** Safety Requirements Team  
**Sent:** Wednesday, June 16, 2010 11:31 AM  
**To:** Wheelous, Teresa A; Summers, Kelly; Yasuda, Sally; Hughes, Alice; Ware, Jacqueline H  
**Cc:** Honig, Susan L; Kashoki, Mwango; Lee, Cathryn; Oussova, Tatiana; Beitz, Julie G; Safety Requirements Team  
**Subject:** RE: Namenda XR; ODE 1 - Tatiana; AP ltr w/ PMR  
**Attachments:** Namenda Approval with PMR 061110 JW.doc

Thanks Teresa. Your letter is cleared, with the revisions to the letter in the eRoom and attached.

[http://erom.fda.gov/eRoom/CDER/CDER-ONDIO/0\\_9f604](http://erom.fda.gov/eRoom/CDER/CDER-ONDIO/0_9f604)

Please copy me (Julie Marchick) in DARRTS when you issue the letter.



Namenda  
val with PMR 06

Thanks,  
Julie

---

**From:** Wheelous, Teresa A  
**Sent:** Wednesday, June 16, 2010 11:09 AM  
**To:** Safety Requirements Team; Summers, Kelly; Yasuda, Sally; Hughes, Alice  
**Cc:** Honig, Susan L; Kashoki, Mwango; Lee, Cathryn; Oussova, Tatiana; Beitz, Julie G; Ware, Jacqueline H  
**Subject:** RE: Namenda XR; ODE 1 - Tatiana; AP ltr w/ PMR

SRT, Kelly, Sally, and Alice,

I checked with Lois Freed, the nonclinical supervisor, and the following is her response:

Yes, thanks. It's only one study. And the sponsor is aware that we are making our previous study request a PMR for the NDA.

Teresa

---

**From:** Wheelous, Teresa A  
**Sent:** Wednesday, June 16, 2010 10:44 AM  
**To:** Freed, Lois M  
**Subject:** FW: Namenda XR; ODE 1 - Tatiana; AP ltr w/ PMR

Lois,

You may be interested in this.

eresa

---

**From:** Safety Requirements Team  
**Sent:** Wednesday, June 16, 2010 9:36 AM  
**To:** Summers, Kelly; Ware, Jacqueline H; Yasuda, Sally; Wheelous, Teresa A; Hughes, Alice  
**Cc:** Safety Requirements Team; Honig, Susan L; Kashoki, Mwango; Lee, Cathryn; Oussova, Tatiana; Beitz, Julie G  
**Subject:** Namenda XR; ODE 1 - Tatiana; AP ltr w/ PMR

Hi Kelly,

We have questions for you in the draft letter in the eRoom. Please respond to the questions and then we'll take another look at the letter.

Basically, our question is whether there is one study or two? Will there be one study for Namenda and one for Namenda XR, or will there only be one study? If there is only one study, we may decide to leave the letter as originally written.

[http://eroom.fda.gov/eRoom/CDER/CDER-ONDIO/0\\_9f604](http://eroom.fda.gov/eRoom/CDER/CDER-ONDIO/0_9f604)

Thanks,  
Julie

---

**From:** Summers, Kelly  
**Sent:** Monday, June 14, 2010 2:07 PM  
**To:** Safety Requirements Team  
**Cc:** Ware, Jacqueline H; Yasuda, Sally; Wheelous, Teresa A  
**Subject:** Namenda XR AP ltr w/ PMR

Please find attached the approval letter with a PMR for NDA 22525, Namenda XR.

PDUFA date is 6/21/10 though we'd love to be able to act on it by Friday.

Many thanks,  
Kelly

LT Kelly Summers, PharmD, USPHS  
Safety Project Manager  
Division of Neurology Products  
OND / CDER / FDA  
White Oak Bldg 22, Room 4321  
301-796-5264 (Office)  
301-796-9842 (Fax)

## Wheelous, Teresa A

---

**From:** Chan, Irene Z.  
**nt:** Wednesday, June 16, 2010 10:19 AM  
**o:** Wheelous, Teresa A  
**Cc:** Mani, Ranjit B; Kozauer, Nicholas; Kelley, Laurie; Griffis, Melina  
**Subject:** Insert Labeling for Namenda XR NDA 022525

Hello Teresa,

I have had an opportunity to look at the revised insert labeling submitted by Forest Laboratories on June 15, 2010. The only comment I have is to consider adding a statement to the dosage and administration section of the "Highlights of Prescribing Information" similar to the following:

*Namenda XR capsules should be swallowed whole or opened and sprinkled on applesauce, then swallowed. The entire contents should be consumed. Namenda XR capsules should not be divided, crushed, or chewed.*

Thanks and have a great day.

Irene Z. Chan, Pharm.D., BCPS  
LCDR, U.S. Public Health Service  
Drug Safety Evaluator  
Division of Medication Error Prevention and Analysis  
Office of Surveillance and Epidemiology  
Center for Drug Evaluation and Research  
Food and Drug Administration

The Federal Research Center at White Oak  
903 New Hampshire Avenue  
Building 22, Rm. #4421 MS4447  
Silver Spring, Maryland 20993-0002  
[Irene.Chan2@fda.hhs.gov](mailto:Irene.Chan2@fda.hhs.gov)  
Office 301.796.3962  
Fax 301.796.9865

## Wheelous, Teresa A

---

**From:** Niebo, Michael [Michael.Niebo@frx.com]  
**Sent:** Tuesday, June 15, 2010 4:33 PM  
**To:** Wheelous, Teresa A  
**Subject:** RE: NDA 22525 Namenda XR; Carton & Container Labeling , Follow-Up to Labeling Discussions

**Attachments:** draft-labeling-text-tracked.doc; emfalert.txt



draft-labeling-te mfalert.txt (855  
xt-tracked.do... B)

Teresa-

Attached is the latest version of the PI label, with revisions as requested below. This label is being submitted via the electronic gateway this afternoon.

Thanks,

Michael P. Niebo, RAC

Asst. Director, Regulatory Affairs

Forest Research Institute

A Subsidiary of Forest Laboratories, Inc.

Harborside Financial Center

Plaza V, Suite 1900

Jersey City, NJ 07311

Office: 201-386-2046

Fax: 201-524-9711/9712

---

**From:** Wheelous, Teresa A [mailto:Teresa.Wheelous@fda.hhs.gov]

**Sent:** Friday, June 11, 2010 2:30 PM

**To:** Niebo, Michael

**Subject:** NDA 22525 Namenda XR; Carton & Container Labeling , Follow-Up to Labeling Discussions

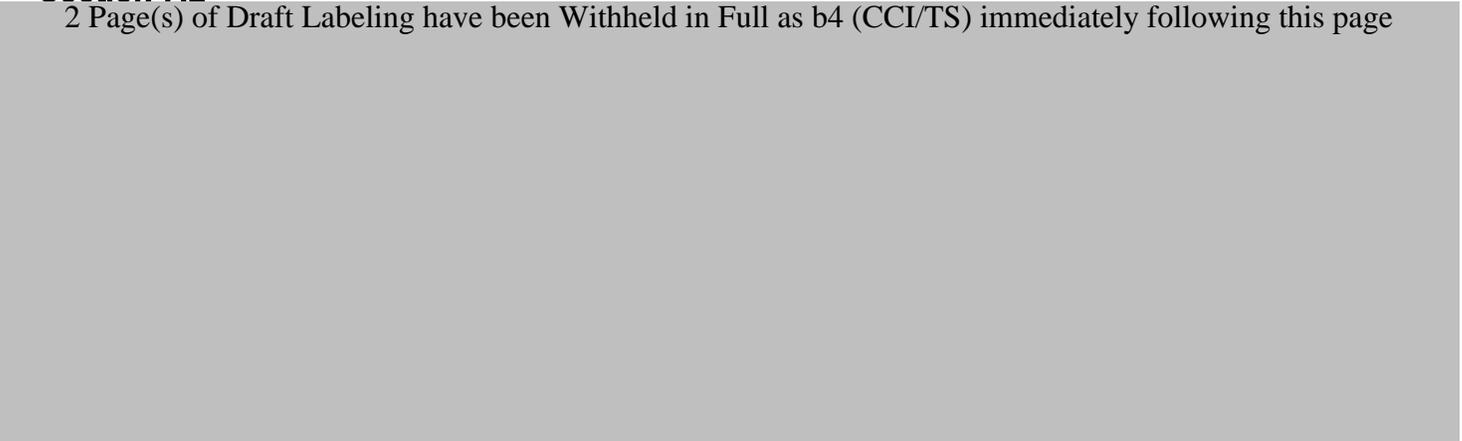
Michael,

The following are additional labeling revisions (that was not discussed this morning) and the Carton & Container labeling recommendations that were mentioned during our telecon:

## **ADDITIONAL LABELING REVISIONS**

### **Section 7.2**

2 Page(s) of Draft Labeling have been Withheld in Full as b4 (CCI/TS) immediately following this page



3. See comment E above.
4. See comment F(3) above.

## Wheelous, Teresa A

---

**From:** Niebo, Michael [Michael.Niebo@frx.com]  
**Sent:** Tuesday, June 15, 2010 4:29 PM  
**To:** Wheelous, Teresa A  
**Cc:** DeMartino, James  
**Subject:** RE: Labeling Discussion

**Attachments:** emfalert.txt



mfalert.txt (855  
B)

Teresa-

For the teleconference at 9am tomorrow, please use the following number: 201-427-8972.

Thanks,

Michael P. Niebo, RAC

Asst. Director, Regulatory Affairs

Forest Research Institute

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Plaza V, Suite 1900

Jersey City, NJ 07311

Office: 201-386-2046

Fax: 201-524-9711/9712

---

**From:** Wheelous, Teresa A [mailto:Teresa.Wheelous@fda.hhs.gov]

**Sent:** Monday, June 14, 2010 3:25 PM

**To:** Niebo, Michael

**Subject:** Labeling Discussion

Michael,

The Division would like to have a follow-up labeling discussion for Namenda XR. Specifically, we'd like to discuss the proposed Carton and Container labeling recommendations that were sent to you on Friday.

Please let me know if Wed, 6/16/10 at 9 AM is a good time for you.

Regards,

*CDR Teresa Wheelous, R. Ph.*  
*Sr. Program Management Officer Consultant*  
*FDA*  
*Division of Neurology*  
*10903 New Hampshire Avenue, Bldg. #22, Room 4344*  
*Silver Spring, MD 20993-0002*  
*(telephone) 301-796-1161*  
*(fax) 301-796-9842*

## **Wheelous, Teresa A**

---

**From:** ias@fdssa087  
**Sent:** Tuesday, June 15, 2010 12:35 PM  
**:** Mani, Ranjit B; Wheelous, Teresa A; CDER-DDMAC-RPM; Nighswander, Robbin M  
**Subject:** Finalized - NDA 22525 General Review (REV-CLINICAL-03)  
**Attachments:** NDA 22525 Review.pdf



NDA 22525  
Review.pdf (2 MB)

[http://darrts/images/new\\_DARRTS\\_Logo.jpg](http://darrts/images/new_DARRTS_Logo.jpg)

[Proceed to DARRTS Login](#)

(b) (4)

**Wheelous, Teresa A**

---

**From:** ias@fdssa088  
**Sent:** Tuesday, June 15, 2010 8:22 AM  
**To:** Freed, Lois M; Wheelous, Teresa A; Nighswander, Robbin M  
**Subject:** Finalized - NDA 22525 General Review (REV-NONCLINICAL-03)

**Attachments:** N22525 memo.pdf



N22525  
emo.pdf (22 KB)

[http://darrts/images/new\\_DARRTS\\_Logo.jpg](http://darrts/images/new_DARRTS_Logo.jpg)

[Proceed to DARRTS Login](#)

**Wheelous, Teresa A**

---

**From:** ias@fdssa088  
**Sent:** Tuesday, June 15, 2010 7:24 AM  
**To:** Mani, Ranjit B; Freed, Lois M; Hawver, David; Wheelous, Teresa A; Nighswander, Robbin M  
**Subject:** Finalized - NDA 22525 General Review (REV-NONCLINICAL-03)

**Attachments:** PharmTox Review of NDA 22-525 Memantine XR for AD.pdf



PharmTox  
w of NDA 22-52

[http://darrts/images/new\\_DARRTS\\_Logo.jpg](http://darrts/images/new_DARRTS_Logo.jpg)

[Proceed to DARRTS Login](#)

## Wheelous, Teresa A

---

**From:** Summers, Kelly  
**Sent:** Monday, June 14, 2010 2:07 PM  
**To:** Summers, Kelly; Safety Requirements Team  
**Cc:** Ware, Jacqueline H; Yasuda, Sally; Wheelous, Teresa A  
**Subject:** RE: Namenda XR AP ltr w/ PMR

**Attachments:** Namenda Approval with PMR 061110 JW.doc



Namenda  
Approval with PMR 06

Now attached!

---

**From:** Summers, Kelly  
**Sent:** Monday, June 14, 2010 2:07 PM  
**To:** Safety Requirements Team  
**Cc:** Ware, Jacqueline H; Yasuda, Sally; Wheelous, Teresa A  
**Subject:** Namenda XR AP ltr w/ PMR

Please find attached the approval letter with a PMR for NDA 22525, Namenda XR.

PDUFA date is 6/21/10 though we'd love to be able to act on it by Friday.

Many thanks,  
Kelly

Kelly Summers, PharmD, USPHS  
Safety Project Manager  
Division of Neurology Products  
OND / CDER / FDA  
White Oak Bldg 22, Room 4321  
301-796-5264 (Office)  
301-796-9842 (Fax)

## Wheelous, Teresa A

---

**From:** Wheelous, Teresa A  
**Sent:** Monday, June 14, 2010 1:59 PM  
**To:** Ware, Jacqueline H  
**Subject:** FW: NDA 22525 Namenda XR - Advisory Committee Statement

**Attachments:** FW: Language in AP letter for not going to Advisory Committee mtg

Jackie

The language for Namenda AC is in Colleen's email below.

Teresa

---

**From:** Locicero, Colleen L  
**Sent:** Friday, June 11, 2010 9:01 PM

**To:** Wheelous, Teresa A  
**Subject:** RE: NDA 22525 Namenda XR - Advisory Committee Statement

Teresa,

Please see the attached. I believe this is the most recent language. Per Kim's e-mail, no need to run it by her unless you plan to deviate from/add to the language. If you have any questions, let me know.

thanks,  
colleen



FW: Language  
in AP letter for ...

---

**From:** Wheelous, Teresa A  
**Sent:** Friday, June 11, 2010 3:59 PM  
**To:** Locicero, Colleen L  
**Subject:** NDA 22525 Namenda XR - Advisory Committee Statement

Colleen

I'm working on the action letter for Namenda XR, and I need your assistance with language in the Advisory Committee portion of the letter: This application did not go to an advisory committee.

(b) (4)

I have attached the a copy of the draft letter as it is today.

<< File: Approval with PMR 061110.doc >>

Thanks,

*CDR Teresa Wheelous, R. Ph.*  
*Sr. Program Management Officer Consultant*  
*FDA*  
*Division of Neurology*  
*10903 New Hampshire Avenue, Bldg. #22, Room 4344*  
*Silver Spring, MD 20993-0002*  
*(telephone) 301-796-1161*  
*(fax) 301-796-9842*

**Wheelous, Teresa A**

---

**From:** ias@fdssa088  
**nt:** Monday, June 14, 2010 1:17 PM  
**.o:** McLamore, Sherita; Sood, Ramesh; Heimann, Martha R; Wheelous, Teresa A; Bouie, Teshara  
**Subject:** Finalized - NDA 22525 Memorandum to File (FRM-ADMIN-01)  
**Attachments:** NDA 22-525 Compliance Memo.pdf



NDA 22-525  
pliance Memo.pdf

[http://darrts/images/new\\_DARRTS\\_Logo.jpg](http://darrts/images/new_DARRTS_Logo.jpg)

[Proceed to DARRTS Login](#)

(b) (4)

**Wheelous, Teresa A**

---

**From:** Locicero, Colleen L  
**Sent:** Friday, June 11, 2010 9:01 PM  
**To:** Wheelous, Teresa A  
**Subject:** RE: NDA 22525 Namenda XR - Advisory Committee Statement

**Attachments:** FW: Language in AP letter for not going to Advisory Committee mtg

Teresa,

Please see the attached. I believe this is the most recent language. Per Kim's e-mail, no need to run it by her unless you plan to deviate from/add to the language. If you have any questions, let me know.

thanks,  
colleen



FW: Language  
n AP letter for ...

---

**From:** Wheelous, Teresa A  
**Sent:** Friday, June 11, 2010 3:59 PM  
**To:** Locicero, Colleen L  
**Subject:** NDA 22525 Namenda XR - Advisory Committee Statement

Colleen

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I have attached the a copy of the draft letter as it is today.

<< File: Approval with PMR 061110.doc >>

Thanks,

*CDR Teresa Wheelous, R. Ph.  
Sr. Program Management Officer Consultant  
FDA  
Division of Neurology  
10903 New Hampshire Avenue, Bldg. #22, Room 4344  
Silver Spring, MD 20993-0002  
(telephone) 301-796-1161  
(fax) 301-796-9842*

**Wheelous, Teresa A**

---

**From:** Wheelous, Teresa A  
**nt:** Friday, June 11, 2010 2:30 PM  
**o:** 'Niebo, Michael'  
**Subject:** NDA 22525 Namenda XR; Carton & Container Labeling , Follow-Up to Labeling Discussions

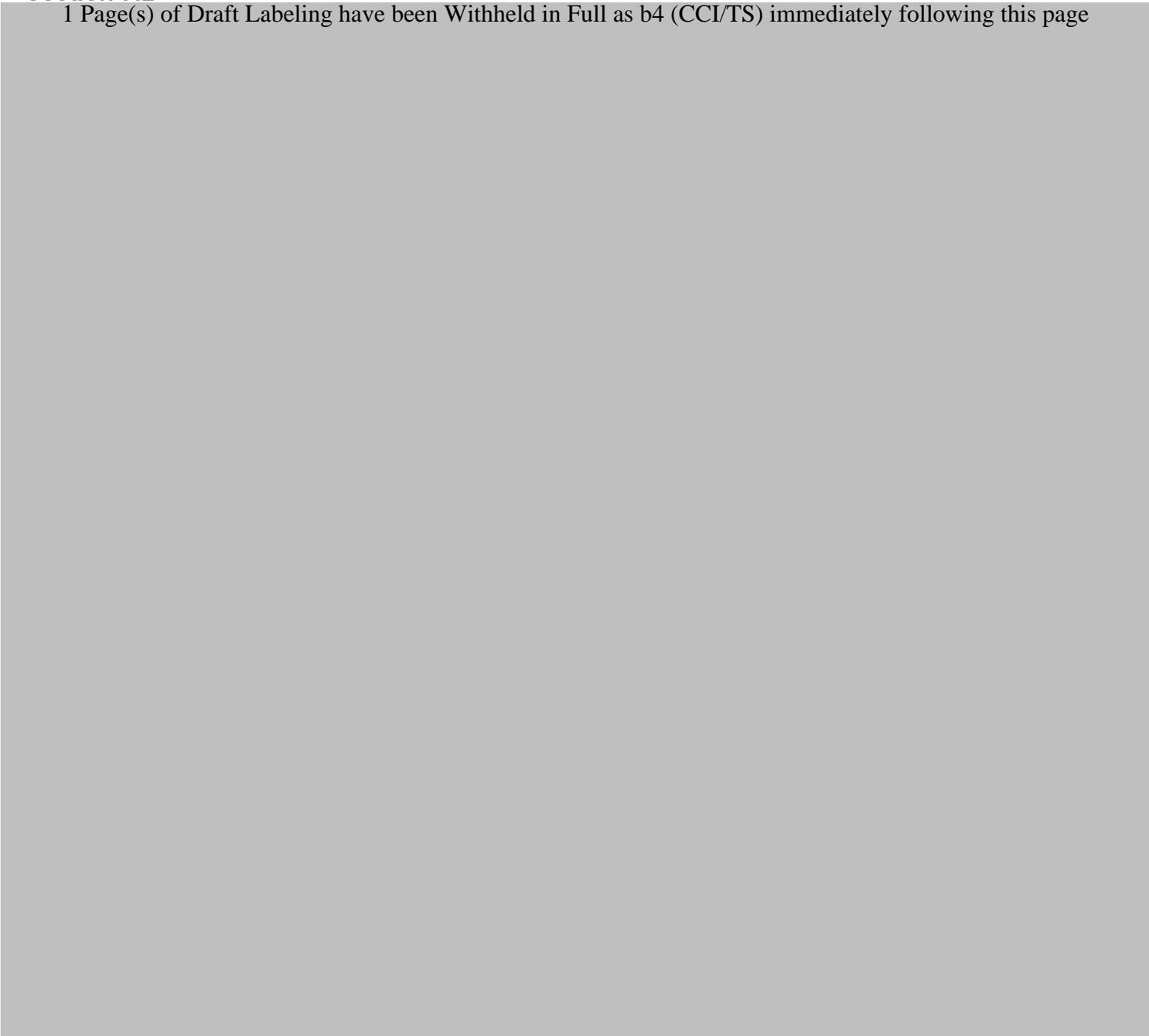
Michael,

The following are additional labeling revisions (that was not discussed this morning) and the Carton & Container labeling recommendations that were mentioned during our telecon:

**ADDITIONAL LABELING REVISIONS**

**Section 7.2**

1 Page(s) of Draft Labeling have been Withheld in Full as b4 (CCI/TS) immediately following this page



**Wheelous, Teresa A**

---

**From:** Niebo, Michael [Michael.Niebo@frx.com]  
**Sent:** Friday, June 11, 2010 12:19 PM  
**To:** Wheelous, Teresa A  
**Subject:** RE: NDA 22525 Namenda Labeling & Tox study dates

**Attachments:** draft-labeling-text-tracked.doc; emfalert.txt



draft-labeling-te mfalert.txt (855  
xt-tracked.do... B)

Teresa-

Below are the proposed dates for single-dose neurotoxicity study timeline, as requested:

Protocol Submission: July 30, 2010

Study End: June 15, 2011

Final Report Submission: December 15, 2011

I've also attached the label as agreed upon this morning. This label has also been formally submitted to the NDA via the electronic gateway this morning.

Please let me know if you have any questions or need any additional information.

Thanks,

Michael P. Niebo, RAC

Asst. Director, Regulatory Affairs

Forest Research Institute

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Harborside Financial Center

Plaza V, Suite 1900

Jersey City, NJ 07311

Office: 201-386-2046

Fax: 201-524-9711/9712

---

**From:** Wheelous, Teresa A [mailto:Teresa.Wheelous@fda.hhs.gov]  
**Sent:** Friday, June 11, 2010 8:32 AM  
**To:** Niebo, Michael  
**Subject:** RE: NDA 22525 Namenda Labeling

Michael,

I'll forward the info to the team.

Thanks,

Teresa

---

**From:** Niebo, Michael [mailto:Michael.Niebo@frx.com]  
**Sent:** Friday, June 11, 2010 8:27 AM  
**To:** Wheelous, Teresa A  
**Subject:** RE: NDA 22525 Namenda Labeling

Teresa-

Forest has decided to go along with the Agency's original revision to delete Section 14.3.2. See revised label attached.

Thanks,

Michael P. Niebo, RAC

Asst. Director, Regulatory Affairs

Forest Research Institute

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Harborside Financial Center

Plaza V, Suite 1900

Jersey City, NJ 07311

Office: 201-386-2046

Fax: 201-524-9711/9712

---

**From:** Wheelous, Teresa A [mailto:Teresa.Wheelous@fda.hhs.gov]  
**Sent:** Thursday, June 10, 2010 5:41 PM  
**To:** Niebo, Michael  
**Subject:** RE: NDA 22525 Namenda Labeling

Thank you

---

**From:** Niebo, Michael [mailto:Michael.Niebo@frx.com]  
**Sent:** Thursday, June 10, 2010 5:28 PM  
**To:** Wheelous, Teresa A  
**Subject:** RE: NDA 22525 Namenda Labeling

Teresa-

Attached are the draft revised label and the draft cover letter for the submission. The only item that Forest is pending verification is the revision from (b) (4) to "3.2 units" in Section 14.3.2. Forest will make every effort to have this value verified before 9am so that we can discuss during the 9am-10am timeslot if necessary.

Thanks,

Michael P. Niebo, RAC

Asst. Director, Regulatory Affairs

Forest Research Institute

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Harborside Financial Center

Plaza V, Suite 1900

Jersey City, NJ 07311

Office: 201-386-2046

Fax: 201-524-9711/9712

---

**From:** Wheelous, Teresa A [mailto:Teresa.Wheelous@fda.hhs.gov]  
**Sent:** Thursday, June 10, 2010 5:14 PM  
**To:** Niebo, Michael  
**Subject:** RE: NDA 22525 Namenda Labeling

Michael,

If possible, the relevant reviewers will meet at 9 AM to go over your revised labeling. If there are minor issues then we may call you sometime between 9 AM -10 AM. If the review team is not able to review the revised labeling by 9 AM on Friday, then we will meet at 3 PM. If needed we will contact you sometime between 3 PM - 4PM.

Teresa

---

**From:** Niebo, Michael [mailto:Michael.Niebo@frx.com]  
**Sent:** Thursday, June 10, 2010 5:09 PM  
**To:** Wheelous, Teresa A; DeMartino, James  
**Subject:** RE: NDA 22525 Namenda Labeling

Teresa-

I have received the label, and we do have some minor comments/revisions, mainly pertaining to sections 7.2, 7.7, 13 and 14.3.2. The revised label will be ready first thing tomorrow (Friday) morning. I'm not sure if the revisions require negotiation via teleconference or not; I can leave that to your discretion. Approximately what time of the day have you set aside for discussion?

Thanks,

Michael P. Niebo, RAC

Asst. Director, Regulatory Affairs

Forest Research Institute

A Subsidiary of Forest Laboratories, Inc.

Harborside Financial Center

Plaza V, Suite 1900

Jersey City, NJ 07311

Office: 201-386-2046

Fax: 201-524-9711/9712

---

**From:** Wheelous, Teresa A [mailto:Teresa.Wheelous@fda.hhs.gov]  
**Sent:** Thursday, June 10, 2010 4:48 PM  
**To:** DeMartino, James; Niebo, Michael  
**Subject:** NDA 22525 Namenda Labeling

James and Michael,

Please acknowledge receipt of labeling for Namenda XR NDA 22525 that was sent yesterday. Also, let me know if there are changes to labeling that require negotiation. I have scheduled some time for discussion on Friday, if we needed.

Thank you,

Teresa

## Wheelous, Teresa A

---

**From:** Mani, Ranjit B  
**nt:** Friday, June 11, 2010 11:59 AM  
**o:** Wheelous, Teresa A  
**Cc:** Mani, Ranjit B  
**Subject:** NDA 22525; Namenda XR; Draft Review (FOR RUSTY)  
**Attachments:** NDA 22525 Review DRAFT.doc

Teresa,

My draft review is attached. Please include it in the package for Rusty.

Ranjit



NDA 22525  
ew DRAFT.doc (2)

## Wheelous, Teresa A

---

**From:** Niebo, Michael [Michael.Niebo@frx.com]  
**Sent:** Friday, June 11, 2010 8:27 AM  
**To:** Wheelous, Teresa A  
**Subject:** RE: NDA 22525 Namenda Labeling  
**Attachments:** draft-labeling-text-tracked 6.11.10.doc; emfalert.txt



draft-labeling-te mfalert.txt (855  
xt-tracked 6.... B)

Teresa-

Forest has decided to go along with the Agency's original revision to delete Section 14.3.2. See revised label attached.

Thanks,

Michael P. Niebo, RAC

Asst. Director, Regulatory Affairs

Forest Research Institute

A Subsidiary of Forest Laboratories, Inc.

Harborside Financial Center

aza V, Suite 1900

Jersey City, NJ 07311

Office: 201-386-2046

Fax: 201-524-9711/9712

---

**From:** Wheelous, Teresa A [mailto:Teresa.Wheelous@fda.hhs.gov]  
**Sent:** Thursday, June 10, 2010 5:41 PM  
**To:** Niebo, Michael  
**Subject:** RE: NDA 22525 Namenda Labeling

Thank you

---

**From:** Niebo, Michael [mailto:Michael.Niebo@frx.com]  
**Sent:** Thursday, June 10, 2010 5:28 PM  
**To:** Wheelous, Teresa A  
**Subject:** RE: NDA 22525 Namenda Labeling

Teresa-

Attached are the draft revised label and the draft cover letter for the submission. The only item that Forest is pending verification is the revision from (b)(4) to "3.2 units" in Section 14.3.2. Forest will make every effort to have this value verified before 9am so that we can discuss during the 9am-10am timeslot if necessary.

Thanks,

Michael P. Niebo, RAC

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Jersey City, NJ 07311

Office: 201-386-2046

Fax: 201-524-9711/9712

---

**From:** Wheelous, Teresa A [mailto:Teresa.Wheelous@fda.hhs.gov]  
**Sent:** Thursday, June 10, 2010 5:14 PM  
**To:** Niebo, Michael  
**Subject:** RE: NDA 22525 Namenda Labeling

Michael,

If possible, the relevant reviewers will meet at 9 AM to go over your revised labeling. If there are minor issues then we may call you sometime between 9 AM -10 AM. If the review team is not able to review the revised labeling by 9 AM on Friday, then we will meet at 3 PM. If needed we will contact you sometime between 3 PM - 4PM.

Teresa

---

**From:** Niebo, Michael [mailto:Michael.Niebo@frx.com]  
**Sent:** Thursday, June 10, 2010 5:09 PM  
**To:** Wheelous, Teresa A; DeMartino, James  
**Subject:** RE: NDA 22525 Namenda Labeling

Teresa-

I have received the label, and we do have some minor comments/revisions, mainly pertaining to sections 7.2, 7.7, 13 and 14.3.2. The revised label will be ready first thing tomorrow (Friday) morning. I'm not sure if the revisions require negotiation via teleconference or not; I can leave that to your discretion. Approximately what time of the day have you set aside for discussion?

Thanks,

Michael P. Niebo, RAC

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Fax: 201-524-9711/9712

---

**From:** Wheelous, Teresa A [mailto:Teresa.Wheelous@fda.hhs.gov]

**Sent:** Thursday, June 10, 2010 4:48 PM

**To:** DeMartino, James; Niebo, Michael

**Subject:** NDA 22525 Namenda Labeling

James and Michael,

Please acknowledge receipt of labeling for Namenda XR NDA 22525 that was sent yesterday. Also, let me know if there are changes to labeling that require negotiation. I have scheduled some time for discussion on Friday, if we needed.

Thank you,

Teresa

## Wheelous, Teresa A

---

**From:** Niebo, Michael [Michael.Niebo@frx.com]  
**Sent:** Thursday, June 10, 2010 5:28 PM  
**To:** Wheelous, Teresa A  
**Subject:** RE: NDA 22525 Namenda Labeling

**Attachments:** draft-labeling-text-tracked.doc; 1 2 Cover letter 6.11.2010.doc; emfalert.txt



draft-labeling-te 1 2 Cover letter malert.txt (855  
xt-tracked.do... 6.11.2010.doc... B)

Teresa-

Attached are the draft revised label and the draft cover letter for the submission. The only item that Forest is pending verification is the revision from (b) (4) to "3.2 units" in Section 14.3.2. Forest will make every effort to have this value verified before 9am so that we can discuss during the 9am-10am timeslot if necessary.

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**Sent:** Thursday, June 10, 2010 5:09 PM  
**To:** Wheelous, Teresa A; DeMartino, James  
**Subject:** RE: NDA 22525 Namenda Labeling

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Office: 201-386-2046

Fax: 201-524-9711/9712

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**To:** DeMartino, James; Niebo, Michael  
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---

#### Wheelous, Teresa A

**From:** Niebo, Michael [Michael.Niebo@frx.com]  
**Sent:** Thursday, June 10, 2010 5:09 PM  
**To:** Wheelous, Teresa A; DeMartino, James  
**Subject:** RE: NDA 22525 Namenda Labeling

**Attachments:** emfalert.txt



mfalert.txt (795  
B)

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Michael P. Niebo, RAC

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Fax: 201-524-9711/9712

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**To:** DeMartino, James; Niebo, Michael  
**Subject:** NDA 22525 Namenda Labeling

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**Sent:** Thursday, June 10, 2010 5:09 PM  
**To:** Wheelous, Teresa A; DeMartino, James  
**Subject:** RE: NDA 22525 Namenda Labeling

**Attachments:** emfalert.txt



mfalert.txt (795  
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Michael P. Niebo, RAC

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**Subject:** NDA 22525 Namenda Labeling

James and Michael,

Please acknowledge receipt of labeling for Namenda XR NDA 22525 that was sent yesterday. Also, let me know if there are changes to labeling that require negotiation. I have scheduled some time for discussion on Friday, if we needed.

Thank you,

Teresa

## Wheelous, Teresa A

---

**From:** Beitzell, Debra  
**nt:** Thursday, June 10, 2010 1:30 PM  
**o:** Wheelous, Teresa A  
**Subject:** RE: NDA 22-525 (Namenda)

Teresa,

I am off tomorrow and at DIA next week (Mon-Wed.); therefore, at this point, a SEALD review may not be possible. If you do move toward approval, I could do a quick PLR check for HL on 6/17 (next Thursday) if you would like.

Debbie

---

**From:** Wheelous, Teresa A  
**Sent:** Thursday, June 10, 2010 12:38 PM  
**To:** Beitzell, Debra  
**Subject:** RE: NDA 22-525 (Namenda)

Debra,

We have not issued a letter yet, but I expect the letter to issue on 6/21/09. At this point the final action decision has not been made.

Teresa

---

**From:** Beitzell, Debra  
**Sent:** Thursday, June 10, 2010 12:11 PM  
**To:** Wheelous, Teresa A  
**Subject:** RE: NDA 22-525 (Namenda)

Hi Teresa,

Has a decision been reached on this application? Will a CR letter be issuing?

Debbie

---

**From:** Wheelous, Teresa A  
**Sent:** Thursday, May 20, 2010 3:23 PM  
**To:** Beitzell, Debra  
**Subject:** RE: NDA 22-525 (Namenda)

Debbie,

There has been no movement on this application. The clinical reviewer is still working on his review.

Teresa

---

**From:** Beitzell, Debra  
**Sent:** Thursday, May 20, 2010 11:57 AM  
**To:** Wheelous, Teresa A  
**Subject:** FW: NDA 22-525 (Namenda)

Hi Teresa,

Could you please give me an update on the status of the Namenda labeling.

Thanks, Debbie

---

**From:** Beitzell, Debra  
**Sent:** Wednesday, March 24, 2010 2:08 PM  
**To:** Wheelous, Teresa A  
**Subject:** RE: NDA 22-525 (Namenda)

Thanks for the update. Please send me a marked-up label once the team has finished editing. Please allow SEALD 5 working days to complete the review.

Thanks, Debbie

---

**From:** Wheelous, Teresa A  
**Sent:** Wednesday, March 24, 2010 9:59 AM  
**To:** Beitzell, Debra  
**Subject:** RE: NDA 22-525 (Namenda)

Debra,

I wanted to let you know that the Division has decided to act on this application NDA 22525 earlier than the PDUFA goal date. We are targeting May 28, 2010 as the action date. Also, the sponsor has submitted a revised labeling in an electronic submission dated 12/17/10.

The Division has not yet worked on labeling so I guess that the Division will not have labeling until early May.

Regards,

Teresa

---

**From:** Beitzell, Debra  
**Sent:** Wednesday, December 16, 2009 10:23 AM  
**To:** Wheelous, Teresa A  
**Subject:** NDA 22-525 (Namenda)

Hello,

I am the PLR content reviewer from SEALD (labeling team) that has been assigned to the Namenda XR application that is due on June 21, 2010. SEALD conducts content reviews **AFTER** the division review team completes their initial draft review **BUT BEFORE** labeling content comments are sent to the applicant. Could you please send me the most recent version of the marked-up label (Highlights, Contents, and FPI) once your team has finished editing? A MS word file is preferable.

Also, do you have an estimate as to when you might take an action on this application and what type of action you will be taking? If you are planning to take a CR action, we will wait until the next review cycle to complete our review, unless you plan on conducting labeling negotiations with the firm this cycle.

Thanks in advance for your time and help.

Debbie Beitzell  
Labeling Reviewer  
SEALD/OND/CDER

## Wheelous, Teresa A

---

**From:** Mani, Ranjit B  
**Content:** Tuesday, June 08, 2010 1:03 PM  
**To:** Katz, Russell G  
**Cc:** Wheelous, Teresa A; Mani, Ranjit B; Kozauer, Nicholas  
**Subject:** NDA 22525; Namenda XR; Draft Labeling

**Attachments:** NDA 22525 Editing Labeling.doc; NDA 22525 Labeling Review (Extracted).doc

Rusty,

Based on our conversation earlier today, I am attaching the following.

1. Draft labeling for Namenda XR. The changes that I have made to the base document submitted by the sponsor incorporate my own recommendations as well as those from other reviewers.
2. A separate document extracted from my review which explains in part the changes that I have made to the labeling.

I will be leaving printed copies of both documents under your door.

Ranjit



NDA 22525      NDA 22525  
ting Labeling.doc      eling Review (Ex

## Wheelous, Teresa A

---

**From:** Summers, Kelly  
**Sent:** Tuesday, June 08, 2010 11:52 AM  
**To:** Wheelous, Teresa A  
**Cc:** Yasuda, Sally  
**Subject:** RE: NDA 22525 Namenda XR - PMC or PMR template request

**Attachments:** PMR-PMC Development Template.doc; New and post Approval PMR mult and single Template (Revised 3.31.09).doc

Teresa,

Sorry just getting back into the office! Attached are the latest letter and justification templates for PMRs. You're right, they aren't in CST as of now, you have to get the most recent templates from me.

Kelly



PMR-PMC      New and post  
opment Templat proval PMR mult

---

**From:** Wheelous, Teresa A  
**Sent:** Tuesday, June 01, 2010 4:39 PM  
**To:** Summers, Kelly  
**Subject:** NDA 22525 Namenda XR - PMC or PMR template request

Kelly,

The review team for NDA 22525 Namenda XR has decided that a post marketing commitment or requirement (not sure which) for a nonclinical animal study is needed. I spoke with Sally and she requested a completed template. Do you have a copy of the recent SRT template or should I check the CST forms?

Thanks,

Teresa

## Wheelous, Teresa A

---

**From:** Niebo, Michael [Michael.Niebo@frx.com]  
**Sent:** Thursday, June 03, 2010 4:11 PM  
**To:** Wheelous, Teresa A  
**Cc:** DeMartino, James  
**Subject:** Namenda XR NDA 22-525

**Attachments:** emfalert.txt



mfalert.txt (952  
B)

Teresa-

As a follow-up to my voicemail this afternoon, I am providing James DeMartino's contact information in case you need to contact Forest regarding NDA 22-525 for Namenda XR during my absence (June 4 and 7). I will be returning to the office on Tuesday June 8.

James L. DeMartino, PhD  
Sr. Director, Regulatory Affairs  
Forest Research Institute  
Harborside Financial Center, Plaza 5  
24th Fl, Room 56  
Jersey City, NJ 07311

tel (201) 386-2131  
cell (917) 692-6456  
fax (201) 524-9711/9712

[james.demartino@frx.com](mailto:james.demartino@frx.com)

Thanks,

Michael P. Niebo, RAC

Asst. Director, Regulatory Affairs

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1200 Broad Street, Suite 1900

Jersey City, NJ 07311

Office: 201-386-2046

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---

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**Wheelous, Teresa A**

---

**From:** Nighswander, Robbin M  
**Sent:** Tuesday, May 25, 2010 11:01 AM  
**To:** Wheelous, Teresa A  
**Subject:** FW: Finalized - NDA 22525 General Review (REV-QUALITY-03)

**Attachments:** NDA 22-525 review2.pdf



NDA 22-525  
review2.pdf (112 KB)

---

**From:** ias@fdssa087 [mailto:ias@fdssa087]  
**Sent:** Tuesday, May 25, 2010 10:58 AM  
**To:** McLamore, Sherita; Sood, Ramesh; Nighswander, Robbin M  
**Subject:** Finalized - NDA 22525 General Review (REV-QUALITY-03)

[http://darrts/images/new\\_DARRTS\\_Logo.jpg](http://darrts/images/new_DARRTS_Logo.jpg)

[Proceed to DARRTS Login](#)



## Wheelous, Teresa A

---

**From:** Nighswander, Robbin M  
**nt:** Friday, May 07, 2010 12:08 PM  
**o:** Wheelous, Teresa A  
**Subject:** FW: Finalized - NDA 22525 General Review (REV-BIOMETRICS-01)

**Attachments:** NDA 22-525 Memantine Final.pdf



NDA 22-525  
mantine Final.pdf  
fyi

---

**From:** ias@fdssa088 [mailto:ias@fdssa088]  
**Sent:** Friday, May 07, 2010 10:48 AM  
**To:** Jin, Kun; Mahjoob, Kooros; Katz, Russell G; Mani, Ranjit B; Patrician, Lillian; Luan, Jingyu (Julia); Bastings, Eric; Nighswander, Robbin M; Hung, Hsien Ming J  
**Subject:** Finalized - NDA 22525 General Review (REV-BIOMETRICS-01)

[http://darrts/images/new\\_DARRTS\\_Logo.jpg](http://darrts/images/new_DARRTS_Logo.jpg)

[Proceed to DARRTS Login](#)

(b) (4)

**Wheelous, Teresa A**

---

**From:** ias@fdssa087  
**Sent:** Friday, May 07, 2010 10:11 AM  
**To:** Mulinde, Jean; Mani, Ranjit B; Wheelous, Teresa A; El Hage, Antoine N; Peacock, Joseph; Walters, Dana L; Nighswander, Robbin M  
**Subject:** Finalized - NDA 22525 Clinical Inspection Summary (CONSULT REV-DSI-02)  
**Attachments:** AEH.jm cis22-525,10.pdf



AEH.jm  
-525,10.pdf (34

[http://darrts/images/new\\_DARRTS\\_Logo.jpg](http://darrts/images/new_DARRTS_Logo.jpg)

[Proceed to DARRTS Login](#)

**Wheelous, Teresa A**

---

**From:** ias@fdssa087  
**Sent:** Monday, May 03, 2010 3:50 PM  
**To:** Uppoor, Ramana S; Katz, Russell G; Mani, Ranjit B; Wang, Yaning; Zhu, Hao; Wheelous, Teresa A; Bastings, Eric; Mehta, Mehul U; Baweja, Raman K; Zhang, Huixia; Nighswander, Robbin M  
**Subject:** Finalized - NDA 22525 General Review (REV-CLINPHARM-01)  
**Attachments:** 05032010 final \_ Namenda XR NDA22525\_Review.pdf



5032010 final \_  
amenda XR ND..

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[Proceed to DARRTS Login](#)

**Wheelous, Teresa A**

---

**From:** ias@fdssa088  
**Sent:** Tuesday, April 27, 2010 12:56 PM  
**To:** Kelley, Laurie; Katz, Russell G; CDER OSE CONSULTS; Chan, Irene Z.; Wheelous, Teresa A; Holquist, Carol A; Griffis, Melina; Toyer, Denise P; Jenkins, Darrell  
**Subject:** Finalized - NDA 22525 Proprietary Name Review (REV-EPIPOSTMKT-10)  
**Attachments:** 2010-453 Namenda XR Name Review.pdf



2010-453  
nda XR Name Re

[http://darrts/images/new\\_DARRTS\\_Logo.jpg](http://darrts/images/new_DARRTS_Logo.jpg)

[Proceed to DARRTS Login](#)

**Wheelous, Teresa A**

---

**From:** Nighswander, Robbin M  
**Sent:** Wednesday, April 21, 2010 1:05 PM  
**To:** Wheelous, Teresa A  
**Subject:** FW: Finalized - NDA 22525 Review Noted (NAI) (REV-CLINICAL-04)

**Attachments:** Communication2770320.pdf



Communication2  
0320.pdf (6 KB.

FYI

---

**From:** ias@fdssa088 [mailto:ias@fdssa088]  
**Sent:** Wednesday, April 21, 2010 12:59 PM  
**To:** Mani, Ranjit B; Nighswander, Robbin M  
**Subject:** Finalized - NDA 22525 Review Noted (NAI) (REV-CLINICAL-04)

[http://darrts/images/new\\_DARRTS\\_Logo.jpg](http://darrts/images/new_DARRTS_Logo.jpg)

[Proceed to DARRTS Login](#)



(b) (4)

## Wheelous, Teresa A

---

**From:** Nighswander, Robbin M  
**nt:** Wednesday, April 14, 2010 5:00 PM  
**o:** Wheelous, Teresa A  
**Subject:** FW: Finalized - NDA 22525 Information Request (COR-NDAIR-01)

**Attachments:** NDA 22-525 IR letter #3.pdf



NDA 22-525 IR  
etter #3.pdf (2...

[more...](#)

---

**From:** ias@fdssa087 [mailto:ias@fdssa087]  
**Sent:** Wednesday, April 14, 2010 3:38 PM  
**To:** McLamore, Sherita; Henry, Don; Sood, Ramesh; Heimann, Martha R; Nighswander, Robbin M  
**Subject:** Finalized - NDA 22525 Information Request (COR-NDAIR-01)

[http://darrts/images/new\\_DARRTS\\_Logo.jpg](http://darrts/images/new_DARRTS_Logo.jpg)

[Proceed to DARRTS Login](#)

(b) (4)

**Wheelous, Teresa A**

---

**From:** Nighswander, Robbin M  
**Sent:** Wednesday, April 14, 2010 10:36 AM  
**To:** Wheelous, Teresa A  
**Subject:** FW: Finalized - NDA 22525 General Review (REV-QUALITY-03)  
**Attachments:** NDA 22-525.pdf



NDA 22-525.pdf  
(2 MB)

Teresa... yet another one that is not being cc'd to you.

Robbin

---

**From:** ias@fdssa087 [mailto:ias@fdssa087]  
**Sent:** Wednesday, April 14, 2010 9:42 AM  
**To:** McLamore, Sherita; Heimann, Martha R; Nighswander, Robbin M  
**Subject:** Finalized - NDA 22525 General Review (REV-QUALITY-03)

[http://darrts/images/new\\_DARRTS\\_Logo.jpg](http://darrts/images/new_DARRTS_Logo.jpg)

[Proceed to DARRTS Login](#)

**Wheelous, Teresa A**

---

**From:** Wheelous, Teresa A  
**Sent:** Thursday, April 08, 2010 12:13 PM  
**To:** 'Niebo, Michael'  
**Subject:** NDA 22525 Namenda XR Statistical Info Request

**Attachments:** 040810 ReqForInfo #3.pdf



040810  
orInfo #3.pdf (6

Michael,

The following and the attached is a clinical / statistical request for info for Namenda XR:

Section 11.4.1.5.4 of the study report for MEM-MD-50 contained in your submission, you include a table that displays similar differences between US and non-US centers on the SIB analysis, while noting the lack of a statistically significant treatment group-by-country interaction for the change from

baseline in SIB.

**Question**

Do you have an explanation for the inter-country differences in effect of treatment on the Severe Impairment Battery displayed in Agency Figure 2 above?

Regards,

Teresa

**Wheelous, Teresa A**

---

**From:** Suarez, Sandra  
**Sent:** Wednesday, April 07, 2010 8:36 AM  
**To:** Wheelous, Teresa A  
**Subject:** NEW version: Biopharm slides for NDA 22-525 WU Meeting

**Attachments:** Biopharm\_namenda\_WU.ppt



Biopharm\_name  
\_WU.ppt (401 K)

---

**From:** Suarez, Sandra  
**Sent:** Tuesday, April 06, 2010 2:22 PM  
**To:** Wheelous, Teresa A  
**Cc:** Marroum, Patrick J; Dorantes, Angelica  
**Subject:** Biopharm slides for NDA 22-525 WU Meeting

Hi Theresa,  
Please find attached the slides for tomorrow's WU meeting.

Thanks.  
Sandra

<< File: Biopharm\_namenda\_WU.ppt >>

## Wheelous, Teresa A

---

**From:** Zhang, Huixia  
**Sent:** Tuesday, April 06, 2010 3:28 PM  
**To:** Wheelous, Teresa A  
**Cc:** Baweja, Raman K  
**Subject:** Slide for tomorrow's meeting (NDA22-525)

**Attachments:** standard curve preparation procedure.ppt

Hi Teresa,

We have a slide (pls see attachment below) that we'd like to share with everybody in tomorrow's meeting. Wondering if you could pls save it on your laptop and bring it to the meeting tomorrow?

Thanks a lot,  
Huixia



standard curve  
preparation proce..

## Wheelous, Teresa A

---

**From:** Suarez, Sandra  
**Sent:** Tuesday, April 06, 2010 2:22 PM  
**To:** Wheelous, Teresa A  
**Cc:** Marroum, Patrick J; Dorantes, Angelica  
**Subject:** Biopharm slides for NDA 22-525 WU Meeting

**Attachments:** Biopharm\_namenda\_WU.ppt

Hi Theresa,  
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Thanks.  
Sandra



Biopharm\_name  
\_WU.ppt (474 K)

## Wheelous, Teresa A

---

**From:** Nighswander, Robbin M  
**nt:** Tuesday, April 06, 2010 1:56 PM  
**o:** Wheelous, Teresa A  
**Cc:** Ware, Jacqueline H  
**Subject:** FW: Finalized - NDA 22525 Information Request (COR-NDAIR-01)

**Attachments:** NDA 22-525 IR letter #2.pdf



NDA 22-525 IR  
etter #2.pdf (2...

Teresa:

Interesting.. as you are listed as the PM in DARRTS for this application.

I'm not sure now why you are not on the automatic cc: lists.

Jackie: Are you aware of this phenomena where the PM is not automatically copied but is the PM of record?

---

**From:** ias@fdssa087 [mailto:ias@fdssa087]

**Sent:** Tuesday, April 06, 2010 10:22 AM

**To:** McLamore, Sherita; Henry, Don; Marroum, Patrick J; Heimann, Martha R; Suarez, Sandra; Dorantes, Angelica; Nighswander, Robbin M

**Subject:** Finalized - NDA 22525 Information Request (COR-NDAIR-01)

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[Proceed to DARRTS Login](#)

(b) (4)

**Wheelous, Teresa A**

---

**From:** Nighswander, Robbin M  
**Sent:** Tuesday, April 06, 2010 1:53 PM  
**To:** Wheelous, Teresa A  
**Subject:** FW: Finalized - NDA 22525 Information Request (COR-NDAIR-01)

**Attachments:** NDA 22-525 IR letter #2.pdf



NDA 22-525 IR  
letter #2.pdf (2...

Teresa:

FYI

I'm wondering whether or not you are listed as the PM for this in DARRTS as you don't seem to be getting any of the emails for this.

I'll check.

Robbin

---

**From:** ias@fdssa087 [mailto:ias@fdssa087]  
**Sent:** Tuesday, April 06, 2010 10:22 AM  
**To:** McLamore, Sherita; Henry, Don; Marroum, Patrick J; Heimann, Martha R; Suarez, Sandra; Dorantes, Angelica; Nighswander, Robbin M  
**Subject:** Finalized - NDA 22525 Information Request (COR-NDAIR-01)

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(b) (4)



**Wheelous, Teresa A**

---

**From:** Wheelous, Teresa A  
**Sent:** Monday, April 05, 2010 2:49 PM  
**To:** 'Niebo, Michael'  
**Subject:** NDA 22525 Namenda XR Info Request

Michael,

The following is an info request from the medical reviewer:

**NDA 22525**  
**Namenda® XR**  
**Forest Laboratories**  
**Request For Information: Final Protocol For Study MEM-MD-50**

Please submit the final complete version of the study protocol for MEM-MD-50. This version should incorporate all amendments.

Regards,

*CDR Teresa Wheelous, R. Ph.*  
*Sr. Program Management Officer Consultant*  
*FDA*  
*Division of Neurology*  
*1903 New Hampshire Avenue, Bldg. #22, Room 4344*  
*Silver Spring, MD 20993-0002*  
*(telephone) 301-796-1161*  
*(fax) 301-796-9842*

**Wheelous, Teresa A**

---

**From:** Mani, Ranjit B  
**Sent:** Monday, April 05, 2010 2:45 PM  
**To:** Wheelous, Teresa A  
**Subject:** FW: Finalized - NDA 22525 General Review (REV-QUALITY-03)

**Attachments:** NDA22525\_namenda\_final.pdf



NDA22525\_namenda\_final.pdf (44.

Teresa,

We have a "wrap-up" meeting for this application scheduled for April 7; we can discuss it then. Could you also forward this to the Clinical Pharmacology team leader (I think it is still Ray Baweja and not Angela) and primary reviewer (I am not sure who it is from list for the April 7 meeting)?

Ranjit

---

**From:** Wheelous, Teresa A  
**Sent:** Monday, April 05, 2010 2:38 PM  
**To:** Mani, Ranjit B  
**Subject:** FW: Finalized - NDA 22525 General Review (REV-QUALITY-03)

Ranjit,

There are recommendations to be forwarded to the sponsor in this attached review. Let me know if they should be sent to the sponsor in the action letter, or prior to the action letter.

Thanks

Teresa

---

**From:** Nighswander, Robbin M  
**Sent:** Monday, April 05, 2010 2:23 PM  
**To:** Wheelous, Teresa A  
**Subject:** FW: Finalized - NDA 22525 General Review (REV-QUALITY-03)

Teresa:

Not sure why you were not copied on this.

Robbin

---

**From:** Heimann, Martha R  
**Sent:** Monday, April 05, 2010 11:21 AM  
**To:** Henry, Don  
**Cc:** McLamore, Sherita; Marroum, Patrick J; Suarez, Sandra; Dorantes, Angelica; Nighswander, Robbin M  
**Subject:** FW: Finalized - NDA 22525 General Review (REV-QUALITY-03)

Don-

Can you please arrange to forward the Biopharmaceutics comments on p. 3 of the attachment to the firm.

Thanks,  
*Martha*

---

**From:** [ias@fdssa088](mailto:ias@fdssa088) [mailto:[ias@fdssa088](mailto:ias@fdssa088)]  
**Sent:** Monday, April 05, 2010 9:10 AM  
**To:** McLamore, Sherita; Marroum, Patrick J; Heimann, Martha R; Suarez, Sandra; Dorantes, Angelica; Nighswander, Robbin M  
**Subject:** Finalized - NDA 22525 General Review (REV-QUALITY-03)

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[Proceed to DARRTS Login](#)

(b) (4)

## Wheelous, Teresa A

---

**From:** Nighswander, Robbin M  
**nt:** Monday, April 05, 2010 2:23 PM  
**o:** Wheelous, Teresa A  
**Subject:** FW: Finalized - NDA 22525 General Review (REV-QUALITY-03)

**Attachments:** NDA22525\_namenda\_final.pdf



NDA22525\_nam  
da\_final.pdf (44.

Teresa:

Not sure why you were not copied on this.

Robbin

---

**From:** Heimann, Martha R  
**Sent:** Monday, April 05, 2010 11:21 AM  
**To:** Henry, Don  
**Cc:** McLamore, Sherita; Marroum, Patrick J; Suarez, Sandra; Dorantes, Angelica; Nighswander, Robbin M  
**Subject:** FW: Finalized - NDA 22525 General Review (REV-QUALITY-03)

Jon-

Can you please arrange to forward the Biopharmaceutics comments on p. 3 of the attachment to the firm.

Thanks,  
Martha

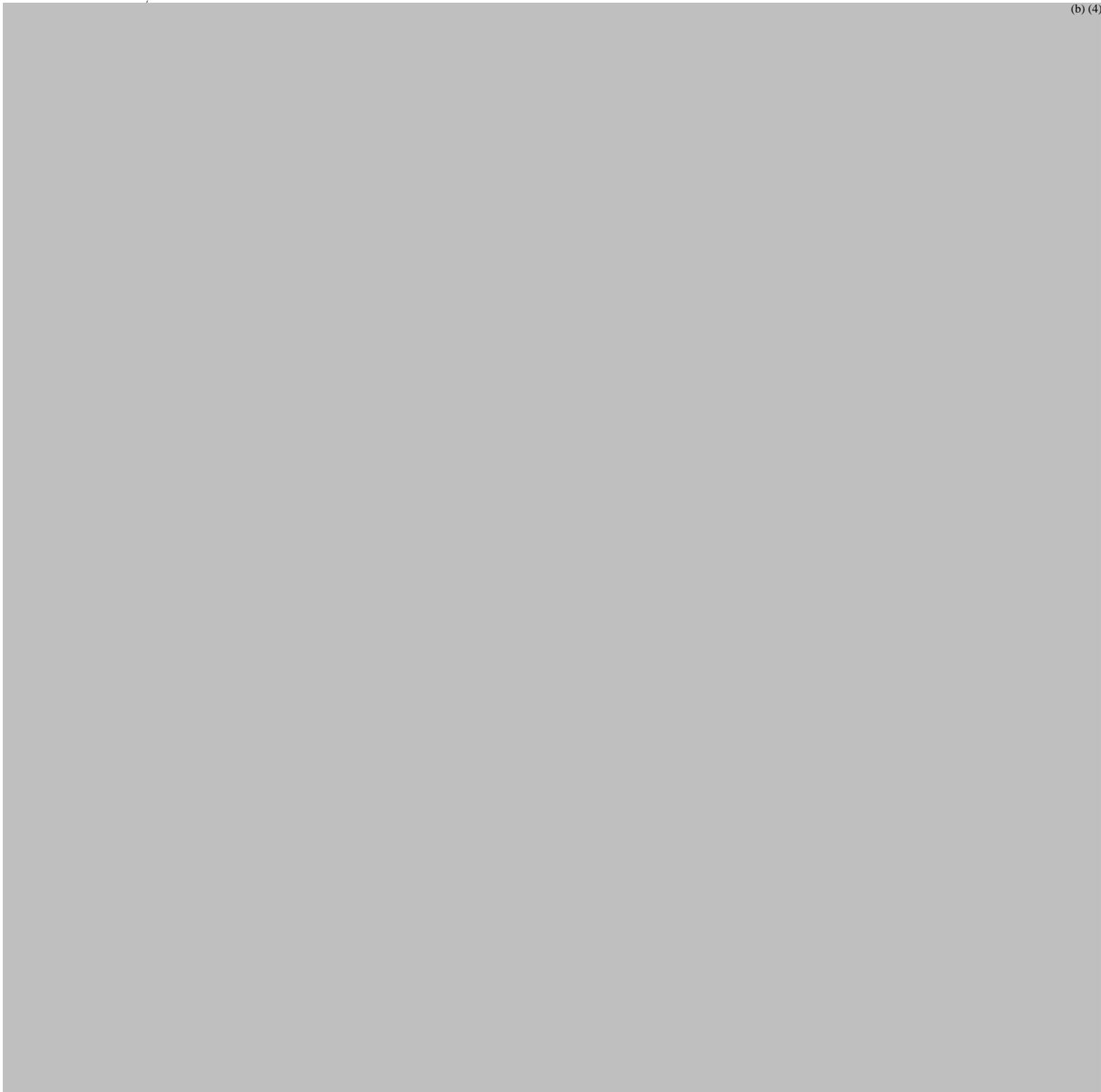
---

**From:** ias@fdssa088 [mailto:ias@fdssa088]  
**Sent:** Monday, April 05, 2010 9:10 AM  
**To:** McLamore, Sherita; Marroum, Patrick J; Heimann, Martha R; Suarez, Sandra; Dorantes, Angelica; Nighswander, Robbin M  
**Subject:** Finalized - NDA 22525 General Review (REV-QUALITY-03)

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[Proceed to DARRTS Login](#)

(b) (4)



**Wheelous, Teresa A**

---

**From:** Stowe, Ginneh D.  
**nt:** Wednesday, March 31, 2010 5:00 PM  
**o:** Wheelous, Teresa A  
**Cc:** Greeley, George  
**Subject:** RE: Namenda XR PeRC Materials-PLEASE REVIEW-ACTION REQUIRED BY APRIL 7th

Great. The documents will be submitted to PeRC as is. Your Division will not have to attend the PeRC meeting in-person, the PeRC's recommendations will be sent to you via email after the meeting on April 21<sup>st</sup>.

---

**From:** Wheelous, Teresa A  
**Sent:** Wednesday, March 31, 2010 9:02 AM  
**To:** Stowe, Ginneh D.  
**Subject:** FW: Namenda XR PeRC Materials-PLEASE REVIEW-ACTION REQUIRED BY APRIL 7th

Ginneh,

The Division has no revisions to the Namenda XR PeRC materials.

Thank you,

Teresa

---

**From:** Mani, Ranjit B  
**Sent:** Wednesday, March 31, 2010 8:49 AM  
**To:** Wheelous, Teresa A  
**Cc:** Mani, Ranjit B  
**Subject:** RE: Namenda XR PeRC Materials-PLEASE REVIEW-ACTION REQUIRED BY APRIL 7th

Teresa,

The documents are acceptable to me.

Ranjit

---

**From:** Wheelous, Teresa A  
**Sent:** Wednesday, March 31, 2010 8:46 AM  
**To:** Mani, Ranjit B  
**Subject:** FW: Namenda XR PeRC Materials-PLEASE REVIEW-ACTION REQUIRED BY APRIL 7th  
**Importance:** High

Ranjit,

Please review the attached documents and let me know if they are acceptable as drafted.

Thanks

Teresa

---

**From:** Stowe, Ginneh D.  
**Sent:** Tuesday, March 30, 2010 6:18 PM  
**To:** Wheelous, Teresa A  
**Cc:** Collins, Felicia  
**Subject:** Namenda XR PeRC Materials-PLEASE REVIEW-ACTION REQUIRED BY APRIL 7th  
**Importance:** High

Hi Teresa,

I have attached the required PeRC materials for the review of a full waiver of pediatric studies for Namenda XR (NDA 22-525). Please review the attached documents and let me know if you would like to make any revisions to the attached documents by the close of business on **Wednesday, April 7<sup>th</sup>**. If the documents are fine as is, please send me an email indicating that you don't have any revisions.

The PeRC will be reviewing this waiver on **April 21, 2010**.

Please note that I will be sending you the PeRC materials for (b) (4) a separate email.

Thanks so much.

Ginneh

---

Ginneh D. Stowe, MS

Public Health Analyst, Regulatory Affairs Team

Pediatric and Maternal Health Staff

Office of New Drugs

FDA-Center for Drug Evaluation and Research

White Oak Complex

Building #22 , Room 6481

Office: 301-796-4049

Fax: 301-796-9855

Email: [Ginneh.Stowe@fda.hhs.gov](mailto:Ginneh.Stowe@fda.hhs.gov)

**Wheelous, Teresa A**

---

**From:** ias@fdssa087  
**Int:** Wednesday, March 31, 2010 12:58 PM  
**To:** Kelley, Laurie; Katz, Russell G; CDER OSE CONSULTS; Chan, Irene Z.; Wheelous, Teresa A; CDER-DDMAC-RPM; Holquist, Carol A; Griffis, Melina; Taylor, Kellie; Jenkins, Darrell  
**Subject:** Finalized - NDA 22525 Labeling Review (REV-EPIPOSTMKT-06)  
**Attachments:** 2009-1915 Namenda XR Label and Labeling Review.pdf



2009-1915  
enda XR Label an

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[Proceed to DARRTS Login](#)

(b) (4)

**Wheelous, Teresa A**

**From:** Stowe, Ginneh D.  
**Sent:** Tuesday, March 30, 2010 6:18 PM  
**To:** Wheelous, Teresa A  
**Cc:** Collins, Felicia  
**Subject:** Namenda XR PeRC Materials-PLEASE REVIEW-ACTION REQUIRED BY APRIL 7th

**Importance:** High

**Follow Up Flag:** Follow up  
**Due By:** Wednesday, April 07, 2010 12:00 PM  
**Flag Status:** Flagged

**Attachments:** Namenda\_PEDIATRIC\_PAGE\_REPORT.pdf; 1\_Supplemental Pediatric Record Information\_Namenda.doc; PREA Waiver\_Namenda\_To be Reviewed.doc; PREA\_Lang for AP Letter.doc



amenda\_PEDIA1\_Supplemental PAGE\_REPORT  
^ PAGE\_REPORT ediatic Recor... Namenda\_To beP Letter.doc (4..

Hi Teresa,

I have attached the required PeRC materials for the review of a full waiver of pediatric studies for Namenda XR (NDA 22-525). Please review the attached documents and let me know if you would like to make any revisions to the attached documents by the close of business on **Wednesday, April 7<sup>th</sup>**. If the documents are fine as is, please send me an email indicating that you don't have any revisions.

The PeRC will be reviewing this waiver on **April 21, 2010**.

Please note that I will be sending you the PeRC materials for (b) (4) a separate email.

Thanks so much.

Ginneh

---

Ginneh D. Stowe, MS

Public Health Analyst, Regulatory Affairs Team

Pediatric and Maternal Health Staff

Office of New Drugs

FDA-Center for Drug Evaluation and Research

White Oak Complex

Building #22 , Room 6481

Office: 301-796-4049

Fax: 301-796-9855

Email: [Ginneh.Stowe@fda.hhs.gov](mailto:Ginneh.Stowe@fda.hhs.gov)

## **Wheelous, Teresa A**

---

**From:** ias@fdssa087  
**Sent:** Friday, March 26, 2010 11:03 AM  
**To:** Mani, Ranjit B; Katz, Russell G; Rivera-Lopez, Carol; Salewski, Joseph; Ayala, Dianiris C; Yau, Martin K; Steyert, Robert C; Nighswander, Robbin M; Chen, Xikui; Torres, Brunilda; Wheelous, Teresa A; Baweja, Raman K; Hansen, Thomas P  
**Subject:** Finalized - NDA 22525 Bioequivalence Establishment Inspection Report Review (CONSULT REV-DSI-05)  
**Attachments:** NDA22525.pdf



NDA22525.pdf  
(302 KB)

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(b) (4)



**Wheelous, Teresa A**

---

**From:** Beitzell, Debra  
**Sent:** Wednesday, March 24, 2010 2:08 PM  
**To:** Wheelous, Teresa A  
**Subject:** RE: NDA 22-525 (Namenda)

**Follow Up Flag:** Follow up  
**Due By:** Thursday, April 22, 2010 12:00 AM  
**Flag Status:** Red

Thanks for the update. Please send me a marked-up label once the team has finished editing. Please allow SEALD 5 working days to complete the review.

Thanks, Debbie

---

**From:** Wheelous, Teresa A  
**Sent:** Wednesday, March 24, 2010 9:59 AM

**To:** Beitzell, Debra  
**Subject:** RE: NDA 22-525 (Namenda)

Debra,

. wanted to let you know that the Division has decided to act on this application NDA 22525 earlier than the PDUFA goal date. We are targeting (b) (4) 2010 as the action date. Also, the sponsor has submitted a revised labeling in an electronic submission dated (b) (4) 10.

The Division has not yet worked on labeling so I guess that the Division will not have labeling until early May.

Regards,

Teresa

---

**From:** Beitzell, Debra  
**Sent:** Wednesday, December 16, 2009 10:23 AM  
**To:** Wheelous, Teresa A  
**Subject:** NDA 22-525 (Namenda)

Hello,

I am the PLR content reviewer from SEALD (labeling team) that has been assigned to the Namenda XR application that is due on June 21, 2010. SEALD conducts content reviews **AFTER** the division review team completes their initial draft review **BUT BEFORE** labeling content comments are sent to the applicant. Could you please send me the most recent version of the marked-up label (Highlights, Contents, and FPI) once your team has finished editing? A MS word file is preferable.

Also, do you have an estimate as to when you might take an action on this application and what type of action you will be taking? If you are planning to take a CR action, we will wait until the next review cycle to complete our review, unless you plan on conducting labeling negotiations with the firm this cycle.

Thanks in advance for your time and help.

Debbie Beitzell  
Labeling Reviewer  
SEALD/OND/CDER

**Wheelous, Teresa A**

---

**From:** Wheelous, Teresa A  
**Sent:** Wednesday, March 24, 2010 10:42 AM  
**To:** Yau, Martin K  
**Subject:** RE: Namendar XR, NDA 22525; (1) Mid-Cycle Meeting (2) Add P'Metrics Colleagues to Outlook calendar notices for Namenda XR

Martin,

Just wanted to let you know that the Division has decided to act on NDA 22525 Namenda XR at the end of (b) (4) 2010. Are you able to provide the status of the Bioequivalence inspection?

Thanks

Teresa

---

**From:** Yau, Martin K  
**Sent:** Monday, January 11, 2010 10:00 AM  
**To:** Wheelous, Teresa A  
**Cc:** Skelly, Michael F  
**Subject:** RE: Namendar XR, NDA 22525; (1) Mid-Cycle Meeting (2) Add P'Metrics Colleagues to Outlook calendar notices for Namenda XR

Hi Teresa:

Thanks. Either me, Mike, or a representative from our group will attend the meeting.

Martin

---

**From:** Wheelous, Teresa A  
**Sent:** Monday, January 11, 2010 9:55 AM  
**To:** Skelly, Michael F; Yau, Martin K  
**Subject:** FW: Namendar XR, NDA 22525; (1) Mid-Cycle Meeting (2) Add P'Metrics Colleagues to Outlook calendar notices for Namenda XR

Mike and Martin,

The Biopharm team leader for NDA 22525 has requested the Bioequivalence DSI colleague to join us on Thursday at the midterm meeting. Should I send the meeting notice to both of you?

Thanks,

Teresa

---

**From:** El Hage, Antoine N  
**Sent:** Monday, January 11, 2010 9:51 AM  
**To:** Wheelous, Teresa A  
**Subject:** RE: Namendar XR, NDA 22525; (1) Mid-Cycle Meeting (2) Add P'Metrics Colleagues to Outlook calendar notices for Namenda XR

Check with Mike Skelly or Marin Yau

---

**From:** Wheelous, Teresa A  
**Sent:** Monday, January 11, 2010 9:50 AM  
**To:** El Hage, Antoine N  
**Subject:** FW: Namendar XR, NDA 22525; (1) Mid-Cycle Meeting (2) Add P'Metrics Colleagues to Outlook calendar notices for Namenda XR

Tony,

Do you know who the DSI Bioequivalence contact is for Namenda XR 22525?

Thanks,  
Teresa

---

**From:** Baweja, Raman K  
**Sent:** Friday, January 08, 2010 2:50 PM  
**To:** Wheelous, Teresa A  
**Cc:** Katz, Russell G; Mani, Ranjit B; Men, Angela; Wang, Yaning; Zhu, Hao; Zhang, Huixia; Baweja, Raman K  
**Subject:** Namendar XR, NDA 22525; (1) Mid-Cycle Meeting (2) Add P'Metrics Colleagues to Outlook calendar notices for Namenda XR

Hi Teresa

Two items related to this NDA:

1) For the midcycle meeting for Namenda XR for next week, January 14, please make sure that DSI colleagues from the BE group (i.e., those doing the inspection of the biostudy) are present at the midcycle meeting.

2) On the Outlook calendar notices for this drug, please also include Pharmacometrics colleagues Drs. Yaning Wang, and Hao Zhu.

Thanks

Ray

## Wheelous, Teresa A

---

**From:** El Hage, Antoine N  
**Sent:** Wednesday, March 24, 2010 10:25 AM  
**To:** Wheelous, Teresa A  
**Subject:** RE: DSI Inspections for NDA 22525 Namenda XR

Hi Teresa,

The clinical sites are completed and no issues. I'll provide the CIS a month before the due date

Take care,  
tony

---

**From:** Wheelous, Teresa A  
**Sent:** Wednesday, March 24, 2010 10:11 AM  
**To:** El Hage, Antoine N  
**Subject:** DSI Inspections for NDA 22525 Namenda XR

Toni,

Do you know the status of the DSI inspections for NDA 22525? There are two consults, a bioequivalence consult and a clinical consult. I have attached copies of both consults.

The Division is targeting an action date of May 28, 2010.

Thanks

Teresa

<< File: DSI Clinical Sites Audit Request (FRM-CONSULT-08).doc >> << File: DSI Bioequivalence CONSULT.doc >>

**Wheelous, Teresa A**

---

**From:** Wheelous, Teresa A  
**Sent:** Wednesday, March 24, 2010 10:11 AM  
**To:** El Hage, Antoine N  
**Subject:** DSI Inspections for NDA 22525 Namenda XR

**Attachments:** DSI Clinical Sites Audit Request (FRM-CONSULT-08).doc; DSI Bioequivalence CONSULT.doc

Toni,

Do you know the status of the DSI inspections for NDA 22525? There are two consults, a bioequivalence consult and a clinical consult. I have attached copies of both consults.

The Division is targeting an action date of May 28, 2010.

Thanks

Teresa



SI Clinical Sites  
Audit Reque...



DSI  
alence CONSULT

**Wheelous, Teresa A**

---

**From:** Wheelous, Teresa A  
**Sent:** Wednesday, March 24, 2010 9:59 AM  
**To:** Beitzell, Debra  
**Subject:** RE: NDA 22-525 (Namenda)

Debra,

I wanted to let you know that the Division has decided to act on this application NDA 22525 earlier than the PDUFA goal date. We are targeting May 28, 2010 as the action date. Also, the sponsor has submitted a revised labeling in an electronic submission dated 12/17/10.

The Division has not yet worked on labeling so I guess that the Division will not have labeling until early May.

Regards,

Teresa

---

**From:** Beitzell, Debra  
**Sent:** Wednesday, December 16, 2009 10:23 AM  
**To:** Wheelous, Teresa A  
**Subject:** NDA 22-525 (Namenda)

Hello,

I am the PLR content reviewer from SEALD (labeling team) that has been assigned to the Namenda XR application that is due on June 21, 2010. SEALD conducts content reviews **AFTER** the division review team completes their initial draft review **BUT BEFORE** labeling content comments are sent to the applicant. Could you please send me the most recent version of the marked-up label (Highlights, Contents, and FPI) once your team has finished editing? A MS word file is preferable.

Also, do you have an estimate as to when you might take an action on this application and what type of action you will be taking? If you are planning to take a CR action, we will wait until the next review cycle to complete our review, unless you plan on conducting labeling negotiations with the firm this cycle.

Thanks in advance for your time and help.

Debbie Beitzell  
Labeling Reviewer  
SEALD/OND/CDER

## **Wheelous, Teresa A**

---

**From:** ias@fdssa087  
**Sent:** Tuesday, March 23, 2010 3:03 PM  
**To:** Wheelous, Teresa A; Nighswander, Robbin M  
**Subject:** Finalized - NDA 22525 Filing Review (REV-RPM-03)

**Attachments:** PM Filing Review .pdf



Filing Review  
.pdf (134 KB)...

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[Proceed to DARRTS Login](#)

(b) (4)

**Wheelous, Teresa A**

---

**From:** Nighswander, Robbin M  
**Sent:** Monday, March 22, 2010 11:43 AM  
**To:** Wheelous, Teresa A  
**Subject:** FW: Finalized - NDA 22525 Information Request (COR-NDAIR-01)

**Attachments:** NDA 22-525 IR letter.pdf



NDA 22-525 IR  
letter.pdf (21 K...

Teresa:

FYI... not sure why you were not automatically copied on this .  
Robbin

---

**From:** ias@fdssa088 [mailto:ias@fdssa088]  
**Sent:** Monday, March 22, 2010 10:15 AM  
**To:** Henry, Don; Sood, Ramesh; Nighswander, Robbin M  
**Subject:** Finalized - NDA 22525 Information Request (COR-NDAIR-01)

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**Wheelous, Teresa A**

---

**From:** ias@fdssa088  
**Sent:** Monday, March 15, 2010 11:24 AM  
**To:** Wheelous, Teresa A; CDER-DDMAC-RPM; Nighswander, Robbin M  
**Subject:** Finalized - NDA 22525 DDMAC Labeling Consult Request Form (FRM-CONSULT-21)

**Attachments:** DDMAC Labeling Consult Request Form (FRM-CONSULT-21).pdf



DMAC Labeling  
onsult Request..

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**Wheelous, Teresa A**

---

**From:** Niebo, Michael [Michael.Niebo@frx.com]  
**Sent:** Wednesday, March 03, 2010 4:37 PM  
**To:** Wheelous, Teresa A  
**Cc:** DeMartino, James  
**Subject:** NDA 22525 Namenda XR Biopharm request

Hi Teresa-

As a follow-up to the voicemail I've just left for you, I see that you sent me an email this afternoon, but yet again, I am having problems with my digital security certificate and cannot open your email. Can you please forward the request to James DeMartino at [james.demartino@frx.com](mailto:james.demartino@frx.com) (also copied on this email), or fax the request to 631-858-7921?

I apologize for the inconvenience. I've contacted Patrick Jalbert and Wendy Lee at FDA to try to help me with this recurring problem.

Thanks,

Michael P. Niebo, RAC

Asst. Director, Regulatory Affairs

Forest Research Institute

A Subsidiary of Forest Laboratories, Inc.

Harborside Financial Center

Plaza V, Suite 1900

Jersey City, NJ 07311

Office: 201-386-2046

Fax: 201-524-9711/9712

---

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## **Wheelous, Teresa A**

---

**From:** Wheelous, Teresa A  
**Sent:** Wednesday, March 03, 2010 9:02 AM  
**To:** (b) (4)  
**Subject:** RE: Review of NDA (b) (4)

(b) (4)

The following is a Biopharmaceutics comment regarding the proposed IVIVC to NDA (b) (4)

We note that the validation of your proposed IVIVC for Namenda XR ER capsules was conducted by comparing the mean predicted PK parameters for the individual subjects. Please conduct the assessment of predictability using convolved mean values not the mean of the convolved individual values.

Regards,

Teresa

---

**From:** [REDACTED] (b) (4)  
**Sent:** Monday, March 01, 2010 2:45 PM  
**To:** Wheelous, Teresa A  
**Subject:** RE: Review of NDA [REDACTED] (b) (4)

Teresa,  
Thanks for your prompt reply.

I have one more question:

As with every NDA submission, our company is preparing itself for a possible Advisory Committee Meeting. Do you already know if [REDACTED] (b) (4) will be invited to present at an Advisory Committee meeting, or if there is no need to have an Advisory Committee Meeting for the above NDA?

thanks

[REDACTED] (b) (4)

From: "Wheelous, Teresa A" <Teresa.Wheelous@fda.hhs.gov>  
To: [REDACTED] (b) (4)  
Date: 02/26/2010 09:33 AM  
Subject: RE: Review of NDA [REDACTED] (b) (4)8

---

[REDACTED] (b) (4)

Yes, we had the mid-cycle meeting and there are no comments to be relayed, at this time.

Teresa

---

**From:** [REDACTED] (b) (4)  
**Sent:** Wednesday, February 24, 2010 5:07 PM  
**To:** Wheelous, Teresa A  
**Cc:** [REDACTED] (b) (4)  
**Subject:** Review of NDA [REDACTED] (b) (4)

Teresa,

NDA [REDACTED] (b) (4) extended release tablets was submitted about five months ago on Sept 24, 2009. Has a Mid-Cycle Review Meeting already been scheduled?

I am asking because I will be traveling the next two weeks, but I can be reached by e-mail or on my cell phone

[REDACTED] (b) (4)  
If you need immediate assistance with any questions regarding this NDA please contact [REDACTED] (b) (4)  
[REDACTED]

Thanks

[REDACTED] (b) (4)

**Wheelous, Teresa A**

---

**From:** ias@fdssa087  
**Sent:** Wednesday, January 20, 2010 3:52 PM  
**To:** Wheelous, Teresa A  
**Subject:** Finalized - NDA 22525 Internal Meeting Minutes (FRM-MINUTES-01)

**Attachments:** Mid-cycle meeting.pdf



Mid-cycle  
meeting.pdf (274 KB)

[http://darrrts/images/new\\_DARRTS\\_Logo.jpg](http://darrrts/images/new_DARRTS_Logo.jpg)

[Proceed to DARRTS Login](#)

(b) (4)

**Wheelous, Teresa A**

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**From:** WHEELOUST [Teresa.Wheelous@fda.hhs.gov]  
**Sent:** Thursday, January 14, 2010 9:59 AM  
**To:** Wheelous, Teresa A  
**Subject:** Scanned document from WHEELOUST

**Attachments:** nonclinical midcycle handout ScanDoc.PDF



nonclinical  
dcycle handout S

**Wheelous, Teresa A**

---

**From:** Yau, Martin K  
**Sent:** Monday, January 11, 2010 10:00 AM  
**To:** Wheelous, Teresa A  
**Cc:** Skelly, Michael F  
**Subject:** RE: Namendar XR, NDA 22525; (1) Mid-Cycle Meeting (2) Add P'Metrics Colleagues to Outlook calendar notices for Namenda XR

Teresa:

Thanks. Either me, Mike, or a representative from our group will attend the meeting.

Martin

---

**From:** Wheelous, Teresa A  
**Sent:** Monday, January 11, 2010 9:55 AM  
**To:** Skelly, Michael F; Yau, Martin K  
**Subject:** FW: Namendar XR, NDA 22525; (1) Mid-Cycle Meeting (2) Add P'Metrics Colleagues to Outlook calendar notices for Namenda XR

Mike and Martin,

The Bipolar team leader for NDA 22525 has requested the Bioequivalence DSI colleague to join us on Thursday at the midterm meeting. Should I send the meeting notice to both of you?

Thanks,

Teresa

---

**From:** El Hage, Antoine N  
**Sent:** Monday, January 11, 2010 9:51 AM  
**To:** Wheelous, Teresa A  
**Subject:** RE: Namendar XR, NDA 22525; (1) Mid-Cycle Meeting (2) Add P'Metrics Colleagues to Outlook calendar notices for Namenda XR

Check with Mike Skelly or Marin Yau

---

**From:** Wheelous, Teresa A

**Sent:** Monday, January 11, 2010 9:50 AM  
**To:** El Hage, Antoine N  
**Subject:** FW: Namendar XR, NDA 22525; (1) Mid-Cycle Meeting (2) Add P'Metrics Colleagues to Outlook calendar notices for Namenda XR

Tony,

Do you know who the DSI Bioequivalence contact is for Namenda XR 22525?

Thanks,  
Teresa

---

**From:** Baweja, Raman K  
**Sent:** Friday, January 08, 2010 2:50 PM  
**To:** Wheelous, Teresa A  
**Cc:** Katz, Russell G; Mani, Ranjit B; Men, Angela; Wang, Yaning; Zhu, Hao; Zhang, Huixia; Baweja, Raman K  
**Subject:** Namendar XR, NDA 22525; (1) Mid-Cycle Meeting (2) Add P'Metrics Colleagues to Outlook calendar notices for Namenda XR

Hi Teresa

Two items related to this NDA:

- 1) For the midcycle meeting for Namenda XR for next week, January 14, please make sure that DSI colleagues from the BE group (i.e., those doing the inspection of the biostudy) are present at the midcycle meeting.
- 2) On the Outlook calendar notices for this drug, please also include Pharmacometrics colleagues Drs. Yaning Wang, and Hao Zhu.

Thanks

Ray

## **Wheelous, Teresa A**

---

**From:** ias@fdssa087  
**Sent:** Tuesday, December 29, 2009 3:23 PM  
**To:** Kelley, Laurie; Katz, Russell G; Chan, Irene Z.; Bates, Doris J; Wheelous, Teresa A; Tandon, Veneeta; Holquist, Carol A; Nighswander, Robbin M; Griffis, Melina; Toyer, Denise P; Wasilik, Maria  
**Subject:** Finalized - NDA 22525 Proprietary Name Granted (COR-NAME-02)  
**Attachments:** 2009-1914 Namenda NDA 22525 TN Granted clean (2).pdf



2009-1914  
nda NDA 22525

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**Wheelous, Teresa A**

---

**From:** ias@fdssa088  
**nt:** Tuesday, December 29, 2009 12:41 PM  
**.o:** Kelley, Laurie; Katz, Russell G; CDER OSE CONSULTS; Bates, Doris J; Chan, Irene; Wheelous, Teresa A; Nighswander, Robbin M; Holquist, Carol A; Griffis, Melina; Toyer, Denise P; Wasilik, Maria  
**Subject:** Finalized - NDA 22525 Proprietary Name Review (REV-EPIPOSTMKT-10)  
**Attachments:** 2009-1914-Namenda XR Name Review.pdf



2009-1914-Nam  
a XR Name Rev

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(b) (4)

**Wheelous, Teresa A**

---

**From:** Beitzell, Debra  
**Sent:** Wednesday, December 16, 2009 10:23 AM  
**To:** Wheelous, Teresa A  
**Subject:** NDA 22-525 (Namenda)

**Follow Up Flag:** Follow up  
**Due By:** Friday, December 18, 2009 12:00 AM  
**Flag Status:** Red

Hello,

I am the PLR content reviewer from SEALD (labeling team) that has been assigned to the Namenda XR application that is due on June 21, 2010. SEALD conducts content reviews **AFTER** the division review team completes their initial draft review **BUT BEFORE** labeling content comments are sent to the applicant. Could you please send me the most recent version of the marked-up label (Highlights, Contents, and FPI) once your team has finished editing? A MS word file is preferable.

Also, do you have an estimate as to when you might take an action on this application and what type of action you will be taking? If you are planning to take a CR action, we will wait until the next review cycle to complete our review, unless you plan on conducting labeling negotiations with the firm this cycle.

Thanks in advance for your time and help.

Debbie Beitzell  
 Labeling Reviewer  
 SEALD/OND/CDER

**Wheelous, Teresa A**

---

**From:** DeMartino, James [James.DeMartino@frx.com]  
**Sent:** Tuesday, December 08, 2009 12:42 PM  
**To:** Wheelous, Teresa A  
**Cc:** Niebo, Michael; Gill, Wendy  
**Subject:** RE: NDA 22-525 NAMENDA XR Info Request

**Attachments:** NDA 22-525 Memantine XR MEM-MD-50 Argentina Investigator List 12 07 09.rtf; emfalert.txt



NDA 22-525 memfalert.txt (855  
 antine XR MEM-M B)

Dear Teresa,

For your information, I am forwarding a desk copy of the information you requested concerning the contact information for each Clinical Investigator at sites in Argentina for Study MEM-MD-50. An official copy will be filed to the NDA later today, or more likely tomorrow.

Please let me know if you have any questions.

.1

---

James L. DeMartino, PhD  
Sr. Director, Regulatory Affairs  
Forest Research Institute  
Harborside Financial Center, Plaza 5  
24th Fl, Room 56  
Jersey City, NJ 07311

tel (201) 386-2131  
cell (917) 692-6456  
fax (201) 524-9711/9712

[james.demartino@frx.com](mailto:james.demartino@frx.com)

---

**From:** Wheelous, Teresa A [mailto:Teresa.Wheelous@fda.hhs.gov]  
**Sent:** Thursday, December 03, 2009 2:16 PM  
**To:** DeMartino, James; Niebo, Michael  
**Subject:** FW: NDA 22-525 [REDACTED] (b) (4) Info Request

Michael,

As requested, this is a copy of the info request that was sent on Wed. before Thanksgiving.

Teresa

---

**From:** Wheelous, Teresa A  
**Sent:** Wednesday, November 25, 2009 11:20 AM  
**To:** 'Niebo, Michael'  
**Subject:** NDA 22 [REDACTED] (b) (4)g Info Request

Michael,

Please send me the following information regarding NDA 22525 Aricept extended release:

The phone number, fax number, and e-mail address for each CI at the Argentina sites for MEM-MD-50.

Regards,

*CDR Teresa Wheelous, R. Ph.*  
*Sr. Program Management Officer Consultant*  
*FDA*  
*Division of Neurology*  
*10903 New Hampshire Avenue, Bldg. #22, Room 4344*  
*Silver Spring, MD 20993-0002*

(telephone) 301-796-1161  
(fax) 301-796-9842

**Wheelous, Teresa A**

---

**From:** Chan, Irene Z.  
**Sent:** Friday, November 13, 2009 1:52 PM  
**To:** Wheelous, Teresa A  
**Cc:** Griffis, Melina; Toyer, Denise P; Holquist, Carol A; Katz, Russell G; Kelley, Laurie; Wheeler, Chris  
**Subject:** Proprietary Name Review: Namenda XR (memantine hydrochloride) NDA 022525  
**Attachments:** Namenda XR Charts.doc

Dear Teresa,

This e-mail is to notify you that the Division of Medication Error Prevention and Analysis (DMEPA) has completed evaluation of the proposed proprietary name Namenda XR (memantine hydrochloride) and finds the name Namenda XR acceptable. Our decision is based on the information submitted by the applicant, preliminary comments from your division, DDMAC's promotional and DMEPA's safety evaluation. We have attached tables that summarize our analysis of the names found to look and/or sound similar to Namenda XR. In addition, our evaluation did not identify any other factors that would render the name unacceptable at this time.

Please share this information with the Namenda XR review team, and provide a response indicating concurrence with our assessment. If the review team identifies any factors that render the name unacceptable (e.g., clinical, chemistry, etc) please provide the rationale for their non-concurrence.

Given the OSE PDUFA timelines associated with this proprietary name review, we ask that you respond to this request within 7 days of receipt of this communication. We are willing to meet with the division to discuss this analysis, if needed. Thank you.



Namenda XR  
Charts.doc (103 KB)

Sincerely,  
Irene Chan

Irene Z. Chan, Pharm.D., BCPS  
LCDR, U.S. Public Health Service  
Drug Safety Evaluator  
Division of Medication Error Prevention and Analysis  
Office of Surveillance and Epidemiology  
Center for Drug Evaluation and Research  
Food and Drug Administration

Federal Research Center at White Oak  
10903 New Hampshire Avenue  
Building 22, Rm. #4421 MS4447  
Silver Spring, Maryland 20993-0002

Irene.Chan2@fda.hhs.gov  
Office 301.796.3962  
Fax 301.796.9865

**Wheelous, Teresa A**

---

**From:** ias@fdssa087  
**Sent:** Friday, November 13, 2009 12:34 PM  
**To:** Katz, Russell G; joanne.rhoads@fda.hhs.gov; CDER DSI; Wheelous, Teresa A; Purohit-Sheth, Tejashri; Nighswander, Robbin M; Lewin, Constance; ddrdsi@cder.fda.gov  
**Subject:** Finalized - NDA 22525 DSI Clinical Sites Audit Request (FRM-CONSULT-08)  
**Attachments:** DSI Clinical Sites Audit Request (FRM-CONSULT-08).pdf



SI Clinical Sites  
Audit Reque...

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(b) (4)

**Wheelous, Teresa A**

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**From:** ias@fdssa087  
**Sent:** Monday, November 02, 2009 9:41 AM  
**To:** Katz, Russell G; Wheelous, Teresa A; CDER PMHS; Nighswander, Robbin M  
**Subject:** Finalized - NDA 22525 No Filing Issues Identified (COR-NDAFILE-05)

**Attachments:** No Filing Issues Identified (COR-NDAFILE-05).pdf



No Filing Issues  
Identified (C...

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**Wheelous, Teresa A**

---

**From:** Stowe, Ginneh D.  
**Sent:** Friday, October 23, 2009 3:44 PM  
**To:** Wheelous, Teresa A  
**Cc:** Collins, Felicia  
**Subject:** RE: PeRC Schedule- NDA 22525 Namenda XR

Hi Teresa,

Our records indicate that this product is being addressed in the pilot project. Felicia Collins (PMHS medical officer who attended the filing meeting) has been assigned to this product. A future meeting will be set up as we get closer to the PeRC date to discuss this product and we will be drafting the required documents for the PeRC review. In the interim, feel free to contact me if you have any questions.

Thanks,

Ginneh

---

**From:** Wheelous, Teresa A  
**Sent:** Friday, October 23, 2009 10:47 AM  
**To:** Stowe, Ginneh D.  
**Subject:** RE: PeRC Schedule- NDA 22525 Namenda XR

Ginneh,

I spoke with Jackie and I wanted to inform (remind) you that this will be one of the Division's pilot applications.

Thanks,

Teresa

---

**From:** Stowe, Ginneh D.  
**Sent:** Wednesday, October 14, 2009 6:18 PM  
**To:** Wheelous, Teresa A  
**Cc:** Greeley, George  
**Subject:** PeRC Schedule- NDA 22525 Namenda XR

Hi Teresa,

Namenda XR is on the PeRC schedule for April 21, 2010. PeRC is usually held from 9 am to 11 am on Wednesdays, you will be notified of a specific time closer to the meeting date. Please send the completed documents covering ages birth to 16 years to be reviewed no later than

**April 12, 2010. Failure to do so will result in your product being rescheduled to a later date.**

**The information entered into the PREA Pediatric Record in DARRTS should reflect the opinions of the Division for each product and not merely those of the sponsor.**

-  
Here is the link to the PREA templates.  
<http://wcms.fda.gov/InsideFDA/CDER/OfficeofNewDrugs/PediatricandMaternalHealthStaff/UCM027829>.

**Please note that the templates in CDER Standard Letters (CSL) are not current so please be sure to use the forms on the PMHS website.**

**The Pediatric Plan submitted for deferrals MUST include a brief description of studies in addition to:**

**Protocol Submission Date**

**Study Start Date**

**Final Report Submission Date**

Here is the link to the webpage where the most current PREA language for the approval letters can be found.  
<http://wcms.fda.gov/InsideFDA/CDER/OfficeofNewDrugs/PediatricandMaternalHealthStaff/UCM027839>.

Thanks,

Ginneh

---

Ginneh D. Stowe, MS

Public Health Analyst, Regulatory Affairs Team

Pediatric and Maternal Health Staff

Office of New Drugs

FDA-Center for Drug Evaluation and Research

White Oak Complex

Building #22 , Room 6481

Office: 301-796-4049

Fax: 301-796-9855

Email: [Ginneh.Stowe@fda.hhs.gov](mailto:Ginneh.Stowe@fda.hhs.gov)

## Wheelous, Teresa A

---

**From:** Wheelous, Teresa A  
**nt:** Friday, October 23, 2009 10:47 AM  
**o:** Stowe, Ginneh D.  
**Subject:** RE: PeRC Schedule- NDA 22525 Namenda XR

Ginneh,

I spoke with Jackie and I wanted to inform (remind) you that this will be one of the Division's pilot applications.

Thanks,

Teresa

---

**From:** Stowe, Ginneh D.  
**Sent:** Wednesday, October 14, 2009 6:18 PM  
**To:** Wheelous, Teresa A  
**Cc:** Greeley, George  
**Subject:** PeRC Schedule- NDA 22525 Namenda XR

Hi Teresa,

Namenda XR is on the PeRC schedule for April 21, 2010. PeRC is usually held from 9 am to 11 am on Wednesdays, you will be notified of a specific time closer to the meeting date. Please send the completed documents covering ages birth to 16 years to be reviewed no later than

**April 12, 2010. Failure to do so will result in your product being rescheduled to a later date.**

**The information entered into the PREA Pediatric Record in DARRTS should reflect the opinions of the Division for each product and not merely those of the sponsor.**

Here is the link to the PREA templates.  
<http://wcms.fda.gov/InsideFDA/CDER/OfficeofNewDrugs/PediatricandMaternalHealthStaff/UCM027829>.

**Please note that the templates in CDER Standard Letters (CSL) are not current so please be sure to use the forms on the PMHS website.**

**The Pediatric Plan submitted for deferrals MUST include a brief description of studies in addition to:**

**Protocol Submission Date**

**Study Start Date**

**Final Report Submission Date**

Here is the link to the webpage where the most current PREA language for the approval letters can be found.  
<http://wcms.fda.gov/InsideFDA/CDER/OfficeofNewDrugs/PediatricandMaternalHealthStaff/UCM027839>.

Thanks,

Ginneh

---

Ginneh D. Stowe, MS

Public Health Analyst, Regulatory Affairs Team

Pediatric and Maternal Health Staff

Office of New Drugs

FDA-Center for Drug Evaluation and Research

White Oak Complex

Building #22 , Room 6481

Office: 301-796-4049

Fax: 301-796-9855

Email: [Ginneh.Stowe@fda.hhs.gov](mailto:Ginneh.Stowe@fda.hhs.gov)

## Wheelous, Teresa A

---

**From:** ias@fdssa087  
**Sent:** Wednesday, October 21, 2009 1:17 PM  
**To:** Henry, Don; Marroum, Patrick J; Heimann, Martha R; Wheelous, Teresa A; Suarez, Sandra; Dorantes, Angelica; Nighswander, Robbin M  
**Subject:** Finalized - NDA 22525 General Review (REV-QUALITY-03)  
**Attachments:** NDA22525\_namenda\_final.pdf



NDA22525\_nam  
da\_final.pdf (11.

[http://darrts/images/new\\_DARRTS\\_Logo.jpg](http://darrts/images/new_DARRTS_Logo.jpg)

[Proceed to DARRTS Login](#)

(b) (4)

**Wheelous, Teresa A**

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**From:** Kelley, Laurie  
**Sent:** Tuesday, October 20, 2009 12:21 PM  
**To:** Wheelous, Teresa A  
**Cc:** Chan, Irene Z.; Griffis, Melina  
**Subject:** NDA 22525 Proprietary Name Request for Review

Hello Teresa,

OSE has received a submission for a proposed proprietary name:

Submission Date: 10/06/2009  
Stamp Date: 10/07/2009  
Proposed Proprietary Name: Namenda XR  
Established Name: memantine HCL  
Application Type/Number: NDA 22525  
Mid-Review Date: 11/21/2009  
DMEPA Safety Evaluator: Irene Chan  
DMEPA Team Leader: Melina Griffis

DDMAC does not have any promotional issues with this name. We realize it is early in your application review cycle, but OSE would like to hear any preliminary concerns your review team may have with the proposed proprietary name at this time. Also, please keep us informed of any emerging issues that may affect our name review as you review the application. As our timeframes are short, please send us any preliminary comments within 7 days.

, nanks,  
Laurie

Laurie Kelley, PA-C  
Safety Regulatory Project Manager  
CDER, Office of Surveillance and Epidemiology  
10903 New Hampshire Ave.  
Bldg. 22, Rm 4435  
Silver Spring, MD 20993  
Phone: 301-796-5068  
Email: laurie.kelley@fda.hhs.gov

**Wheelous, Teresa A**

---

**From:** Zhu, Hao  
**Sent:** Friday, October 16, 2009 1:21 PM  
**To:** Wheelous, Teresa A  
**Cc:** Wang, Yaning  
**Subject:** NDA 22525 (Memantine XR formulation)

Dear Teresa,

I am the pharmacometrics review for NDA 22525 (Memantine XR). Will you please include me in the future team meetings? Thank you,

Hao

Hao Zhu, Ph.D.

Division of Pharmacometrics,  
Office of Clinical Pharmacology,  
U.S. Food and Drug Administration

10903 New Hampshire Ave,  
Bldg 51, Room 3150,  
Silver Spring, MD, 20993

Phone: (301)796-2772  
Fax: (301) 847-8720  
Email: Hao.Zhu@fda.hhs.gov

**Wheelous, Teresa A**

---

**From:** Stowe, Ginneh D.  
**Sent:** Wednesday, October 14, 2009 6:18 PM  
**To:** Wheelous, Teresa A  
**Cc:** Greeley, George  
**Subject:** PeRC Schedule- NDA 22525 Namenda XR

**Follow Up Flag:** Follow up  
**Due By:** Friday, March 05, 2010 12:00 AM  
**Flag Status:** Red

Hi Teresa,

Namenda XR is on the PeRC schedule for April 21, 2010. PeRC is usually held from 9 am to 11 am on Wednesdays, you will be notified of a specific time closer to the meeting date. Please send the completed documents covering ages birth to 16 years to be reviewed no later than

**April 12, 2010. Failure to do so will result in your product being rescheduled to a later date.**

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-  
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**Study Start Date**

**Final Report Submission Date**

Here is the link to the webpage where the most current PREA language for the approval letters can be found.

<http://wcms.fda.gov/InsideFDA/CDER/OfficeofNewDrugs/PediatricandMaternalHealthStaff/UCM027839>.

Thanks,

nneh

---

Ginneh D. Stowe, MS

Public Health Analyst, Regulatory Affairs Team

Pediatric and Maternal Health Staff

Office of New Drugs

FDA-Center for Drug Evaluation and Research

White Oak Complex

Building #22 , Room 6481

Office: 301-796-4049

Fax: 301-796-9855

✉mail: [Ginneh.Stowe@fda.hhs.gov](mailto:Ginneh.Stowe@fda.hhs.gov)



NDA 22-525

**INFORMATION REQUEST**

Forest Laboratories, Inc.  
Attention: Michael P. Niebo  
Asst. Director, Regulatory Affairs  
Harborside Financial Center  
Plaza V, Suite 1900  
Jersey City, NJ 07311

Dear Mr. Niebo:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Namenda XR (memantine hydrochloride) extended release capsules.

We are reviewing the Chemistry, Manufacturing, and Controls sections of your submission and have the following comments and information requests. We request a prompt written response in order to continue our evaluation of your NDA.

- In your April 2, 2010 response, you indicated that Microbial testing will be performed on the validation batches and the first three commercial batches for each strength of the drug product at release. You further indicate that if all batches show no microbial growth, the Microbial testing will be removed from the specification and the updated specification will be included in the next Annual Report. Be advised that that in the absence of providing justification, microbial limit testing should be performed at release and on stability. Moreover, removing a test from the regulatory specification is not an annual reportable change. As such, we suggest that you provide acceptable scientific justification for removing the microbial limit test and submit this change post-approval in the form of a Prior Approval supplement.

If you have any questions, call Don Henry, Regulatory Project Manager, at (301) 796-4227.

Sincerely,

*{See appended electronic signature page}*

Ramesh Sood, Ph.D.  
Branch Chief  
Division of Pre-Marketing Assessment I  
Office of New Drug Quality Assessment  
Center for Drug Evaluation and Research

Application  
Type/Number

Submission  
Type/Number

Submitter Name

Product Name

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NDA-22525

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LABORATORIES  
INC

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/s/  
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MARTHA R HEIMANN  
04/14/2010  
for Ramesh Sood



NDA 22-525

**INFORMATION REQUEST**

Forest Laboratories, Inc.  
Attention: Michael P. Niebo  
Asst. Director, Regulatory Affairs  
Harborside Financial Center  
Plaza V, Suite 1900  
Jersey City, NJ 07311

Dear Mr. Niebo:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Namenda XR (memantine hydrochloride) extended release capsules.

We are reviewing the Chemistry, Manufacturing, and Controls sections of your submission and have the following comments and information requests. We request a prompt written response in order to continue our evaluation of your NDA.



(b) (4)

If you have any questions, call Don Henry, Regulatory Project Manager, at (301) 796-4227.

Sincerely,

*{See appended electronic signature page}*

Ramesh Sood, Ph.D.  
Branch Chief  
Division of Pre-Marketing Assessment I  
Office of New Drug Quality Assessment  
Center for Drug Evaluation and Research

Application  
Type/Number

Submission  
Type/Number

Submitter Name

Product Name

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NDA-22525

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/s/  
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MARTHA R HEIMANN

04/06/2010



NDA 22-525

**INFORMATION REQUEST**

Forest Laboratories, Inc.  
Attention: Michael P. Niebo  
Asst. Director, Regulatory Affairs  
Harborside Financial Center  
Plaza V, Suite 1900  
Jersey City, NJ 07311

Dear Mr. Niebo:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Namenda XR (memantine hydrochloride) extended release capsules.

We are reviewing the Chemistry, Manufacturing, and Controls sections of your submission and have the following comments and information requests. We request a prompt written response in order to continue our evaluation of your NDA.

1. Provide certificates of analyses for the drug substance lots used in the manufacture of the primary stability batches and in the clinical study.
2. The validation report of the (b) (4) procedure used for identification and degradation product determination is devoid of the following validation characteristics: linearity, precision, sensitivity (LOD and LOQ), accuracy and selectivity. Provide complete validation data for the (b) (4) procedure.
3. Include a test and an acceptance criterion for the microbial limits in the drug product specification or provide justification for the exclusion as per ICH Q6A.
4. Update the post-approval stability commitment to include storage under accelerated conditions for the first three commercial batches as per ICH Q1A (R2).
5. Update the current stability protocol and the post-approval stability protocol to include a (b) (4) time point to confirm the proposed expiration period since you are seeking (b) (4) expiration dating period for your product.
6. You indicate that the stability samples employed the (b) (4) seal and that the (b) (4) inner seal will be used for the commercial product. Explain the impact of this seal change on the protective ability of the container closure system and provide supporting data.

If you have any questions, call Don Henry, Regulatory Project Manager, at (301) 796-4227.

Sincerely,

*{See appended electronic signature page}*

Ramesh Sood, Ph.D.  
Branch Chief  
Division of Pre-Marketing Assessment I  
Office of New Drug Quality Assessment  
Center for Drug Evaluation and Research

Application  
Type/Number

Submission  
Type/Number

Submitter Name

Product Name

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NDA-22525

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HCL)ER CAPSULES

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/s/  
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RAMESH K SOOD

03/22/2010

## **NDA 22-525 Namenda extended release**

**Date: Thursday, January 14, 2010**

### **FDA Attendees:**

Katz, Russell – Division Director; Mani, Ranjit – CDTL and Clinical Reviewer; Freed, Lois – Nonclinical Supervisor; Hawver, David – Nonclinical Reviewer; Heimann, Martha - CMC PAL; Men, Angela – Clinical Pharmacology Supervisor; Jin, Kun - Biometrics Team Leader; Purohit-Sheth, Tejashri; El Hage, Antoine N – DSI Reviewer; Suarez, Sandra – Biopharmaceutics Reviewer; Baweja, Raman – Clinical Pharmacology Team Leader; McLamore, Sherita – CMC Reviewer; Kelley, Laurie; M; Kortepeter, Cindy; Chan, Irene Z.; Yu, Bei; Zhang, Huixia; Zhu, Hao - Pharmacometrics; Mehta, Mehul U; Wang, Yaning - Pharmacometrics; Skelly, Michael F – DSI, Bioequivalence; Yau, Martin- DSI, Bioequivalence

## **Mid-Cycle Meeting Agenda Template**

### 1. Important Goal Dates

*Review Completion Goal Date according to GRMP: May 24, 2010*

*PDUFA Goal Date: June 21, 2010*

### 2. Discipline Specific Reviews of Application (handouts provided)

- Applicable studies/information submitted
- Status of your review of the data
- Discussion of findings so far
- Identification of need for additional input from review team or through additional consults
- Information requests to be sent to sponsor
  - a. CMC – Sherita McLamore – no issues
  - b. P/T – Dave Hawver – dose adjustment based on exposure not considered by sponsor. (see handout). This may need to be addressed either in labeling or as a phase 4 study
  - c. Clin Pharm/Biopharm – Mehta, Mehul U; Wang, Yaning (see handout) – alcohol dose dumping may require a phase 4 PMR
  - d. Clinical – Ranjit Mani – no issues
  - e. Labeling – animal exposure date may considered for labeling

### 3. Pending Consults

- Tradename (DDMETS) – 90-day consult should be submitted early, if Division plans to act early
- DSI Inspection- Due date – April 1, 2010 (El Hage, Antoine N), Clinical Pharmacology Bioequivalence Inspection - Skelly, Michael F – DSI, Bioequivalence; Yau, Martin- DSI, Bioequivalence

### 4. Issues Requiring Resolution - name/time required on agenda

- If Namenda (approved label) is changed to incorporate animal exposure concern, then the Generics Division should be informed.

5. Labeling Issues - name/time required on agenda

- See #4

6. Scheduled Meetings

Team Meetings:

Wrap-Up: March 29, 2010

Labeling: May 24, 2010

## NDA 22-525 Namenda XR Capsules for Moderate to Severe AD

The majority of the following label information is extracted verbatim from the currently approved Namenda label, Rev. 04/2007 and thus is not annotated. The abbreviation CL (current label) is used to show completeness.

| Draft Text   | Annotation  |
|--|---|
| <p><b>13.2 Animal Toxicology</b></p> <p>Memantine induced neuronal lesions (vacuolation and necrosis) in the multipolar and pyramidal cells in cortical layers III and IV of the posterior cingulate and retrosplenial neocortices in rats, similar to those which are known to occur in rodents administered other NMDA receptor antagonists. Lesions were seen after a single dose of memantine. In a study in which rats were given daily oral doses of memantine for 14 days, the no-effect dose for neuronal necrosis was 4 times the maximum recommended human dose on a mg/m<sup>2</sup> basis. In a juvenile rat toxicity study, memantine induced neuronal lesions in the anterior ventral nucleus of the thalamus and the lateral nucleus of the mammillary bodies of the brain in pups of age 15 and/or 17 days. The no effect dose for neuronal degeneration was 5 times the MRHD on a mg/m<sup>2</sup> basis. The potential for induction of central neurodegenerative lesions by NMDA receptor antagonists in humans is unknown.</p> | <p>CL<br/>(calculations revised based on MRHD of 28 mg/day)</p> |

Exposure ratios for NOAELs for brain lesions in the 28-Day oral combination toxicity study in rat, compared to steady state levels at the maximum recommended dose of 28 mg/day ER Memantine + 10 mg/day Donepezil:

10 mg/kg/day MEM,                      Day 28 Cmax = ~**3.3X**                      Day 28 AUC<sub>0-24 hr</sub> = ~**1.2X**

+ 3 mg/kg/day DPZ,                      Day 28 Cmax = ~**1.8X**                      Day 28 AUC<sub>0-24 hr</sub> = ~**0.6X**

Exposure ratios at the LOEL for lesions:

30 mg/kg/day MEM,                      Day 28 Cmax = ~**8.5X**                      Day 28 AUC<sub>0-24 hr</sub> = ~**4.6X**

+ 10 mg/kg/day DPZ,                      Day 28 Cmax = ~**5.7X**                      Day 28 AUC<sub>0-24 hr</sub> = ~**2.7X**

(Note: Cmax and AUC ratios above were means of 3 groups for each MEM dose [0, 3, & 10 mg/day DPZ] and 5 groups for each DPZ dose [0, 3, 10, 30, & 60 mg/day MEM])

|  | MEM Cmax      |               | MEM AUC         |              | DPZ Cmax    |             | DPZ AUC <sub>0-24</sub> |             |
|--|---------------|---------------|-----------------|--------------|-------------|-------------|-------------------------|-------------|
|  | ng/mL         | Margin        | ng*hr/<br>mL    | margin       | ng/mL       | margin      | ng*hr/<br>mL            | margin      |
| Estimated Maximal Human Plasma Exposure Steady State (28 QD MEM + 10 QD DPZ) | 163           | --            | 3058            | --           | 61          | --          | 1128                    | --          |
| No Neurodegeneration (Rat: 0 MEM + 3 DPZ)                                    | 0             | --            | 0               | --           | 118-<br>93  | 1.9-<br>1.5 | 425-<br>505             | 0.4-<br>0.4 |
| No Neurodegeneration (Rat: 0 MEM + 10 DPZ)                                   | 0             | --            | 0               | --           | 218-<br>398 | 3.6-<br>6.5 | 1522-<br>2170           | 1.3-<br>1.9 |
| No Neurodegeneration (Rat: 3 MEM + 0 DPZ)                                    | 98-<br>184    | 0.6-<br>1.1   | 527-<br>681     | 0.2-<br>0.2  | 0           | --          | 0                       | --          |
| No Neurodegeneration (Rat: 3 MEM + 3 DPZ)                                    | 94-<br>140    | 0.6-<br>0.9   | 673-<br>776     | 0.2-<br>0.3  | 75-<br>110  | 1.2-<br>1.8 | 450-<br>508             | 0.4-<br>0.5 |
| No Neurodegeneration (Rat: 3 MEM + 10 DPZ)                                   | 94-<br>128    | 0.6-<br>0.8   | 722-<br>905     | 0.2-<br>0.3  | 218-<br>386 | 3.6-<br>6.3 | 2049-<br>2618           | 1.8-<br>2.3 |
| No Neurodegeneration (Rat: 10 MEM + 0 DPZ)                                   | 389-<br>516   | 2.4-<br>3.2   | 2852-<br>3464   | 0.9-<br>1.1  | 0           | --          | 0                       | --          |
| No Neurodegeneration (Rat: 10 MEM + 3 DPZ)                                   | 399-<br>684   | 2.4-<br>4.2   | 3042-<br>3841   | 1.0-<br>1.3  | 96-<br>147  | 1.6-<br>2.4 | 534-<br>687             | 0.5-<br>0.6 |
| No Neurodegeneration (Rat: 10 MEM + 10 DPZ)                                  | 324-<br>428   | 2.0-<br>2.6   | 2821-<br>3449   | 0.9-<br>1.1  | 265-<br>467 | 4.3-<br>7.7 | 2348-<br>3035           | 2.1-<br>2.7 |
| No Neurodegeneration (Rat: 30 MEM + 0 DPZ)                                   | 1024-<br>1988 | 6.3-<br>12.2  | 9571-<br>15595  | 3.1-<br>5.1  | 0           | --          | 0                       | --          |
| No Neurodegeneration (Rat: 30 MEM + 3 DPZ)                                   | 878-<br>2171  | 5.4-<br>13.3  | 9785-<br>16092  | 3.2-<br>5.3  | 52-<br>148  | 0.9-<br>2.4 | 427-<br>756             | 0.4-<br>0.7 |
| Marked Neurodegeneration in Entorhinal Ctx of 1/9 (Rat: 30 MEM + 10 DPZ)     | 1048-<br>1390 | 6.4-<br>8.5   | 10553-<br>13948 | 3.5-<br>4.6  | 241-<br>347 | 4.0-<br>5.7 | 2107-<br>2993           | 1.9-<br>2.7 |
| Mild or Marked Neurodegeneration in 2/7 (Rat: 60 MEM + 10 DPZ)               | 1656-<br>3822 | 10.2-<br>23.4 | 24607-<br>40610 | 8.0-<br>13.3 | 203-<br>475 | 3.3-<br>7.8 | 2254-<br>4309           | 2.0-<br>3.8 |
| Mild Neurodegeneration in Retrosplenial Ctx of 1/10 (Rat: 60 MEM + 3 DPZ)    | 1863-<br>3388 | 11.4-<br>20.8 | 28279-<br>43805 | 9.2-<br>14.3 | 68-<br>59   | 1.1-<br>1.0 | 666-<br>754             | 0.6-<br>0.7 |
| Mild Neurodegeneration in Retrosplenial Ctx of 1/9 (Rat: 60 MEM + 0 DPZ)     | 1724-<br>3046 | 10.6-<br>18.7 | 19429-<br>37774 | 6.4-<br>12.4 | 0           | --          | 0                       | --          |

(Note: Ranges represent Day 1-Day 28 values; Reviewer's Table)

In Study MEM-PK-23 (NDA 22-525 Namenda XR for AD, submitted 20 AUG 2009), oral administration of 28 mg q.d. ER Memantine in healthy subjects resulted in mean steady state C<sub>max</sub> = 163 ng/mL and mean AUC<sub>0-24 hr</sub> = 3058 ng\*hr/mL (see table below); individual C<sub>max</sub> values were as high as 381 ng/mL.

| Mean Steady-State Pharmacokinetic Parameters of Memantine on Day 29 Following Administration of either 10-mg IR (Treatment A) Memantine HCl Tablet or 28-mg ER (Treatment B) Memantine HCl Capsule |   |  |                                   |                      |
|--|---|--|-----------------------------------|----------------------|
| PK Parameter   | 10-mg IR Tablet,<br>Mean ± SD<br>(N = 20)   | 28-mg ER Capsule,<br>Mean ± SD<br>(N = 20) | Ratio of Geometric<br>Means,<br>% | 90% CI or<br>p-Value |
| C <sub>max,ss</sub> , ng/mL  | 109.19 ± 36.62                              | 163.06 ± 68.17                             | 147.9                             | 134.51-162.66        |
| C <sub>min,ss</sub> , ng/mL  | 95.90 ± 27.19                               | 113.54 ± 35.19                             | 116.4                             | 104.23-130.01        |
| C <sub>av</sub> , ng/mL  | 93.46 ± 25.50                               | 127.41 ± 34.73                             | —                                 | —                    |
| AUC <sub>0-τ</sub> , ng*hr/mL  | 1121.47 ± 306.06                            | 3057.87 ± 833.39                           | —                                 | —                    |
| AUC <sub>0-24</sub> , ng*hr/mL   | 2324.62 ± 652.68                            | 3057.87 ± 833.39                           | 132.7                             | 123.08-143.13        |
| T <sub>½</sub> , h   | 58.47 ± 10.88                               | 56.69 ± 8.44                               | —                                 | —                    |
| T <sub>max,ss</sub> , h  | 6.59 ± 3.71<br>7.0 (2.0-11.95) <sup>a</sup> | 9.45 ± 3.79<br>9.0 (6.0-16.0) <sup>a</sup> | —                                 | p = 0.100            |
| Swing  | 0.15 ± 0.12 <sup>b</sup>                    | 0.48 ± 0.50                                | —                                 | —                    |
| Fluctuation  | 0.15 ± 0.11 <sup>b</sup>                    | 0.37 ± 0.29                                | —                                 | —                    |
| AI   | 7.27 ± 1.42                                 | 4.62 ± 1.34                                | —                                 | —                    |
| CL/F, L/h  | 7.87 ± 1.83                                 | 8.20 ± 2.38                                | —                                 | —                    |

a Median (range).  
b N = 17.  
AI = accumulation index; AUC<sub>0,τ</sub> = area under the plasma concentration versus time during the dosing interval τ at steady state;  
C<sub>av</sub> = average steady-state plasma drug concentration; CL/F = oral plasma clearance; C<sub>max,ss</sub> = maximum plasma drug concentration at steady state; C<sub>min,ss</sub> = minimum plasma drug concentration at steady state; PK = pharmacokinetic; T<sub>½</sub> = terminal elimination half-life; T<sub>max,ss</sub> = time of maximum plasma drug concentration following administration at steady state.  
Cross-reference: Tables 14.2-8 and 14.2-9.

(page 5 of Study MEM-PK-23)

8 Page(s) has been Withheld in Full as b4 (CCI/TS) immediately following this page

Application  
Type/Number

Submission  
Type/Number

Submitter Name

Product Name

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NDA-22525

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NAMENDA XR(MEMANTINE  
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TERESA A WHEELOUS

01/20/2010



NDA 022525

**PROPRIETARY NAME REQUEST  
CONDITIONALLY ACCEPTABLE**

Forest Laboratories, Inc.  
Harborside Financial Center  
Plaza Five, Suite 1900  
Jersey City, New Jersey 07311

ATTENTION: Michael P. Niebo  
Assistant Director, Regulatory Affairs

Dear Mr. Niebo:

Please refer to your New Drug Application (NDA) dated August 21, 2009, received August 21, 2009, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Memantine Hydrochloride Extended-release Capsules 7 mg, 14 mg, 21 mg and 28 mg.

We also refer to your October 6, 2009, correspondence, received October 7, 2009, requesting review of your proposed proprietary name, Namenda XR. We have completed our review of the proposed proprietary name, Namenda XR and have concluded that it is acceptable.

The proposed proprietary name, Namenda XR, will be re-reviewed 90 days prior to the approval of the NDA. If we find the name unacceptable following the re-review, we will notify you.

If **any** of the proposed product characteristics as stated in your October 6, 2009 submission are altered prior to approval of the marketing application, the proprietary name should be resubmitted for review.

If you have any questions regarding the contents of this letter or any other aspects of the proprietary name review process, contact Laurie Kelley, Safety Regulatory Project Manager in the Office of Surveillance and Epidemiology, at (301) 796-5068.

For any other information regarding this application contact the Office of New Drugs (OND) Regulatory Project Manager, Teresa Wheelous at (301) 796-1161.

Sincerely,

*{See appended electronic signature page}*

Carol Holquist, RPh

Director

Division of Medication Error Prevention and Analysis

Office of Surveillance and Epidemiology

Center for Drug Evaluation and Research

| Application Type/Number | Submission Type/Number | Submitter Name          | Product Name                         |
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DENISE P TOYER on behalf of CAROL A HOLQUIST  
12/29/2009



NDA 22-525

**FILING COMMUNICATION**

Forest Laboratories, Inc.  
Attention: Michael P. Niebo  
Asst. Director, Regulatory Affairs  
Harborside Financial Center  
Plaza V, Suite 1900  
Jersey City, NJ 07311

Dear Mr. Niebo:

Please refer to your new drug application (NDA) dated August 21, 2009 received August 21, 2009, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act, for Namenda XR (memantine hydrochloride) extended release capsules 7 mg, 14 mg, 21 mg, & 28 mg.

We also refer to your submission dated October 19, 2009, which provides the requested clinical pharmacology information regarding dose dumping.

We have completed our filing review and have determined that your application is sufficiently complete to permit a substantive review. Therefore, this application is considered filed 60 days after the date we received your application in accordance with 21 CFR 314.101(a). The review classification for this application is **Standard**. Therefore, the user fee goal date is June 21, 2010.

We are reviewing your application according to the processes described in the Guidance for Review Staff and Industry: Good Review Management Principles and Practices for PDUFA Products. Therefore, we have established internal review timelines as described in the guidance, which includes the timeframes for FDA internal milestone meetings (e.g., filing, planning, mid-cycle, team and wrap-up meetings). Please be aware that the timelines described in the guidance are flexible and subject to change based on workload and other potential review issues (e.g., submission of amendments). We will inform you of any necessary information requests or status updates following the milestone meetings or at other times, as needed, during the process. If major deficiencies are not identified during the review, we plan to communicate proposed labeling and, if necessary, any postmarketing commitment requests by May 21, 2010.

We have the following information requests:

**CLINICAL PHARMACOLOGY**

Please provide the full and complete study report of the in vitro dose-dumping alcohol effect study for all strengths of Memantine XR. This report should be submitted to the NDA within 30 days of the receipt of the 74-day letter.

**BIOPHARMACEUTICS**

(b) (4)

**REQUIRED PEDIATRIC ASSESSMENTS**

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We acknowledge receipt of your request for a full waiver of pediatric studies for this application. Once we have reviewed your request, we will notify you if the full waiver request is denied and a pediatric drug development plan is required.

If you have any questions, call Teresa Wheelous, Sr. Regulatory Management Officer, at (301) 796-1161.

Sincerely,

*{See appended electronic signature page}*

Russell Katz, M.D.  
Director  
Division of Neurology Products  
Office of Drug Evaluation 1  
Center for Drug Evaluation and Research

Application  
Type/Number

Submission  
Type/Number

Submitter Name

Product Name

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NDA-22525

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RUSSELL G KATZ

11/02/2009

**DSI CONSULT**  
**Request for Biopharmaceutical Inspections**

**DATE:** October 23, 2009

**TO:** Associate Director for Bioequivalence  
Division of Scientific Investigations, HFD-48

**THROUGH:** Russell Katz, M.D.  
Director, Review Division, HFD-120  
  
Director, Division of Pharmaceutical Evaluation, HFD-120

**FROM:** Teresa Wheelous, Sr. Regulatory Management Officer, Division of Neurology Products,  
HFD-120

**SUBJECT: Request for Biopharmaceutical Inspections**  
NDA 22-525  
Namenda XR (memantine hydrochloride) extended release capsules 7 mg, 14 mg, 21 mg,  
& 28 mg.  
  
Forest Laboratories, Inc.

**Study/Site Identification:**

OCP requests the inspection of the following Bio-study for both its clinical and analytical aspects:

**Study number:** MEM-PK-17

**Title:** Study MEM-PK-17: A Randomized, Open-label, Three-Way Crossover, Single-Dose Bioequivalence and Food-Effect Study of the Clinical Formulation and the to-Be-Marketed Modified-Release Formulation of Memantine HCl in Healthy Human Subjects.

The study is found in module 5.3.1.2 mem-pk-17.

The following was obtained from the jacket but DSI should confirm the locations before they go for the inspection:

Clinical site: [REDACTED] (b) (4) [REDACTED]  
Analytical site: Forest Research Institute

The NDA is an electronic submission. The necessary information can be found in the network location as follows: [http://edr.fda.gov:7777/edr/EDR\\_Main.jsp](http://edr.fda.gov:7777/edr/EDR_Main.jsp)

**Goal Date for Completion:**

OCP requests that the inspection report be sent by **April 1, 2010**. The clinical division intends to issue an action letter on this application by **June 21, 2010**.

Should you require any additional information, please contact the following:

Concurrence: (Optional)

Name - Clinical Pharmacology Team Leader: Raman Baweja 301-796-1503

Name - Medical Reviewer: Ranjit Mani

Name – PM – Teresa Wheelous 301-796-1161

| Application Type/Number | Submission Type/Number | Submitter Name          | Product Name                         |
|-------------------------|------------------------|-------------------------|--------------------------------------|
| NDA-22525               | ORIG-1                 | FOREST LABORATORIES INC | NAMENDA XR(MEMANTINE HCL)ER CAPSULES |

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/s/

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TERESA A WHEELOUS  
10/22/2009

RUSSELL G KATZ  
11/02/2009



NDA 22-525

**NDA ACKNOWLEDGMENT**

Forest Laboratories, Inc.  
Attention: Michael P. Niebo  
Asst. Director, Regulatory Affairs  
Harborside Financial Center  
Plaza V, Suite 1900  
Jersey City, NJ 07311

Dear Mr. Niebo:

We have received your new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for the following:

Name of Drug Product: Namenda XR (memantine hydrochloride) 7 mg, 14 mg, 21 mg, & 28 mg extended release capsules

Date of Application: August 20, 2009

Date of Receipt: August 21, 2009

Our Reference Number: NDA 22-525

Unless we notify you within 60 days of the receipt date that the application is not sufficiently complete to permit a substantive review, we will file the application on October 20, 2009 in accordance with 21 CFR 314.101(a).

If you have not already done so, promptly submit the content of labeling [21 CFR 314.50(l)(1)(i)] in structured product labeling (SPL) format as described at <http://www.fda.gov/oc/datacouncil/spl.html>. Failure to submit the content of labeling in SPL format may result in a refusal-to-file action under 21 CFR 314.101(d)(3). The content of labeling must conform to the content and format requirements of revised 21 CFR 201.56-57.

Please note that you are responsible for complying with the applicable provisions of sections 402(i) and 402(j) of the Public Health Service Act (PHS Act) (42 USC §§ 282(i) and (j)), which was amended by Title VIII of the Food and Drug Administration Amendments Act of 2007 (FDAAA) (Public Law No. 110-85, 121 Stat. 904). Title VIII of FDAAA amended the PHS Act by adding new section 402(j) (42 USC § 282(j)), which expanded the current database known as ClinicalTrials.gov to include mandatory registration and reporting of results for applicable clinical trials of human drugs (including biological products) and devices. FDAAA requires that, at the time of submission of an application under section 505 of the FDCA, the application must be accompanied by a certification that all applicable requirements of 42 USC § 282(j) have been met. Where available, the certification must include the appropriate National Clinical Trial

(NCT) control numbers. 42 USC 282(j)(5)(B). You did not include such certification when you submitted this application. You may use Form FDA 3674, *Certification of Compliance, under 42 U.S.C. § 282(j)(5)(B), with Requirements of ClinicalTrials.gov Data Bank*, to comply with the certification requirement. The form may be found at <http://www.fda.gov/opacom/morechoices/fdaforms/default.html>.

In completing Form FDA 3674, you should review 42 USC § 282(j) to determine whether the requirements of FDAAA apply to any clinical trials referenced in this application. Additional information regarding the certification form is available at: [http://internet-dev.fda.gov/cder/regulatory/FDAAA\\_certification.htm](http://internet-dev.fda.gov/cder/regulatory/FDAAA_certification.htm). Additional information regarding Title VIII of FDAAA is available at: <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-08-014.html>. Additional information on registering your clinical trials is available at the Protocol Registration System website <http://prsinfo.clinicaltrials.gov/>.

The NDA number provided above should be cited at the top of the first page of all submissions to this application. Send all submissions, electronic or paper, including those sent by overnight mail or courier, to the following address:

Food and Drug Administration  
Center for Drug Evaluation and Research  
Division of Neurology Products  
5901-B Ammendale Road  
Beltsville, MD 20705-1266

All regulatory documents submitted in paper should be three-hole punched on the left side of the page and bound. The left margin should be at least three-fourths of an inch to assure text is not obscured in the fastened area. Standard paper size (8-1/2 by 11 inches) should be used; however, it may occasionally be necessary to use individual pages larger than standard paper size. Non-standard, large pages should be folded and mounted to allow the page to be opened for review without disassembling the jacket and refolded without damage when the volume is shelved. Shipping unbound documents may result in the loss of portions of the submission or an unnecessary delay in processing which could have an adverse impact on the review of the submission. For additional information, please see <http://www.fda.gov/cder/ddms/binders.htm>.

If you have any questions, call me at (301) 796-1161.

Sincerely,

*{See appended electronic signature page}*

Teresa Wheelous, R. Ph  
Sr. Regulatory Management Officer  
Division of Neurology Products  
Office of Drug Evaluation 1  
Center for Drug Evaluation and Research

Application  
Type/Number

Submission  
Type/Number

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/s/  
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TERESA A WHEELOUS

09/29/2009

### CERTIFICATION: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

TO BE COMPLETED BY APPLICANT

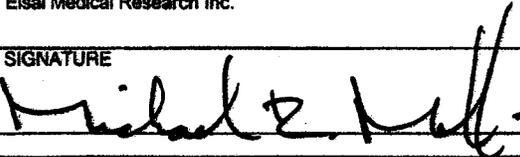
With respect to all covered clinical studies (or specific clinical studies listed below (if appropriate)) submitted in support of this application, I certify to one of the statements below as appropriate. I understand that this certification is made in compliance with 21 CFR part 54 and that for the purposes of this statement, a clinical investigator includes the spouse and each dependent child of the investigator as defined in 21 CFR 54.2(d).

Please mark the applicable checkbox.

- (1) As the sponsor of the submitted studies, I certify that I have not entered into any financial arrangement with the listed clinical investigators (enter names of clinical investigators below or attach list of names to this form) whereby the value of compensation to the investigator could be affected by the outcome of the study as defined in 21 CFR 54.2(a). I also certify that each listed clinical investigator required to disclose to the sponsor whether the investigator had a proprietary interest in this product or a significant equity in the sponsor as defined in 21 CFR 54.2(b) did not disclose any such interests. I further certify that no listed investigator was the recipient of significant payments of other sorts as defined in 21 CFR 54.2(f).

|                        |                   |  |
|------------------------|-------------------|--|
| Clinical Investigators | see attached list |  |
|                        |                   |  |
|                        |                   |  |

- (2) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that based on information obtained from the sponsor or from participating clinical investigators, the listed clinical investigators (attach list of names to this form) did not participate in any financial arrangement with the sponsor of a covered study whereby the value of compensation to the investigator for conducting the study could be affected by the outcome of the study (as defined in 21 CFR 54.2(a)); had no proprietary interest in this product or significant equity interest in the sponsor of the covered study (as defined in 21 CFR 54.2(b)); and was not the recipient of significant payments of other sorts (as defined in 21 CFR 54.2(f)).
- (3) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that I have acted with due diligence to obtain from the listed clinical investigators (attach list of names) or from the sponsor the information required under 54.4 and it was not possible to do so. The reason why this information could not be obtained is attached.

|  |   |
|--|---|
| NAME<br>Michael R. Melfi, CPA  | TITLE<br>Director of Finance and Accounting |
| FIRM/ORGANIZATION<br>Eisai Medical Research Inc.   |   |
| SIGNATURE<br> | DATE<br>Sept. 1, 2009                       |

#### Paperwork Reduction Act Statement

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number. Public reporting burden for this collection of information is estimated to average 1 hour per response, including time for reviewing instructions, searching existing data sources, gathering and maintaining the necessary data, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information to the address to the right:

Department of Health and Human Services  
Food and Drug Administration  
5600 Fishers Lane, Room 14C-03  
Rockville, MD 20857

**Attachment 1 to Form 3454:**

Clinical investigators with no disclosable financial arrangements for the study sponsored by (b) (4)

**E2020-G000-326**

| Site # | Investigator Names | Facility |
|--------|--------------------|----------|
|--------|--------------------|----------|



(b) (4)

34 Pages withheld in full immediately following this page as (b)(6).



**Form 3455:**

FDA Form 3455 does not apply to any investigator who participated in study E2020-G000-326, as there were no financial interests or arrangements to be disclosed as defined in 21 CFR 54.2.