

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

203340Orig1s000

**ADMINISTRATIVE and CORRESPONDENCE
DOCUMENTS**



DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

NDA 203340

**PROPRIETARY NAME REQUEST
CONDITIONALLY ACCEPTABLE**

Arbor Pharmaceuticals, Inc.
980 Hammond Drive, Suite 1250
Atlanta, GA 30328

ATTENTION: Allison Lowry
Director, Regulatory Affairs

Dear Ms. Lowry:

Please refer to your New Drug Application (NDA) submitted and received November 20, 2012, submitted under section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Nimodipine Oral Solution, 60 mg/20 mL.

We also refer to your correspondence, submitted and received November 30, 2012, requesting review of your proposed proprietary name, Nymalize. We have completed our review of the proposed proprietary name, Nymalize and have concluded that it is acceptable.

The proposed proprietary name, Nymalize, 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 November 30, 2012 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, Vanda Kishore, at (301) 796-4193.

Sincerely,

{See appended electronic signature page}

Carol Holquist, RPh

Director

Division of Medication Error Prevention and Analysis

Office of Medication Error Prevention and Risk Management

Office of Surveillance and Epidemiology

Center for Drug Evaluation and Research

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

LAURIE A KELLEY
02/27/2013

CAROL A HOLQUIST
02/27/2013



NDA 203340

**ACKNOWLEDGE –
CLASS 2 RESPONSE**

Arbor Pharmaceuticals
Attention: Allison Lowry
Director, Quality and Regulatory Affairs
980 Hammond Drive, Suite 1250
Atlanta, GA 30328

Dear Ms. Lowry:
:

We acknowledge receipt on November 20, 2012, of your November 20, 2012, resubmission of your new drug application submitted under section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Nymalize, (nimodipine) 60mg/20ml Oral Solution.

We consider this a complete, class 2 response to our August 16, 2012, action letter. Therefore, the user fee goal date is May 19, 2013.

If you have any questions, call me, Vandna Kishore, R.Ph., Regulatory Project Manager, at (301) 796-4193.

Sincerely,

{See appended electronic signature page}

Vandna Kishore, R.Ph.
Regulatory Project Manager
Division of Neurology Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

VANDNA N KISHORE
11/28/2012

ONDQA
request
via email

Kishore, Vandna N

From: Bouie, Teshara
Sent: Monday, July 30, 2012 10:43 AM
To: Allison Lowry
Cc: Kishore, Vandna N
Subject: NDA 203340 - Information Request

Hi Alison,

In the current version of your proposed shelf life specification (Table Fifteen, 3.2.P.8.1 Stability Summary & Conclusion in Amendment #9), (b) (4) does not have an acceptance criterion. Either add the acceptance criterion or remove the test from the specification table. Provide a single consolidated specification for the drug product which would be considered as the regulatory specification for the drug product. This table should include all the tests and acceptance criteria that the product must meet at release and during the shelf-life.

We request a prompt response to this request.

Regards,

Teshara G. Bouie, MSA, OTR/L
CDR, United States Public Health Service
Regulatory Health Project Manager
FDA/CDER/OPS/ONDQA
Division of New Drug Quality Assessment I
Phone (301) 796-1649
Fax (301) 796-9749

Kishore, Vandna N

From: Kishore, Vandna N
Sent: Tuesday, July 10, 2012 2:27 PM
To: 'Allison Lowry'
Cc: Kishore, Vandna N
Subject: RE: NDA 203340 Nimodipine oral solution labeling update request

Hi Allison,

Please see additional comment from our review team in response to your latest labeling submission:

Amber Oral Syringe:

1. Increase the prominence of the established name so it is at least half the size of the proprietary name and has prominence commensurate with the proprietary name taking into account all pertinent factors including typography, layout, contrast and other printing features per 21 CFR 201.10(g)(2).
2. Remove the [REDACTED] ^{(b) (4)} from the oral syringe.
3. Decrease the size of the statement [REDACTED] ^{(b) (4)} on the amber syringe so it has less prominence than that of the established name and proprietary name statements; however it should retain some prominence, as this is an important statement for this device.

Since we are towards the end of the review cycle, I'm going to ask you to submit this updated information as soon as possible please.

Also, was the stability data mentioned below submitted?

Thanks,

Vandna

From: Allison Lowry [mailto:ALowry@arborpharma.com]
Sent: Tuesday, June 26, 2012 11:50 AM
To: Kishore, Vandna N
Subject: RE: NDA 203340 Nimodipine oral solution labeling update request

Thanks, Vandna. I'll get this out to you this week as we are not in the office next week. I'll monitor email though in case there is an urgent request.
Should we be expecting more comments to the package insert that you are aware?

Also, we have another stability report that has some additional data through May. Would the team like us to submit it? If so, I can have it over this Friday.

Thanks
Allison

Allison Lowry
Director, Regulatory Affairs
Arbor Pharmaceuticals, Inc.
678-334-2428

From: Kishore, Vandna N [mailto:Vandna.Kishore@fda.hhs.gov]
Sent: Tuesday, June 26, 2012 10:57 AM
To: Allison Lowry
Subject: RE: NDA 203340 Nimodipine oral solution labeling update request

Hi Allison,

Please find another request regarding the ongoing review of Nymalize. We ask that you submit updated information as soon as possible, but no later than 7/2/12.

16 Ounce Bottle Container Label, 20 mL Unit-Dose Cup Carton Labeling, 20 mL Unit-Dose Cup Label,
(b) (4) Labeling for the Unit-Dose Cup:

The proposed product is a solution. The Applicant states that it will not be necessary to (b) (4)
(b) (4) (b) (4) Therefore, remove
the statement (b) (4) from all container labels and carton labeling.

Thanks,
Vandna

From: Allison Lowry [mailto:ALowry@arborpharma.com]
Sent: Tuesday, June 05, 2012 10:13 AM
To: Kishore, Vandna N
Subject: RE: NDA 203340 Nimodipine oral solution labeling update request

Hi Vandna,

I have attached a picture of the syringe as it looks now with the (b) (4) Do I need to submit this formally?

Thanks
Allison

Allison Lowry
Director, Regulatory Affairs
Arbor Pharmaceuticals, Inc.
678-334-2428

From: Kishore, Vandna N [mailto:Vandna.Kishore@fda.hhs.gov]

Sent: Monday, June 04, 2012 12:42 PM
To: Allison Lowry
Subject: RE: NDA 203340 Nimodipine oral solution labeling update request

Hi Allison,

Thanks for your submission with the updated C&C comments.

One more request for you:

Can you provide another picture of the amber syringe? According to the cover letter, it states (b) (4)
(b) (4)
(b) (4) We cannot see that in the 2 pictures submitted.

Thanks,
Vandna

From: Allison Lowry [mailto:ALowry@arborpharma.com]
Sent: Monday, May 21, 2012 5:12 PM
To: Kishore, Vandna N
Subject: RE: NDA 203340 Nimodipine oral solution labeling update request

Hi Vandna,

We've received the request and will turn it around by the time indicated.

Thanks!
allison

Allison Lowry
Director, Regulatory Affairs
Arbor Pharmaceuticals, Inc.
678-334-2428

From: Kishore, Vandna N [mailto:Vandna.Kishore@fda.hhs.gov]
Sent: Monday, May 21, 2012 3:01 PM
To: Allison Lowry
Subject: NDA 203340 Nimodipine oral solution labeling update request

Hi Allison,

Please find attached comments on the labeling for this application as the review continues.

As usual, please confirm receipt, and advise acceptability of turn around time frame.

Thanks,

Vandna

From: Allison Lowry [mailto:ALowry@arborpharma.com]

Sent: Monday, May 21, 2012 1:35 PM
To: Kishore, Vandna N
Subject: RE: NDA 20334 - Goal Date Extension

Hi Vandna,

Actually, there were a few minor changes to the report. My apologies – I should have pointed that out. They are captured here:

1. In the Administration of Test Materials section of the report (8.7.1), the following sentence was added for clarification:

“The first dose on Day 2 for the Group 1 males and Day 1 for the Group 1 females was at 20 mL/kg and the second dose that day was at 15 mL/kg.”

2. There were a few tissues that were not processed to histo slides for various reasons and these were listed out on the deviations page (Appendix 1).
3. The results in the ophthalmology report for the Group 5 animals near the end of the study stated that there were no differences “among the dose groups”; however, only Group 5 was examined that day. The ophthalmology report was amended for this (Appendix 8, Amendment).
4. The histo report was amended to correct the QA statement and compliance statement (Appendix 14, Amendment 1). They both had some errors.

The only other changes were removing reference to the “draft” report and addition of a person to Responsible personnel. Otherwise, only editorial corrections for misspellings.

I’m hoping your August trip is a fun one! Meanwhile, we’ll see what transpires with the action date – thanks for checking around. I also received your note on changes to the container closure labels and will keep an eye out for them.

As always, many thanks --
Allison

Allison Lowry
Director, Regulatory Affairs
Arbor Pharmaceuticals, Inc.
678-334-2428

From: Kishore, Vandna N [<mailto:Vandna.Kishore@fda.hhs.gov>]
Sent: Monday, May 21, 2012 12:47 PM
To: Allison Lowry
Subject: RE: NDA 20334 - Goal Date Extension

Hi Allison,

I will try to get some answers to your questions below, but I do think it's premature on the expiry right now.

Also, regarding the final tox report just submitted, can you confirm the content is the same as the draft version? If there are changes, can you send us specifics on what they are. As you know, we have been using the draft version to continue the review so we want to confirm the contents.

I'd love to take an action earlier than 8/18 as I personally will be out of the country that week. But, I'm just one piece of the pie! I will talk to the team and see how things are going soon and will keep you posted if anything should change from the 8/18 time frame.

Thanks,

Vandna

From: Allison Lowry [<mailto:ALowry@arborpharma.com>]
Sent: Friday, May 18, 2012 4:40 PM
To: Kishore, Vandna N
Subject: RE: NDA 20334 - Goal Date Extension

Hi Vandna,

I wanted to let you know the Final Report for the 14-day tox study has been dispatched to FDA. Hopefully, you should have it soon.

I have a few questions that I'm hoping you can answer. We have completed validation batches and would like to get them packaged in their finished primary container for the purposes of stability (both 16 oz and 20 mL cup). We would apply the container label (16 oz) to the bottle and seal the 20 mL cup with its printed foil lidding. Would you be able to let me know if these two labeling pieces are considered final or should we anticipate additional changes? Also, I realize it may be premature, but we would also need to know expiry if that has been decided so that we could appropriately stamp the labels.

Also, for planning purposes, do you have a sense of whether review will continue to August 18 per our extension letter or is there a chance an action could occur before then?

Thanks in advance for your help. I also want to thank you again for the many efforts in working with us during the review thus far!
Allison

Allison Lowry
Director, Regulatory Affairs
Arbor Pharmaceuticals, Inc.
678-334-2428

From: Kishore, Vandna N [<mailto:Vandna.Kishore@fda.hhs.gov>]
Sent: Monday, May 14, 2012 3:06 PM
To: Allison Lowry
Subject: RE: NDA 20334 - Goal Date Extension

Thanks Allison. I meant the final signed report as that is what is needed...

Thanks,
Vandna

From: Allison Lowry [<mailto:ALowry@arborpharma.com>]
Sent: Monday, May 14, 2012 3:03 PM
To: Kishore, Vandna N
Subject: RE: NDA 20334 - Goal Date Extension

Hi Vandna,

Thank you for the update and the review work done thus far in moving the application along. I realize we were

working with a tight schedule.

The signed pathology report was included with the audited draft sent last week and we will have the final signed study report this week as promised.

It will be dispatched to the FDA on Friday, the 18th.

Again, thanks for the update and we'll look forward to next steps.

Kind regards,
Allison

Allison Lowry
Director, Regulatory Affairs
Arbor Pharmaceuticals, Inc.
678-334-2428

From: Kishore, Vandna N [<mailto:Vandna.Kishore@fda.hhs.gov>]
Sent: Monday, May 14, 2012 10:28 AM
To: Allison Lowry
Subject: RE: NDA 20334 - Goal Date Extension

Hi Allison,

Please find attached the Goal Date Extension letter for Nymalize as we felt this is the best path forward to continue our review with such a short time left.

We would still like to get the signed path report this week as planned below.

Thanks,
Vandna

From: Allison Lowry [<mailto:ALowry@arborpharma.com>]
Sent: Thursday, May 10, 2012 2:15 PM
To: Kishore, Vandna N
Subject: RE: NDA 20334 - Request for Information

Hi Vandna,

Can you accept the final mid-next week since there will not be any changes? [REDACTED] (b)(4) can get a signed report by the 16th (and we'll still try to get it sooner) and we should be able to get it over without major publishing the same day. Will that work?

Thanks,
Allison

Allison Lowry
Director, Regulatory Affairs
Arbor Pharmaceuticals, Inc.
678-334-2428

From: Kishore, Vandna N [<mailto:Vandna.Kishore@fda.hhs.gov>]
Sent: Thursday, May 10, 2012 2:09 PM
To: Allison Lowry
Subject: RE: NDA 20334 - Request for Information

Hi Allison,

Yes, we need the final signed report for action. Normally, we don't accept the draft versions, but are trying to keep reviewing in this case. End of the week, meaning tomorrow still, correct? If that is not possible, please advise ASAP.

Thanks,
Vandna

From: Allison Lowry [<mailto:ALowry@arborpharma.com>]
Sent: Thursday, May 10, 2012 1:51 PM
To: Kishore, Vandna N
Subject: RE: NDA 20334 - Request for Information

Hi Vandna,

The submission last night was the audited draft with a signed pathology report. Our intent for last night's submission was to get you the signed pathology report with the audited draft. Are you going to need the final signed report in order to potentially grant an approval or can this be a commitment? (b) (4) is checking to see if they can get the final to me within the week (and we do not anticipate any changes).

Thanks
Allison

Allison Lowry
Director, Regulatory Affairs
Arbor Pharmaceuticals, Inc.
678-334-2428

From: Kishore, Vandna N [<mailto:Vandna.Kishore@fda.hhs.gov>]
Sent: Thursday, May 10, 2012 1:32 PM
To: Allison Lowry
Subject: RE: NDA 20334 - Request for Information

Hi Allison,

We got a submission last night, but it wasn't the final signed version. Is this coming soon?

Thanks,
Vandna

From: Allison Lowry [<mailto:ALowry@arborpharma.com>]
Sent: Monday, May 07, 2012 4:58 PM
To: Kishore, Vandna N
Subject: RE: NDA 20334 - Request for Information

Hi Vanda,

(b) (4) was able to furnish the audited draft and it was dispatched this afternoon. Hopefully you'll have it soon.

Note that it did not go through full publishing before submission, but the same audited draft report (with signed

pathology report) will get published tomorrow and should get transmitted to FDA on Wednesday.

I hope this helps!

Thanks
Allison

Allison Lowry
Director, Regulatory Affairs
Arbor Pharmaceuticals, Inc.
678-334-2428

From: Kishore, Vandna N [<mailto:Vandna.Kishore@fda.hhs.gov>]
Sent: Friday, May 04, 2012 1:16 PM
To: Allison Lowry
Subject: RE: NDA 20334 - Request for Information

Sounds like a plan.

Thanks,
Vandna

From: Allison Lowry [<mailto:ALowry@arborpharma.com>]
Sent: Friday, May 04, 2012 9:49 AM
To: Kishore, Vandna N
Subject: RE: NDA 20334 - Request for Information

Hi Vandna,

We had pushed [REDACTED] ^{(b) (4)} from the 14th to the 9th and they've indicated it would be hard for them to move it any earlier. Would the unaudited draft be helpful in the interim?

I could probably get it to you Monday, the 7th if the reviewer would like. The audited draft with signed histo would follow on the 10th.

We also have a summary of the study and results coming to you today.

Thanks
allison

Allison Lowry
Director, Regulatory Affairs
Arbor Pharmaceuticals, Inc.
678-334-2428

From: Kishore, Vandna N [<mailto:Vandna.Kishore@fda.hhs.gov>]
Sent: Thursday, May 03, 2012 3:44 PM
To: Allison Lowry
Subject: RE: NDA 20334 - Request for Information

Thanks Allison.

From: Allison Lowry [<mailto:ALowry@arborpharma.com>]
Sent: Thursday, May 03, 2012 3:40 PM
To: Kishore, Vandna N
Subject: RE: NDA 20334 - Request for Information

Hi Vandna,

I'll do my best and will let you know what I find out. I may be able to get it but without the signed histo which can follow a few days later.

We have a summary coming to you tomorrow and I'll let you know about the audited draft.

Thanks
Allison

Allison Lowry
Director, Regulatory Affairs
Arbor Pharmaceuticals, Inc.
678-334-2428

From: Kishore, Vandna N [<mailto:Vandna.Kishore@fda.hhs.gov>]
Sent: Thursday, May 03, 2012 3:27 PM
To: Allison Lowry
Subject: RE: NDA 20334 - Request for Information

Hi Allison,

The sooner you can get this in, the better. If possible to get it in earlier than May 10, it would be helpful. Is that possible?

Thanks,
Vandna

From: Allison Lowry [<mailto:ALowry@arborpharma.com>]
Sent: Tuesday, May 01, 2012 3:35 PM
To: Kishore, Vandna N
Subject: RE: NDA 20334 - Request for Information

Hi Vandna,

Apologies for the delay in getting back. We have an unaudited draft report just in that we are summarizing. We were hoping to submit a summary of the report this week, then follow up with the Audited Draft Report which we've arranged to get by May 9. We are awaiting confirmation that the Audited draft report will include a signed Histopathology which we will know soon (the signed histo would be there a few days after the 9th if not then). I would then need to get it through publishing quickly and could have it to you late May 10. Will that be acceptable?

Thanks
Allison

Allison Lowry
Director, Regulatory Affairs

Arbor Pharmaceuticals, Inc.
678-334-2428

From: Kishore, Vandna N [mailto:Vandna.Kishore@fda.hhs.gov]
Sent: Tuesday, May 01, 2012 10:36 AM
To: Allison Lowry
Subject: RE: NDA 20334 - Request for Information

Hi Allison,

In regards to the toxicology report, can you be more specific as to when we will see this report as the goal date is approaching near, and the team needs to review this ASAP.

Thanks,
Vandna

From: Allison Lowry [mailto:ALowry@arborpharma.com]
Sent: Monday, April 30, 2012 5:27 PM
To: Bouie, Teshara; Kishore, Vandna N
Subject: RE: NDA 20334 - Request for Information

Good afternoon,

I wanted to let you know that an amendment has been dispatched this afternoon. As mentioned below, the unaudited draft of the toxicology report was received today and will be summarized for a submission this week. Although stability was provided in the amendment today, we'll supplement the report later this week with a summary report of the stability and proposed expiry.

Thanks!
Allison

Allison Lowry
Director, Regulatory Affairs
Arbor Pharmaceuticals, Inc.
678-334-2428

From: Allison Lowry
Sent: Friday, April 20, 2012 3:14 PM
To: 'Bouie, Teshara'; Kishore, Vandna N
Subject: RE: NDA 20334 - Request for Information

Hi Vandna and Teshara,

I have another question for you -

In our recent response (March 30) we updated the finished specifications for the (b)(4) cup to full testing. We noticed today that we inadvertently included the proposed stability specs for the (b)(4) cup rather than finished product specs.

In addition to correcting these, we have some other quicker updates to the application. Would you rather us send these in earlier next week in advance of the

stability update that will come in April 30 and the tox summary? If not, we can include most information at one time.

Also, the request for *Burkeholderia Cepacia* validation and test method (received on the 28th) are underway at both [REDACTED] (b) (4)

Thanks
Allison

Allison Lowry
Director, Regulatory Affairs
Arbor Pharmaceuticals, Inc.
678-334-2428

From: Allison Lowry
Sent: Tuesday, April 03, 2012 5:40 PM
To: 'Bouie, Teshara'; Kishore, Vandna N
Subject: RE: NDA 20334 - Request for Information

Dear Teshara,

I wanted to touch base with you on the recent Information Request letters for Nymalize. You should have received an amendment this last Friday (March 30) in response to the March 16 letter. We received the March 22 letter (by mail) on March 28 and are beginning work on the requested item #2 and can provide answers to 1 and 3 soon since they have recently been completed.

In the response of March 30 (Sequence 0007), item 8 provides a side-by-side comparison of stability data and details on additional testing. In the additional testing, we are including more unit cup analyses in the testing in addition to what is listed and anticipate this testing can be completed, reviewed and published to the FDA by April 30. Testing will be conducted at both [REDACTED] (b) (4). Any other updates mentioned will be provided in the interim prior to April 30.

Vandna,

We anticipate an unaudited report from the tox study by April 30 and can provide a summary of these results to you a few days after. We can then follow up with an audited report.

Many thanks,
Allison

Allison Lowry
Director, Regulatory Affairs
Arbor Pharmaceuticals, Inc.
678-334-2428

From: Allison Lowry
Sent: Thursday, March 22, 2012 8:13 PM
To: 'Bouie, Teshara'
Subject: RE: NDA 20334 - Request for Information

Hi Teshara,

I wanted to update you on timing of the requested information. We will have a submission leaving the publisher next Friday, the 30th, which will address most of the items in the letter. We may have some follow-up information in early April on some testing that is finishing up and

will speak to it in the submission next Friday.

Thanks
Allison

Allison Lowry
Director, Regulatory Affairs
Arbor Pharmaceuticals, Inc.
678-334-2428

From: Bouie, Teshara [<mailto:Teshara.Bouie@fda.hhs.gov>]
Sent: Friday, March 16, 2012 3:58 PM
To: Allison Lowry
Subject: NDA 20334 - Request for Information

Hi Allison,

Please see the attached request for information.
Thanks,

Teshara G. Bouie, MSA, OTR/L
CDR, United States Public Health Service
Regulatory Health Project Manager
FDA/CDER/OPS/ONDQA
Division of New Drug Quality Assessment I
Phone (301) 796-1649
Fax (301) 796-9749

Dear Allison,

In reviewing the proposed labeling for Nymalize, we recommend you make the following changes and submit revised labeling as requested here:

RECOMMENDATIONS TO THE APPLICANT

A. GENERAL COMMENTS

1. We suggest labeling the proposed (b) (4) syringe with the proprietary name, Nymalize, if possible to ensure that the correct dosing device is utilized with the proposed Nymalize oral solution.

B. 16 OUNCE BOTTLE CONTAINER LABEL

1. The dosage form, "ORAL SOLUTION," is in all upper case letters. Revise the presentation of the dosage form to be in title case to improve readability.
2. Revise the statement (b) (4) to "Store at room temperature".

C. 20 ML UNIT-DOSE CARTON LABELING

1. Revise the net quantity statement on the carton to indicate the unit-dose cups and the (b) (4) syringes are included in the box. For example, "Contains 12 Unit-Dose Cups and 12 (b) (4) Syringes."
2. Revise the statement (b) (4) to "Store at room temperature".

D. (b) (4) LABELING

1. Increase the prominence of the proprietary name, established name and statement of strength. Ensure the established name is at least half the size of the proprietary name and has prominence commensurate with the proprietary name taking into account all pertinent factors including typography, layout, contrast and other printing features per 21 CFR 201.10(g)(2).
2. Use consistent wording to describe the accompanying syringe. As currently presented, the container label and carton labeling describe it as "oral syringe" whereas the (b) (4) labeling describes it as "(b) (4) syringe."
3. Revise the statement (b) (4) to "Store at room temperature" because post-marketing medication error reports have shown that negative statements such as (b) (4) may be misinterpreted as (b) (4).
4. As currently presented, the text on the labeling appears crowded but there is plenty of space available on the labeling. In order to improve the readability of the (b) (4) labeling, separate the statements on the labeling with a line space such as the example below:

sent 5/21/12 email

Please address these above comments and submit updated labeling promptly. We request that you consolidate the updates made to the label submitted last, and the recommendations made in this communication and submit an updated labeling submission to this application.

In the interest of time, we request that you submit as soon as possible, but no later than next Tuesday, May 29th, 2012.

Thank you,
Vandna

From: Kishore, Vandna N
Sent: Tuesday, June 26, 2012 10:27 AM
To: 'Allison Lowry'
Subject: RE: NDA 203340 Nimodipine oral solution update

Hi Allison,

The team wants to see a sample of the (b) (4) oral syringe. Can you please send me one ASAP?

Thanks,
Vandna

From: Allison Lowry [mailto:ALowry@arborpharma.com]
Sent: Wednesday, June 20, 2012 4:58 PM
To: Kishore, Vandna N
Subject: RE: NDA 203340 Nimodipine oral solution update

Hi Vandna,

I wanted to update you on some information and also ask a few questions. We'll be submitting the burkholderia cepacia methods, along with their validations this Friday. They will come from both of the labs that are filed (b) (4). We are also finalizing some method transfers between the two labs (from validated methods already submitted). I will include two of these transferred methods from (b) (4) then follow up next week with two updated methods from (b) (4).

For the amber oral syringe that was sent in sequence 0014, we've sought information on having these (b) (4) will be able to perform this for us and I've attached their specification. I also attached the (b) (4) syringe for a visual photos although the actual syringe will be (b) (4). Can we get feedback from the FDA on (b) (4), we would like to proceed with the process. Also, should I submit the new syringe (b) (4) formally?

Lastly, we included a few updates to the container and carton label in 0014. Can we consider those and the cup lidding label final? If we get started on processing them, we would also need expiry dating and I realize you are checking on that. But, if you are able to get an update on those items, we would be most appreciative!

As always, many thanks,
Allison

Allison Lowry
Director, Regulatory Affairs
Arbor Pharmaceuticals, Inc.
678-334-2428

From: Kishore, Vandna N [<mailto:Vandna.Kishore@fda.hhs.gov>]
Sent: Wednesday, June 06, 2012 2:51 PM
To: Allison Lowry
Subject: RE: NDA 203340 Nimodipine oral solution (b) (4) question

Thanks Allison.

One more question, is it necessary to (b) (4) as stated in the initial package insert?

Take care,
Vandna

From: Allison Lowry [<mailto:ALowry@arborpharma.com>]
Sent: Wednesday, June 06, 2012 9:43 AM
To: Kishore, Vandna N
Subject: RE: NDA 203340 Nimodipine oral solution IR update?

Hi Vandna,

We have received the results from (b) (4) and they are in the final stages of writing the Validation Report for us. I anticipate getting the final next week. I am waiting to hear back from (b) (4) but know they are in process of testing which includes additional testing as risk assessment of materials. I'll let you asap once I am able to reach them.

Thanks
Allison

Allison Lowry
Director, Regulatory Affairs
Arbor Pharmaceuticals, Inc.
678-334-2428

From: Kishore, Vandna N [<mailto:Vandna.Kishore@fda.hhs.gov>]
Sent: Tuesday, June 05, 2012 3:56 PM
To: Allison Lowry
Subject: RE: NDA 203340 Nimodipine oral solution IR update?

Hi Allison,

Seems our Micro folks are waiting for a bit of micro data from you pertaining to an IR that we sent on March 20 and regarding testing methods and related validation for the presence of Burkholderia cepacia in this product. Would you find out when we can expect that data please?

Thanks,
Vandna

From: Allison Lowry [<mailto:ALowry@arborpharma.com>]
Sent: Tuesday, June 05, 2012 10:13 AM
To: Kishore, Vandna N
Subject: RE: NDA 203340 Nimodipine oral solution labeling update request

Hi Vandna,

I have attached a picture of the syringe as it looks now with (b) (4). Do I need to submit this formally?

Thanks
Allison

Allison Lowry
Director, Regulatory Affairs
Arbor Pharmaceuticals, Inc.
678-334-2428

From: Kishore, Vandna N [<mailto:Vandna.Kishore@fda.hhs.gov>]
Sent: Monday, June 04, 2012 12:42 PM
To: Allison Lowry
Subject: RE: NDA 203340 Nimodipine oral solution labeling update request

Hi Allison,

Thanks for your submission with the updated C&C comments.

One more request for you:

Can you provide another picture of the amber syringe? According to the cover letter, it states (b) (4)
(b) (4) We
want to see where (b) (4) We cannot see that in the 2 pictures submitted.

Thanks,
Vandna

From: Allison Lowry [<mailto:ALowry@arborpharma.com>]
Sent: Monday, May 21, 2012 5:12 PM
To: Kishore, Vandna N
Subject: RE: NDA 203340 Nimodipine oral solution labeling update request

Hi Vandna,

We've received the request and will turn it around by the time indicated.

Thanks!
allison

Allison Lowry
Director, Regulatory Affairs
Arbor Pharmaceuticals, Inc.
678-334-2428

From: Kishore, Vandna N [<mailto:Vandna.Kishore@fda.hhs.gov>]
Sent: Monday, May 21, 2012 3:01 PM
To: Allison Lowry
Subject: NDA 203340 Nimodipine oral solution labeling update request

Hi Allison,

Please find attached comments on the labeling for this application as the review continues.

As usual, please confirm receipt, and advise acceptability of turn around time frame.

Thanks,

Vandna

From: Allison Lowry [<mailto:ALowry@arborpharma.com>]
Sent: Monday, May 21, 2012 1:35 PM
To: Kishore, Vandna N
Subject: RE: NDA 20334 - Goal Date Extension

Hi Vandna,

Actually, there were a few minor changes to the report. My apologies – I should have pointed that out. They are captured here:

1. In the Administration of Test Materials section of the report (8.7.1), the following sentence was added for clarification:

“The first dose on Day 2 for the Group 1 males and Day 1 for the Group 1 females was at 20 mL/kg and the second dose that day was at 15 mL/kg.”

2. There were a few tissues that were not processed to histo slides for various reasons and these were listed out on the deviations page (Appendix 1).
3. The results in the ophthalmology report for the Group 5 animals near the end of the study stated that there were no differences “among the dose groups”; however, only Group 5 was examined that day. The ophthalmology report was amended for this (Appendix 8, Amendment).
4. The histo report was amended to correct the QA statement and compliance statement (Appendix 14, Amendment 1). They both had some errors.

The only other changes were removing reference to the “draft” report and addition of a person to Responsible personnel. Otherwise, only editorial corrections for misspellings.

I’m hoping your August trip is a fun one! Meanwhile, we’ll see what transpires with the action date – thanks for checking around. I also received your note on changes to the container closure labels and will keep an eye out for them.

As always, many thanks --
Allison

Allison Lowry
Director, Regulatory Affairs
Arbor Pharmaceuticals, Inc.
678-334-2428

From: Kishore, Vandna N [<mailto:Vandna.Kishore@fda.hhs.gov>]
Sent: Monday, May 21, 2012 12:47 PM
To: Allison Lowry
Subject: RE: NDA 20334 - Goal Date Extension

Hi Allison,

I will try to get some answers to your questions below, but I do think it's premature on the expiry right now.

Also, regarding the final tox report just submitted, can you confirm the content is the same as the draft version? If there are changes, can you send us specifics on what they are. As you know, we have been using the draft version to continue the review so we want to confirm the contents.

I'd love to take an action earlier than 8/18 as I personally will be out of the country that week. But, I'm just one piece of the pie! I will talk to the team and see how things are going soon and will keep you posted if anything should change from the 8/18 time frame.

Thanks,
Vandna

From: Allison Lowry [<mailto:ALowry@arborpharma.com>]
Sent: Friday, May 18, 2012 4:40 PM
To: Kishore, Vandna N
Subject: RE: NDA 20334 - Goal Date Extension

Hi Vandna,

I wanted to let you know the Final Report for the 14-day tox study has been dispatched to FDA. Hopefully, you should have it soon.

I have a few questions that I'm hoping you can answer. We have completed validation batches and would like to get them packaged in their finished primary container for the purposes of stability (both 16 oz and 20 mL cup). We would apply the container label (16 oz) to the bottle and seal the 20 mL cup with its printed foil lidding. Would you be able to let me know if these two labeling pieces are considered final or should we anticipate additional changes? Also, I realize it may be premature, but we would also need to know expiry if that has been decided so that we could appropriately stamp the labels.

Also, for planning purposes, do you have a sense of whether review will continue to August 18 per our extension letter or is there a chance an action could occur before then?

Thanks in advance for your help. I also want to thank you again for the many efforts in working with us during the review thus far!
Allison

Allison Lowry
Director, Regulatory Affairs
Arbor Pharmaceuticals, Inc.
678-334-2428

From: Kishore, Vandna N [<mailto:Vandna.Kishore@fda.hhs.gov>]
Sent: Monday, May 14, 2012 3:06 PM
To: Allison Lowry
Subject: RE: NDA 20334 - Goal Date Extension

Thanks Allison. I meant the final signed report as that is what is needed....

Thanks,
Vandna

From: Allison Lowry [<mailto:ALowry@arborpharma.com>]
Sent: Monday, May 14, 2012 3:03 PM
To: Kishore, Vandna N
Subject: RE: NDA 20334 - Goal Date Extension

Hi Vandna,

Thank you for the update and the review work done thus far in moving the application along. I realize we were working with a tight schedule.

The signed pathology report was included with the audited draft sent last week and we will have the final signed study report this week as promised.

It will be dispatched to the FDA on Friday, the 18th.

Again, thanks for the update and we'll look forward to next steps.

Kind regards,
Allison

Allison Lowry
Director, Regulatory Affairs
Arbor Pharmaceuticals, Inc.
678-334-2428

From: Kishore, Vandna N [<mailto:Vandna.Kishore@fda.hhs.gov>]
Sent: Monday, May 14, 2012 10:28 AM
To: Allison Lowry
Subject: RE: NDA 20334 - Goal Date Extension

Hi Allison,

Please find attached the Goal Date Extension letter for Nymalize as we felt this is the best path forward to continue our review with such a short time left.

We would still like to get the signed path report this week as planned below.

Thanks,
Vandna

From: Allison Lowry [<mailto:ALowry@arborpharma.com>]
Sent: Thursday, May 10, 2012 2:15 PM
To: Kishore, Vandna N
Subject: RE: NDA 20334 - Request for Information

Hi Vandna,

Can you accept the final mid-next week since there will not be any changes? [REDACTED] ^{(b) (4)} can get a signed report by the 16th (and we'll still try to get it sooner) and we should be able to get it over without major publishing the same day. Will that work?

Thanks,
Allison

Allison Lowry
Director, Regulatory Affairs
Arbor Pharmaceuticals, Inc.
678-334-2428

From: Kishore, Vandna N [<mailto:Vandna.Kishore@fda.hhs.gov>]
Sent: Thursday, May 10, 2012 2:09 PM
To: Allison Lowry
Subject: RE: NDA 20334 - Request for Information

Hi Allison,

Yes, we need the final signed report for action. Normally, we don't accept the draft versions, but are trying to keep reviewing in this case. End of the week, meaning tomorrow still, correct? If that is not possible, please advise ASAP.

Thanks,
Vandna

From: Allison Lowry [<mailto:ALowry@arborpharma.com>]
Sent: Thursday, May 10, 2012 1:51 PM
To: Kishore, Vandna N
Subject: RE: NDA 20334 - Request for Information

Hi Vandna,

The submission last night was the audited draft with a signed pathology report. Our intent for last night's submission was to get you the signed pathology report with the audited draft. Are you going to need the final signed report in order to potentially grant an approval or can this be a commitment? (b) (4) is checking to see if they can get the final to me within the week (and we do not anticipate any changes).

Thanks
Allison

Allison Lowry
Director, Regulatory Affairs
Arbor Pharmaceuticals, Inc.
678-334-2428

From: Kishore, Vandna N [<mailto:Vandna.Kishore@fda.hhs.gov>]
Sent: Thursday, May 10, 2012 1:32 PM
To: Allison Lowry
Subject: RE: NDA 20334 - Request for Information

Hi Allison,

We got a submission last night, but it wasn't the final signed version. Is this coming soon?

Thanks,
Vandna

From: Allison Lowry [<mailto:ALowry@arborpharma.com>]
Sent: Monday, May 07, 2012 4:58 PM
To: Kishore, Vandna N
Subject: RE: NDA 20334 - Request for Information

Hi Vanda,

(b) (4) was able to furnish the audited draft and it was dispatched this afternoon. Hopefully you'll have it soon.

Note that it did not go through full publishing before submission, but the same audited draft report (with signed pathology report) will get published tomorrow and should get transmitted to FDA on Wednesday.

I hope this helps!

Thanks
Allison

Allison Lowry
Director, Regulatory Affairs
Arbor Pharmaceuticals, Inc.
678-334-2428

From: Kishore, Vandna N [<mailto:Vandna.Kishore@fda.hhs.gov>]
Sent: Friday, May 04, 2012 1:16 PM
To: Allison Lowry
Subject: RE: NDA 20334 - Request for Information

Sounds like a plan.

Thanks,
Vandna

From: Allison Lowry [<mailto:ALowry@arborpharma.com>]
Sent: Friday, May 04, 2012 9:49 AM
To: Kishore, Vandna N
Subject: RE: NDA 20334 - Request for Information

Hi Vandna,

We had pushed (b) (4) from the 14th to the 9th and they've indicated it would be hard for them to move it any earlier. Would the unaudited draft be helpful in the interim? I could probably get it to you Monday, the 7th if the reviewer would like. The audited draft with signed histo would follow on the 10th.

We also have a summary of the study and results coming to you today.

Thanks
allison

Allison Lowry
Director, Regulatory Affairs
Arbor Pharmaceuticals, Inc.
678-334-2428

From: Kishore, Vandna N [<mailto:Vandna.Kishore@fda.hhs.gov>]
Sent: Thursday, May 03, 2012 3:44 PM
To: Allison Lowry
Subject: RE: NDA 20334 - Request for Information

Thanks Allison.

From: Allison Lowry [<mailto:ALowry@arborpharma.com>]
Sent: Thursday, May 03, 2012 3:40 PM
To: Kishore, Vandna N
Subject: RE: NDA 20334 - Request for Information

Hi Vandna,

I'll do my best and will let you know what I find out. I may be able to get it but without the signed histo which can follow a few days later.

We have a summary coming to you tomorrow and I'll let you know about the audited draft.

Thanks
Allison

Allison Lowry
Director, Regulatory Affairs
Arbor Pharmaceuticals, Inc.
678-334-2428

From: Kishore, Vandna N [<mailto:Vandna.Kishore@fda.hhs.gov>]
Sent: Thursday, May 03, 2012 3:27 PM
To: Allison Lowry
Subject: RE: NDA 20334 - Request for Information

Hi Allison,

The sooner you can get this in, the better. If possible to get it in earlier than May 10, it would be helpful. Is that possible?

Thanks,
Vandna

From: Allison Lowry [<mailto:ALowry@arborpharma.com>]
Sent: Tuesday, May 01, 2012 3:35 PM
To: Kishore, Vandna N
Subject: RE: NDA 20334 - Request for Information

Hi Vandna,

Apologies for the delay in getting back. We have an unaudited draft report just in that we are summarizing. We were hoping to submit a summary of the report this week, then follow up with the Audited Draft Report which we've arranged to get by May 9. We are awaiting confirmation that the Audited draft report will include a signed Histopathology

which we will know soon (the signed histo would be there a few days after the 9th if not then). I would then need to get it through publishing quickly and could have it to you late May 10. Will that be acceptable?

Thanks
Allison

Allison Lowry
Director, Regulatory Affairs
Arbor Pharmaceuticals, Inc.
678-334-2428

From: Kishore, Vandna N [<mailto:Vandna.Kishore@fda.hhs.gov>]
Sent: Tuesday, May 01, 2012 10:36 AM
To: Allison Lowry
Subject: RE: NDA 20334 - Request for Information

Hi Allison,

In regards to the toxicology report, can you be more specific as to when we will see this report as the goal date is approaching near, and the team needs to review this ASAP.

Thanks,
Vandna

From: Allison Lowry [<mailto:ALowry@arborpharma.com>]
Sent: Monday, April 30, 2012 5:27 PM
To: Bouie, Teshara; Kishore, Vandna N
Subject: RE: NDA 20334 - Request for Information

Good afternoon,

I wanted to let you know that an amendment has been dispatched this afternoon. As mentioned below, the unaudited draft of the toxicology report was received today and will be summarized for a submission this week. Although stability was provided in the amendment today, we'll supplement the report later this week with a summary report of the stability and proposed expiry.

Thanks!
Allison

Allison Lowry
Director, Regulatory Affairs
Arbor Pharmaceuticals, Inc.
678-334-2428

From: Allison Lowry
Sent: Friday, April 20, 2012 3:14 PM
To: 'Bouie, Teshara'; Kishore, Vandna N
Subject: RE: NDA 20334 - Request for Information

Hi Vandna and Teshara,

I have another question for you -

In our recent response (March 30) we updated the finished specifications for the (b) (4) cup to full testing. We noticed today that we inadvertently included the proposed stability specs for the (b) (4) cup rather than finished product specs.

In addition to correcting these, we have some other quicker updates to the application. Would you rather us send these in earlier next week in advance of the stability update that will come in April 30 and the tox summary? If not, we can include most information at one time.

Also, the request for *Burkeholderia Cepacia* validation and test method (received on the 28th) are underway at both (b) (4)

Thanks
Allison

Allison Lowry
Director, Regulatory Affairs
Arbor Pharmaceuticals, Inc.
678-334-2428

From: Allison Lowry
Sent: Tuesday, April 03, 2012 5:40 PM
To: 'Bouie, Teshara'; Kishore, Vandna N
Subject: RE: NDA 20334 - Request for Information

Dear Teshara,

I wanted to touch base with you on the recent Information Request letters for Nymalize. You should have received an amendment this last Friday (March 30) in response to the March 16 letter. We received the March 22 letter (by mail) on March 28 and are beginning work on the requested item #2 and can provide answers to 1 and 3 soon since they have recently been completed.

In the response of March 30 (Sequence 0007), item 8 provides a side-by-side comparison of stability data and details on additional testing. In the additional testing, we are including more unit cup analyses in the testing in addition to what is listed and anticipate this testing can be completed, reviewed and published to the FDA by April 30. Testing will be conducted at both (b) (4). Any other updates mentioned will be provided in the interim prior to April 30.

Vandna,

We anticipate an unaudited report from the tox study by April 30 and can provide a summary of these results to you a few days after. We can then follow up with an audited report.

Many thanks,
Allison

Allison Lowry
Director, Regulatory Affairs
Arbor Pharmaceuticals, Inc.
678-334-2428

From: Allison Lowry
Sent: Thursday, March 22, 2012 8:13 PM
To: 'Bouie, Teshara'
Subject: RE: NDA 20334 - Request for Information

Hi Teshara,

I wanted to update you on timing of the requested information. We will have a submission leaving the publisher next Friday, the 30th, which will address most of the items in the letter. We may have some follow-up information in early April on some testing that is finishing up and will speak to it in the submission next Friday.

Thanks
Allison

Allison Lowry
Director, Regulatory Affairs
Arbor Pharmaceuticals, Inc.
678-334-2428

From: Bouie, Teshara [<mailto:Teshara.Bouie@fda.hhs.gov>]
Sent: Friday, March 16, 2012 3:58 PM
To: Allison Lowry
Subject: NDA 20334 - Request for Information

Hi Allison,

Please see the attached request for information.
Thanks,

Teshara G. Bouie, MSA, OTR/L
CDR, United States Public Health Service
Regulatory Health Project Manager
FDA/CDER/OPS/ONDQA
Division of New Drug Quality Assessment I
Phone (301) 796-1649
Fax (301) 796-9749



NDA 203340

**REVIEW EXTENSION –
MAJOR AMENDMENT**

Arbor Pharmaceuticals
Attention: Allison Lowry
Director, Quality and Regulatory Affairs
980 Hammond Drive, Suite 1250
Atlanta, GA 30328

Dear Ms. Lowry:

Please refer to your New Drug Application (NDA) dated November 18, 2011, received November 18, 2011, submitted under section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act, for Nimodipine 60 mg/ml Oral Solution.

On May 9, 2012, we received your May 9, 2012, solicited major amendment to this application. The receipt date is within three months of the user fee goal date. Therefore, we are extending the goal date by three months to provide time for a full review of the submission. The extended user fee goal date is August 18, 2012.

In addition, we are establishing a new timeline for communicating labeling changes and/or postmarketing requirements/commitments in accordance with "PDUFA REAUTHORIZATION PERFORMANCE GOALS AND PROCEDURES – FISCAL YEARS 2008 THROUGH 2012." If major deficiencies are not identified during our review, we plan to communicate proposed labeling and, if necessary, any postmarketing requirement/commitment requests by July 18, 2012.

If you have any questions, call Vandna Kishore, R.Ph., Regulatory Project Manager, at (301) 796-4193.

Sincerely,

{See appended electronic signature page}

Russell Katz, MD
Director
Division of Neurology Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

ERIC P BASTINGS on behalf of RUSSELL G KATZ
05/11/2012

Kishore, Vandna N

From: Kishore, Vandna N
Sent: Thursday, March 22, 2012 12:55 PM
To: 'Allison Lowry'
Subject: RE: NDA 203340 Nimodipine oral solution labeling update request
Attachments: NDA 203340 Nimodipine oral solution labeling comments to sponsor(DMEPA) 032212.pdf



NDA 203340
nimodipine oral sol..

Hi Allison,

attached

Please find attached comments on the labeling for this application as the review continues.

As usual, please confirm receipt, and advise acceptability of turn around time frame.

Thanks,
Vandna

-----Original Message-----

From: Allison Lowry [mailto:ALowry@arborpharma.com]
Sent: Wednesday, March 21, 2012 11:11 AM
To: Kishore, Vandna N
Subject: RE: NDA 203340 Nimodipine oral solution filing/designation letter

Oh sure. We have more of the bags coming from the packager tomorrow and I'll get them out to you right away, along with some cups (with generic printing).

Thanks
Allison

Allison Lowry
Director, Regulatory Affairs
Arbor Pharmaceuticals, Inc.
678-334-2428

-----Original Message-----

From: Kishore, Vandna N [mailto:Vandna.Kishore@fda.hhs.gov]
Sent: Wednesday, March 21, 2012 11:08 AM
To: Allison Lowry
Subject: RE: NDA 203340 Nimodipine oral solution filing/designation letter

Can you also send a few samples of the cup/syringe directly to me?

Vandna

-----Original Message-----

From: Allison Lowry [mailto:ALowry@arborpharma.com]
Sent: Wednesday, March 21, 2012 11:07 AM
To: Kishore, Vandna N
Subject: RE: NDA 203340 Nimodipine oral solution filing/designation letter

Hi Vandna,

We'll be submitting some CMC updates next week in response to the Information Request and

will include the cup and syringe information with it.

Thanks!
Allison

Allison Lowry
Director, Regulatory Affairs
Arbor Pharmaceuticals, Inc.
678-334-2428

-----Original Message-----

From: Kishore, Vandna N [mailto:Vandna.Kishore@fda.hhs.gov]
Sent: Wednesday, March 21, 2012 9:53 AM
To: Allison Lowry
Subject: RE: NDA 203340 Nimodipine oral solution filing/designation letter

Hi Allison,

Please go ahead and submit the proposal for the cup/oral syringe components to the application as soon as possible.

I'm also going to send you another email regarding the labeling shortly.

Thanks,

Vandna

-----Original Message-----

From: Allison Lowry [mailto:ALowry@arborpharma.com]
Sent: Thursday, March 15, 2012 6:58 PM
To: Kishore, Vandna N
Subject: RE: NDA 203340 Nimodipine oral solution filing/designation letter

Hi Vandna,

I wanted to touch base with you and provide an update on a few things. The dosing for the tox study is nearing completion soon and the work will get underway so that we can get an analysis by early May as discussed.

You should have received the stability update on the 5th. There is a supporting method qualification report that supports it and we're ready to send it to you. It allows for testing at (b)(4) (which is the change in wavelength from the validated method that was originally submitted in 0000). Also, when submitting our justification to the 74-day letter for the methylparaben specification in amendment 3, we offered that we would make a 50% batch and test it for Anti-microbial effectiveness and microbial limits. The batch was made and the 28-day test for the micro is near final. We would like to provide that C of A.

Lastly, we discussed with the Agency in earlier conversations a route to market a cup and an oral syringe together. We have sourced an oral syringe (b)(4) which will not accommodate a needle-tip syringe. Upon approval, we plan to provide one oral syringe and one 20 mL cup (b)(4). There will be 12 of these combo's per box. We would like to submit these components to the application.

We have the publishing group working on the submission - will it be ok to send these to you next week?

Thanks for your help,
Allison

Allison Lowry
Director, Regulatory Affairs
Arbor Pharmaceuticals, Inc.
678-334-2428

-----Original Message-----

From: Kishore, Vandna N [mailto:Vandna.Kishore@fda.hhs.gov]
Sent: Monday, March 05, 2012 10:17 AM
To: Allison Lowry
Subject: RE: NDA 203340 Nimodipine oral solution filing/designation letter

Thanks Allison. We really need this information ASAP.

Take care,
Vandna

From: Allison Lowry [ALowry@arborpharma.com]
Sent: Monday, March 05, 2012 9:37 AM
To: Kishore, Vandna N
Subject: RE: NDA 203340 Nimodipine oral solution filing/designation letter

Good morning, Vandna,

I hope all is well. Based on our last conversation, you mentioned updated stability data would be needed March 3. I wanted to let you know the data and proposed expiry will be coming in today, via electronic submission as usual. We have included updated data from ongoing studies (b)(4) and also pulled all samples from each storage condition to test with the new wavelength at (b)(4) that was discussed in amendment 2 (Sequence 0002).

We are also finalizing additional testing for the methylparaben limit which will be ready this week and will provide support in favor of the proposed limit. For reference, this was discussed in amendment 3 (Sequence 0003).

Thanks so much and please let me know if you have any questions.
Allison

Allison Lowry
Director, Regulatory Affairs
Arbor Pharmaceuticals, Inc.
678-334-2428

-----Original Message-----

From: Kishore, Vandna N [mailto:Vandna.Kishore@fda.hhs.gov]
Sent: Thursday, February 16, 2012 11:11 AM
To: Allison Lowry
Subject: RE: NDA 203340 Nimodipine oral solution filing/designation letter

Hi Allison,

The proposal to prepare two fresh solutions (one for each 7-day period) instead of daily appears reasonable based on the available stability information. We recommend that you evaluate the impurity profile at the end use for each solution.

Thanks,
Vandna

-----Original Message-----

From: Allison Lowry [mailto:ALowry@arborpharma.com]
Sent: Thursday, February 16, 2012 9:45 AM
To: Kishore, Vandna N
Subject: RE: NDA 203340 Nimodipine oral solution filing/designation letter

Hi Vanda,

I wanted to mention a couple of other points with regards to the control sample. We could open a fresh bottle every day that might limit exposure to light, etc. The total impurity

change over a month time period at 25C is less than (b)(4).

Many thanks,
Allison

Allison Lowry
Director, Regulatory Affairs
Arbor Pharmaceuticals, Inc.
678-334-2428

-----Original Message-----

From: Allison Lowry
Sent: Wednesday, February 15, 2012 6:04 PM
To: 'Kishore, Vandna N'
Subject: RE: NDA 203340 Nimodipine oral solution filing/designation letter

Hi Vandna,

Good news - we'll get started right away. One question - we are preparing our control solution as a lab scale batch, made at the product manufacturer using the same suppliers of raw materials as in the test samples (aged product), then shipping the batch to the tox lab, while at the same time shipping a sample to the analytical testing lab for analysis. Due to the time it takes to ship the batch and samples, and the time it takes to test the batch sample at the analytical lab, we are concerned about making it daily then having shipping / testing delays occur during the 14-day period. Would it be acceptable to prepare two fresh solutions instead of daily solutions? We would prepare a fresh solution per 7-day period. That would allow us prep time, then shipping / testing time over the weekend.

Thanks for your help,
Allison

Allison Lowry
Director, Regulatory Affairs
Arbor Pharmaceuticals, Inc.
678-334-2428

-----Original Message-----

From: Kishore, Vandna N [mailto:Vandna.Kishore@fda.hhs.gov]
Sent: Wednesday, February 15, 2012 4:37 PM
To: Allison Lowry
Subject: RE: NDA 203340 Nimodipine oral solution filing/designation letter

Hi Alison,

We agree with your plan to conduct a 2-week toxicity study using aged solutions stored under accelerated conditions, as long as the impurity levels in the degraded product will provide a reasonable safety margin compared to the proposed specification limits. Also, we would recommend that you prepare fresh control solution daily to minimize formation of impurities in the control.

Thanks,
Vandna

-----Original Message-----

From: Allison Lowry [mailto:ALowry@arborpharma.com]
Sent: Tuesday, February 14, 2012 4:55 PM
To: Kishore, Vandna N
Subject: RE: NDA 203340 Nimodipine oral solution filing/designation letter

Great - thanks!

Allison Lowry
Director, Regulatory Affairs

Arbor Pharmaceuticals, Inc.
678-334-2428

-----Original Message-----

From: Kishore, Vandna N [mailto:Vandna.Kishore@fda.hhs.gov]
Sent: Tuesday, February 14, 2012 4:34 PM
To: Allison Lowry
Subject: RE: NDA 203340 Nimodipine oral solution filing/designation letter

Hi Allison,

I'm waiting for one more response before I can get back to you on the proposal below.
Hopefully, by tomorrow.

Thanks,
Vandna

From: Allison Lowry [ALowry@arborpharma.com]
Sent: Tuesday, February 14, 2012 11:59 AM
To: Kishore, Vandna N
Subject: RE: NDA 203340 Nimodipine oral solution filing/designation letter

Hi Vandna,

I hope all is well. I left you a voicemail regarding feedback on the proposal below to use the aged oral solution (against a fresh product as control) to run the toxicology study.

Have you received feedback? We are hoping to get paperwork signed today to begin but would like to get your feedback on our approach.

Also, I mentioned that we would have the labeling to you this Friday. I hope that will be sufficient.

Many thanks,
Allison

Allison Lowry
Director, Regulatory Affairs
Arbor Pharmaceuticals, Inc.
678-334-2428

-----Original Message-----

From: Allison Lowry
Sent: Wednesday, February 08, 2012 5:10 PM
To: 'Kishore, Vandna N'
Subject: RE: NDA 203340 Nimodipine oral solution filing/designation letter

Hi Vandna,

I have gotten some more details around the toxicology study and wanted to make sure your team is ok with our plan. Since we haven't synthesized the two impurities (other than (b)(4)

(b)(4), we were planning to run aged solutions of product stored at accelerated conditions (current worst-case) and compare it to freshly made product in a 14-day repeat-dose study. If positive, will this approach satisfy the request for qualification of the impurities?

Thanks for your help!
Allison

Allison Lowry
Director, Quality & Regulatory Affairs
Arbor Pharmaceuticals, Inc.
678-334-2428

-----Original Message-----

From: Kishore, Vandna N [mailto:Vandna.Kishore@fda.hhs.gov]
Sent: Wednesday, February 08, 2012 9:53 AM
To: Allison Lowry
Subject: RE: NDA 203340 Nimodipine oral solution filing/designation letter

Hi Allison,

No need to resubmit the Adobe files...both folks that had issues have been resolved it seems.

Let's touch base this afternoon to discuss the dates proposed further. I'm back at 1pm after the next two meetings.

Thanks,
Vandna

-----Original Message-----

From: Allison Lowry [mailto:ALowry@arborpharma.com]
Sent: Tuesday, February 07, 2012 4:11 PM
To: Kishore, Vandna N
Subject: RE: NDA 203340 Nimodipine oral solution filing/designation letter

Hi Vandna,

I'm a little delayed in getting back with you today. Was there any feedback from the meeting this morning regarding the proposed timelines? Also, we are still troubleshooting the Adobe file issue and were wondering if more than one person had experienced difficulties. It looks like we may just resubmit those files, however.

Many thanks,
Allison

Allison Lowry
Director, Quality & Regulatory Affairs
Arbor Pharmaceuticals, Inc.
678-334-2428

-----Original Message-----

From: Kishore, Vandna N [mailto:Vandna.Kishore@fda.hhs.gov]
Sent: Monday, February 06, 2012 2:03 PM
To: Allison Lowry
Subject: RE: NDA 203340 Nimodipine oral solution filing/designation letter

I don't need this formalized.

Let's touch base tomorrow afternoon then.
Vandna

-----Original Message-----

From: Allison Lowry [mailto:ALowry@arborpharma.com]
Sent: Monday, February 06, 2012 1:31 PM
To: Kishore, Vandna N
Subject: RE: NDA 203340 Nimodipine oral solution filing/designation letter

Hi Vandna,

Sure - I'll try to reach you tomorrow after noon EST so that you would have time to meet with the team. We would like to propose several submissions, the first being this Friday in which we would provide answers to 1,2,4, and 5. We would follow up first of next week with labeling revisions (no later than Wednesday).

For stability data and expiration dating (item 3), we plan to evaluate the upcoming stability pulls, and reanalyze some current pulls, with the revised method for testing impurities (used for testing in the last amendment). There are several stability pulls we are evaluating and we should be able to have the revised validated

impurities method and stability data by the end of February, along with more data in early March. We can propose an appropriate expiry period after reviewing the data. Would this approach be acceptable to the Agency?

Lastly, we plan to qualify the noted impurities from CMC/non-clinical item 1. If we have completed toxicological report to the Agency by early May, would this be acceptable for meeting the goal date of 5/18? We are in process of generating the protocol for this study.

I hope this will work for your meeting tomorrow, but please let me know if you would like me to better formalize the proposed timelines and I can do so.

Many thanks!
Allison

Allison Lowry
Director, Quality & Regulatory Affairs
Arbor Pharmaceuticals, Inc.
678-334-2428

-----Original Message-----

From: Kishore, Vandna N [mailto:Vandna.Kishore@fda.hhs.gov]
Sent: Monday, February 06, 2012 12:46 PM
To: Allison Lowry
Subject: RE: NDA 203340 Nimodipine oral solution filing/designation letter

Hi Allison,

I'm in meetings from 1:30 to 5 pm today so this afternoon looks tough. How about tomorrow? I should be in my office until 10 am and then back after noon EST.

If you could email me your proposals for the responses to the 74 day letter, I can share them with the team in our morning meeting. That may be helpful before we discuss further.

Thanks,
Vandna

-----Original Message-----

From: Allison Lowry [mailto:ALowry@arborpharma.com]
Sent: Monday, February 06, 2012 12:41 PM
To: Kishore, Vandna N
Subject: RE: NDA 203340 Nimodipine oral solution filing/designation letter

Hi Vandna,

Thank you -
I also left you a message regarding timing of our response. Hopefully we can speak this afternoon about our plan for action and submitting a response.

Thanks
Allison

Allison Lowry
Director, Quality & Regulatory Affairs
Arbor Pharmaceuticals, Inc.
678-334-2428

-----Original Message-----

From: Kishore, Vandna N [mailto:Vandna.Kishore@fda.hhs.gov]
Sent: Monday, February 06, 2012 12:28 PM
To: Allison Lowry
Subject: RE: NDA 203340 Nimodipine oral solution filing/designation letter

Hi Allison,

I will ask the team in a meeting we have tomorrow, and let you know.

Thanks,

Vandna

-----Original Message-----

From: Allison Lowry [mailto:ALowry@arborpharma.com]
Sent: Thursday, February 02, 2012 11:15 AM
To: Kishore, Vandna N
Subject: Re: NDA 203340 Nimodipine oral solution filing/designation letter

Good morning, Vandna,

In case you get a chance to access this during your conference, I thought I would go ahead and send a question from our team. In working through the question regarding the PDF files, (b)(4) eCTD submission rep) wanted to know if only one person was having issues with files or if there were several persons. I believe that will help them in troubleshooting.

Many thanks and should I not hear from you, I'll be checking in with you Monday also.
Allison

Sent from my iPad

On Jan 31, 2012, at 8:15 AM, "Kishore, Vandna N" <Vandna.Kishore@fda.hhs.gov> wrote:

> Great. I will be at a conference and not really off though!

>

>

> Vandna

>

> -----Original Message-----

> From: Allison Lowry [mailto:ALowry@arborpharma.com]

> Sent: Tuesday, January 31, 2012 10:09 AM

> To: Kishore, Vandna N

> Subject: Re: NDA 203340 Nimodipine oral solution filing/designation
> letter

>

> Good morning Vandna,

>

> Thank you - I've received the letter and will pass it on to the team as I am out of the office. We'll get started right away and work to provide a response quickly. Meanwhile, I will be in touch.

>

> Enjoy your time off!

>

> Thanks,

> Allison

>

> Sent from my iPad

>

> On Jan 31, 2012, at 8:03 AM, "Kishore, Vandna N" <Vandna.Kishore@fda.hhs.gov> wrote:

>

>> Good Morning Allison,

>>

>> Please find attached an e-copy of the filing, 74 day, with issues listed.

>>

>> A response as soon as possible would be appreciated considering the short priority review window.

>>

>> FYI, I will be out of the office rest of this week, and will touch base with you on Monday as needed. I may have access to email periodically.

>>

>> Regards,

>> Vandna

>>

>>
>> -----Original Message-----
>> From: Allison Lowry [mailto:ALowry@arborpharma.com]
>> Sent: Wednesday, January 18, 2012 3:24 PM
>> To: Kishore, Vandna N
>> Subject: RE: NDA 203340 Nimodipine oral solution filing/designation
>> letter
>>
>> Hi Vandna,
>>
>> I received the letter. Many thanks and we'll look forward to your comments on the
>> 31st.
>>
>> Have a great day!
>> Allison
>>
>> Allison Lowry
>> Director, Quality & Regulatory Affairs Arbor Pharmaceuticals, Inc.
>> 678-334-2428
>>
>>
>> -----Original Message-----
>> From: Kishore, Vandna N [mailto:Vandna.Kishore@fda.hhs.gov]
>> Sent: Wednesday, January 18, 2012 2:31 PM
>> To: Allison Lowry
>> Subject: RE: NDA 203340 Nimodipine oral solution filing/designation
>> letter
>>
>> Hi Allison,
>>
>> Attached is the filing/designation letter for this NDA. I should have the next letter
>> with the filing review comments by 1/31/12 to you.
>>
>> Take care,
>> Vandna
>>
>>
>> -----Original Message-----
>> From: Allison Lowry [mailto:ALowry@arborpharma.com]
>> Sent: Tuesday, January 17, 2012 9:37 PM
>> To: Kishore, Vandna N
>> Subject: Re: NDA 203340 Nimodipine oral solution telecon request
>>
>> Thank you, Vandna!
>>
>>
>> Sent from my iPhone
>>
>> On Jan 17, 2012, at 9:07 PM, "Kishore, Vandna N" <Vandna.Kishore@fda.hhs.gov> wrote:
>>
>>> Hi Allison,
>>>
>>> Yes, the application has been filed. I will send you the letter tomorrow.
>>>
>>> Thanks,
>>> Vandna
>>>
>>> -----
>>> From: Allison Lowry [ALowry@arborpharma.com]
>>> Sent: Tuesday, January 17, 2012 5:04 PM
>>> To: Kishore, Vandna N
>>> Subject: RE: NDA 203340 Nimodipine oral solution telecon request
>>>
>>> Hi Vandna,
>>>
>>> I just wanted to touch base with you this afternoon since I am in
>>> and out of meetings. Should we expect to hear from you today regarding the filing or

is there anything you need from me?

>>>

>>> Thanks,

>>> Allison

>>>

>> Allison Lowry

>> Director, Quality & Regulatory Affairs Arbor Pharmaceuticals, Inc.

>>> 678-334-2428

>>>

>>> From: Kishore, Vandna N [mailto:Vandna.Kishore@fda.hhs.gov]

>>> Sent: Friday, January 13, 2012 12:51 PM

>>> To: Allison Lowry

>>> Subject: RE: NDA 203340 Nimodipine oral solution telecon request

>>>

>>> Hi Allison,

>>>

>>> Thank you for the feedback regarding the packaging proposal.

>>>

>>> The team is still reviewing the data submitted, and I hope to be in touch with you this coming Tuesday.

>>>

>>> Have a wonderful weekend.

>>> Vandna

>>>

>>>

>>>

>>>

>>> From: Allison Lowry

>>> [mailto:ALowry@arborpharma.com]<mailto:[mailto:ALowry@arborpharma.co

>>> m]

>>>>

>>> Sent: Friday, January 13, 2012 10:03 AM

>>> To: Kishore, Vandna N

>>> Subject: RE: NDA 203340 Nimodipine oral solution telecon request

>>> Good morning, Vandna,

>>>

>>> I hope all is well. I realize your team is probably still working through the filing decision (keeping my fingers crossed) but I just wanted to drop a quick note and let you know we have checked into the packaging proposal that was discussed at the end of the call Monday.

>>> We believe there is a good solution that will work. The unit-dose

>>> cup can be packaged, along with a 20 mL oral syringe, (b) (4)

(b) (4)

appropriate labeling information on the outside. We anticipate providing 12 of these in a box (similar to the current configuration but with a syringe provided). Of course, we are still nailing down details such as fitting with a naso-gastric tube, (b) (4) etc. but wanted to let you know that we should be able to source something that works. We can provide these soon for the team's review also.

>>>

>>> We had actually begun looking into sources for a (b) (4) but still needed to gather stability data on it, which we will also explore.

>>>

>>> Thanks for everything and we'll look forward to hearing from you

>>> soon, Allison

>>>

>>>

>>> Allison Lowry

>>> Director, Quality & Regulatory Affairs Arbor Pharmaceuticals, Inc.

>>> 678-334-2428

>>>

>>> From: Kishore, Vandna N

>>> [mailto:Vandna.Kishore@fda.hhs.gov]<mailto:[mailto:Vandna.Kishore@fda.

>>> hhs.gov]>

>>> Sent: Tuesday, January 10, 2012 2:12 PM

>>> To: Allison Lowry

>>> Subject: RE: NDA 203340 Nimodipine oral solution telecon request

>>>

>>> Thanks again for getting the team together at a short notice. We will review the data once we receive it, and be in touch.

>>>
>>> Take care,
>>> Vandna

>>
>>
>>>

>>> From: Allison Lowry
>>> [mailto:ALowry@arborpharma.com] <mailto:[mailto:ALowry@arborpharma.co
>>> m]

>>>>
>>> Sent: Tuesday, January 10, 2012 2:06 PM
>>> To: Kishore, Vandna N
>>> Subject: RE: NDA 203340 Nimodipine oral solution telecon request Hi
>>> Vandna,
>>>

>>> I wanted to thank you and the team for the call today and also let you know the submission has been dispatched and has been received at the FDA.

>>>
>>> I will touch base with you later in the week. Meanwhile, please let me know if we can answer any additional questions.

>>>
>>> Thanks again,
>>> Allison

>>>
>>>

>>> Allison Lowry
>>> Director, Quality & Regulatory Affairs Arbor Pharmaceuticals, Inc.
>>> 678-334-2428

>>>
>>> From: Kishore, Vandna N
>>> [mailto:Vandna.Kishore@fda.hhs.gov] <mailto:[mailto:Vandna.Kishore@fda.
>>> hhs.gov]>

>>> Sent: Tuesday, January 10, 2012 11:20 AM
>>> To: Allison Lowry
>>> Subject: RE: NDA 203340 Nimodipine oral solution telecon request

>>>
>>> Hi Allison,
>>>
>>> Here is the call in number to use at 12:30:

>>>
>>>
>>>  (b) (4)

>>>
>>>
>>> Speak to you then.

>>>
>>> Thanks,
>>>
>>> Vandna

>>>
>>>
>>>

>>> From: Allison Lowry
>>> [mailto:ALowry@arborpharma.com] <mailto:[mailto:ALowry@arborpharma.co
>>> m]

>>>>
>>> Sent: Tuesday, January 10, 2012 9:36 AM
>>> To: Kishore, Vandna N
>>> Subject: RE: NDA 203340 Nimodipine oral solution telecon request Hi

>>> Vandna,
>>>
>>> Good morning and Happy New Year to you! I hope you enjoyed the holidays.
>>>
>>> Yes, I was going to send you a note here shortly to update you. We are on track to
>>> submit the electronic submission this afternoon through the gateway.
>>> So I will send you a note when it is transmitted and we'll go from there.
>>>
>>> Thanks so much,
>>> Allison
>>>
>>> Allison Lowry
>>> Director, Quality & Regulatory Affairs Arbor Pharmaceuticals, Inc.
>>> 678-334-2428
>>>
>>> From: Kishore, Vandna N
>>> [mailto:Vandna.Kishore@fda.hhs.gov]<mailto:[mailto:Vandna.Kishore@fda.
>>> hhs.gov]>
>>> Sent: Tuesday, January 10, 2012 9:10 AM
>>> To: Allison Lowry
>>> Subject: RE: NDA 203340 Nimodipine oral solution telecon request
>>>
>>> Happy New Year Allison!
>>>
>>> Will you please send me an email when the data requested is submitted today?
>>>
>>> Thanks,
>>> Vandna
>>>
>>>
>>>
>>>

>>> From: Allison Lowry
>>> [mailto:ALowry@arborpharma.com]<mailto:[mailto:ALowry@arborpharma.co
>>> m]
>>>>
>>> Sent: Wednesday, December 07, 2011 6:51 PM
>>> To: Kishore, Vandna N
>>> Cc: Laurie J. Downey
>>> Subject: RE: NDA 203340 Nimodipine oral solution telecon request Hi
>>> Vandna,
>>>
>>> I want to thank you and the FDA team again for speaking with us
>>> today about solutions for the nimodipine oral solution product. We are moving forward
>>> with some additional testing as we discussed, and gathering ongoing data for submission by
>>> January 10.
>>>
>>> I wanted to let you know that I will be traveling next week (Mon -
>>> Fri) with intermittent access to email and voicemail, so if you have any immediate
>>> questions that might need my attention, please direct them to Dr. Downey and he can get
>>> circle me in.
>>>
>>> Kind regards,
>>> Allison
>>>
>>>
>>>
>>> From: Allison Lowry
>>> Sent: Tuesday, December 06, 2011 1:07 PM
>>> To: Kishore, Vandna N
>>> Cc: Laurie J. Downey
>>> Subject: RE: NDA 203340 Nimodipine oral solution telecon request
>>>
>>>
>>> Hi Vandna,
>>>
>>>

>>>
>>> Great, thank you. We'll look forward to speaking tomorrow at noon and will use the same call-in number unless we hear otherwise.
>>>
>>>
>> Kind regards,
>>>
>>> Allison
>>>
>>>
>>>
>>>
>>>
>>> Allison Lowry
>>>
>>> Director, Quality & Regulatory Affairs
>>>
>>> Arbor Pharmaceuticals, Inc.
>>>
>>> 980 Hammond Drive, Suite 1250
>>>
>>> Atlanta, GA 30328
>>>
>>> Direct: 678-334-2428
>>>
>>> Mobile: 678-316-0097
>>>
>>> Fax: 678-823-7201
>>>
>>> _____
>>> From: Kishore, Vandna N [Vandna.Kishore@fda.hhs.gov]
>>> Sent: Tuesday, December 06, 2011 12:51 PM
>>> To: Allison Lowry
>>> Cc: Laurie J. Downey
>>> Subject: RE: NDA 203340 Nimodipine oral solution telecon request
>>> Hello Allison,
>>>
>>> Let's try this again: Noon tomorrow for the telecon.
>>>
>>> We will have our CMC, non-clinical, and clinical team on hand.
>>>
>>> Thanks,
>>> Vandna
>>>
>>>
>>>
>>> _____
>>> From: Allison Lowry
>>> [mailto:ALowry@arborpharma.com]<mailto:[mailto:ALowry@arborpharma.co
>>> m]
>>>>>
>>> Sent: Tuesday, December 06, 2011 12:04 PM
>>> To: Kishore, Vandna N
>>> Cc: Laurie J. Downey
>>> Subject: RE: NDA 203340 Nimodipine oral solution telecon request
>>>
>>> Hi Vandna,
>>>
>>>
>>>
>>> Thanks for the update. I'll look to hear from you tomorrow.
>>>
>>>
>>>

>>> Kind regards,

>>>

>>> Allison

>>>

>>>

>

>> Allison Lowry

>>>

>>> Director, Quality & Regulatory Affairs

>>>

>>> Arbor Pharmaceuticals, Inc.

>>>

>>> 980 Hammond Drive, Suite 1250

>>>

>>> Atlanta, GA 30328

>>>

>>> Direct: 678-334-2428

>>>

>>> Mobile: 678-316-0097

>>>

>>> Fax: 678-823-7201

>>>

>>>

>>> From: Kishore, Vandna N [Vandna.Kishore@fda.hhs.gov]

>>> Sent: Tuesday, December 06, 2011 12:02 PM

>>> To: Allison Lowry

>>> Cc: Laurie J. Downey

>>> Subject: RE: NDA 203340 Nimodipine oral solution telecon request Hi

>>> Allison,

>>> Looks like we won't be able to call you today due to another conflict. I will keep you posted regarding a possible telecon tomorrow.

>>>

>>> Thanks,

>>> Vandna

>>>

>>>

>>>

>>>

>>> From: Allison Lowry

>>> [mailto:ALowry@arborpharma.com]<mailto:[mailto:ALowry@arborpharma.co

>>> m]

>>>>

>>> Sent: Tuesday, December 06, 2011 11:28 AM

>>> To: Kishore, Vandna N

>>> Cc: Laurie J. Downey

>>> Subject: RE: NDA 203340 Nimodipine oral solution telecon request

>>>

>>> Thank you, Vandna. We'll speak to you then.

>>>

>>>

>>>

>>> Allison Lowry

>>>

>>> Director, Quality & Regulatory Affairs

>>>

>>> Arbor Pharmaceuticals, Inc.

>>>

>>> 980 Hammond Drive, Suite 1250

>>>

>>> Atlanta, GA 30328

>>>

>>> Direct: 678-334-2428

>>>

>>> Mobile: 678-316-0097

>>>

>>> Fax: 678-823-7201

>>>
>>>
>>> From: Kishore, Vandna N [Vandna.Kishore@fda.hhs.gov]
>>> Sent: Tuesday, December 06, 2011 11:06 AM
>>> To: Allison Lowry
>>> Cc: Laurie J. Downey
>>> Subject: NDA 203340 Nimodipine oral solution telecon request Hi
>>> Allison,
>>>
>>> As we spoke earlier today, our team would like to speak with Arbor Pharmaceuticals
briefly this afternoon, around 2:25-2:30 pm, regarding the submission.
>>>
>>> Here is the call in number:
>>>  (b) (4)
>>>
>>> Thank you,
>>> Vandna
>>>
>>> Vandna N. Kishore
>>> Regulatory Project Manager
>>> FDA, Division of Neurology Products
>>> 10903 New Hampshire Avenue
>>> White Oak, CDER Bldg 22, Rm. 4340
>>> Silver Spring, MD 20993
>>> Phone: 301.796.4193
>>> Vandna.Kishore@fda.hhs.gov<mailto:Vandna.Kishore@fda.hhs.gov>
>>>
>>>
>>> <NDA 203340 Nymalize Filing Issues Identified 74 day letter
>>> 013012.pdf - Adobe Acrobat Pro.pdf>

Dear Allison,

In reviewing the proposed labeling for Nymalize, we recommend you make the following changes and submit revised labeling:

Recommendations:

A. 16 OUNCE BOTTLE CONTAINER LABEL

1. The graphic to the left of the proprietary name is overly prominent and distracts from more important information on the label. We recommend removing the graphic, or minimizing and moving the graphic away from the proprietary name so that it does not compete in prominence with the proprietary name, established name, and product strength.
2. The active ingredient and dosage form comprise the established name but are presented in different fonts. Ensure the active ingredient and the dosage form are displayed in the same font as the proprietary name.
3. The statement of strength lacks prominence. In order to increase the prominence of the statement of strength, increase the font size.
4. The distributor's logo and name as presently stated are overly prominent. Decrease the prominence of the distributor's logo and name on the principal display panel.
5. Ensure the lot number and expiration date are printed on the label.
6. Include the inactive ingredients on the side panel as required under 21 CFR 201.10(a).
7. Instructions to [REDACTED] ^{(b)(4)} are contained in the package insert labeling but not on the label. Add the statement [REDACTED] ^{(b)(4)} on the principal display panel.
8. Given the history of erroneous intravenous administration with oral nimodipine, the route of administration statement should be made more prominent by increasing the font size.
9. The "Rx Only" statement is overly prominent. Relocate the "Rx Only" statement to a less prominent location and debold.

B. 20 ML UNIT-DOSE CUP CONTAINER LABEL

1. As currently presented, the label appears cluttered. Ensure information required under 21 CFR 201.10(i) is included on the label. To decrease clutter on the label, remove the "Rx Only", "Package Not Child Resistant", and "Protect from Light" statements.

Labeling Info

Sent 3/22/12 email

2. The net quantity statement is too close to the statement of strength and may cause confusion. (b) (4)

(b) (4)

3. The proprietary name is in all upper case letters. Revise the presentation of the proprietary name from all upper case letters (NYMALIZE) to title case (Nymalize) to improve readability. In addition, increase the size of the proprietary name.

4. See comment A.7 above.

C. 20 ML UNIT-DOSE CARTON LABELING

1. See comments A.1 to A.8 above.

2. Include the statement "Package Not Child Resistant."

D. INSERT LABELING

1. General Comments

a. In general, do not use trailing zeros within the insert labeling. Trailing zeros can lead to 10-fold errors in dosing. We recommend removing all trailing zeros with the exception of when it is required to demonstrate the level of precision of the value being reported, such as for laboratory results, imaging studies that report size of lesions, or catheter/tube sizes.

b. We recommend adding a unit of measure immediately following all numbers, as appropriate. For example under section 14 (Clinical Studies), (b) (4) mg doses" should be revised to read "30 mg, 60 mg, and 90 mg doses."

c. We recommend keeping numbers next to units or symbols within the same line of text. For example under section 8.1 (Pregnancy), 10 mg/kg/day should all be on one line. Revise the layout so 10 is not at the end of the line of text.

2. Under Section ^{2.13 new} (b) (4) (Dosage and Administration), reword the statement (b) (4) (b) (4), to read "Refill the syringe with 20 mL of 0.9% saline (b) (4) solution..." for increased clarity.

3. Under Section 3 (Dosage Forms and Strengths), it appears that information relating to how Nymalize is supplied is included. Consider revising this section so it only includes information pertaining to the dosage form and strength.

Please address these above comments and submit updated labeling promptly. We request that you consolidate the updates made to the label submitted on February 17, 2012, (in response to our comments in the 74 day letter) and the recommendations made in this communication and submit an updated labeling submission to this application.

In the interest of time, we request that you submit as soon as possible, but no later than next Tuesday, March 27, 2012.

An updated package insert submission addressing the comments in D above may be submitted independently from the updated carton and container labeling in order to expedite the submission of an updated package insert.

Thank you,
Vandna



NDA 203340

INFORMATION REQUEST

Arbor Pharmaceuticals, Inc.
Attention: Allison Lowry, Director, Quality & Regulatory Affairs
980 Hammond Drive, Building Two, Suite 1250
Atlanta, GA 30328

Dear Ms. Lowry:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Nimodipine Oral Solution.

We are reviewing the Chemistry, Manufacturing, and Controls section 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. Section 3.2.P.2.5, Microbiological Attributes, states that an antimicrobial effectiveness testing report for the proposed formulation is provided in the application, but the report is not present. Please provide the report. Additionally, the sponsor should validate antimicrobial effectiveness on a batch containing at or below the lowest specified methylparaben concentration and provide the data for review.
2. The application should provide test methods and acceptance criteria to demonstrate the product is free of the objectionable microorganism *Burkholderia cepacia*. We recommend that potential sources are examined and sampled as process controls, and these may include raw materials and the manufacturing environment. A risk assessment for this species in the product and raw materials is recommended to develop sampling procedures and acceptance criteria. Your test method should be validated and a discussion of those methods should be provided. Test methods validation should address multiple strains of the species and cells that are acclimated to the environments (e.g., warm or cold water) that may be tested.
3. The application should include specifications for the (b) (4) ml cup presentation of the drug product. Please provide these specifications.

If you have any questions, contact Teshara G. Bouie, Regulatory Project Manager, at (301) 796-1649.

Sincerely,

{See appended electronic signature page}

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

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

RAMESH K SOOD
03/22/2012



NDA 203340

INFORMATION REQUEST

Arbor Pharmaceuticals, Inc.
Attention: Allison Lowry, Director, Quality & Regulatory Affairs
980 Hammond Drive, Building Two, Suite 1250
Atlanta, GA 30328

Dear Ms. Lowry:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Nimodipine Oral Solution.

We are reviewing the Chemistry, Manufacturing, and Controls section 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. The proposed drug substance specification includes an acceptance criterion of not more than (NMT) (b) (4) % for 'any other impurity'. This limit is inconsistent with ICH identification threshold for identification of impurities, which is 0.10%. Revise the limit to NMT 0.10% to be consistent with the ICH threshold. If there are known impurities which may exceed the identification threshold they should be listed individually in the specification by name or other suitable identifier such as relative retention time (RRT).
2. Provide a detailed description of the packaging process and process controls for the drug product.
3. Revise the proposed specification for Nimodipine Oral Solution packaged in (b) (4) mL cups (Table 2, Module 3.2.P.5.1) to include all test parameters and acceptance criteria (e.g., assay, pH, identification, impurities, etc.) to which the product should conform.
4. Provide a copy of the revised method NPLC-1266 (i.e. detection of impurities at (b) (4) nm) and the validation report for the impurity test section of the method, as committed in the January 10, 2012, amendment (002).
5. The version of method NPLC-1266 submitted in the original application does not include use of the relative response factors (RRFs) to correct the results for known impurities. Use of RRFs should be included in the calculation of known impurities other than (b) (4) (b) (4) for which an authentic reference is used.

6. For validation of method NPLC-1266, solution stability was studied at 4 °C over 3-day and 8-day periods. Provide the details how the samples are handled if precipitation occurs.
7. You proposed the identification test for the drug product based on the HPLC retention time. Identification solely by a single chromatographic retention time is not regarded as a specific identification test. An identification test that is specific to the drug substance, e.g., infrared spectroscopy (IR) should be used. Alternatively, a combination of non-specific identification tests combined into a single procedure (e.g., HPLC/MS or HPLC in conjunction with UV spectroscopy by photodiode array detector) may be acceptable.
8. You stated that the results from the samples at the more specific wavelength of (b) (4) nm showed lower results for the unknown impurities but the results for (b) (4) remained unchanged. For this reason, you proposed a revised specification with lower acceptance criteria for impurities. Your stability data included part of the data analyzed at wavelength of (b) (4) nm and part of the data analyzed at wavelength of (b) (4) nm. Provide comparative impurity data, i.e., side-by-side determination on the same samples, obtained using both wavelengths.
9. Provide an update on the status of your efforts to determine the structures of the unidentified degradants present in the drug product.
10. Provide photostability test results to support that the container closure systems provide adequate light protection for the product.
11. As communicated in the January 30, 2012 Agency letter, revise the primary stability protocol to include leachables testing for the remaining time points.
12. The provided stability data will not support the proposed expiration dating period. Additionally, note that we are not able to complete our evaluation of the proposed specification pending qualification of impurities. Therefore, we are not able to establish the expiration dating period at this time.
13. Different ranges are given in the application as the acceptance criterion for pH. E.g., (b) (4) (original submission, Module 3.2.P.8.1, Table 13), (b) (4) (original submission, Module 3.2.P.5.1), and (b) (4) (March 6, submission, Module 3.2.P.8.1, Table 15). Provide an explanation and clarify whether the proposed regulatory acceptance criterion for pH is (b) (4) or (b) (4).

If you have any questions, contact Teshara G. Bouie, Regulatory Project Manager, at (301) 796-1649.

Sincerely,

{See appended electronic signature page}

Ramesh Sood, Ph.D.

Branch Chief
Division of New Drug Quality Assessment I
Office of New Drug Quality Assessment
Center for Drug Evaluation and Research

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

RAMESH K SOOD
03/16/2012



NDA 203340

**PROPRIETARY NAME REQUEST
CONDITIONALLY ACCEPTABLE**

Arbor Pharmaceuticals, Inc.
980 Hammond Drive
Suite 1250
Atlanta, Georgia 30328

ATTENTION: Allison Lowry
Director, Quality & Regulatory Affairs

Dear Ms. Lowry:

Please refer to your New Drug Application (NDA) dated and received November 18, 2011, submitted under section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Nimodipine Oral Solution, 60 mg/20 mL.

We also refer to your correspondence, dated and received November 21, 2011, requesting review of your proposed proprietary name, Nymalize. We have completed our review of the proposed proprietary name and have concluded that it is acceptable.

The proposed proprietary name, Nymalize, 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 November 18, 2011, 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, Vandna Kishore at (301) 796-4193.

Sincerely,

{See appended electronic signature page}

Carol Holquist, RPh
Director
Division of Medication Error Prevention and Analysis
Office of Medication Error Prevention and Risk Management
Office of Surveillance and Epidemiology
Center for Drug Evaluation and Research

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

LAURIE A KELLEY
02/13/2012

CAROL A HOLQUIST
02/13/2012



NDA 203340

FILING COMMUNICATION

Arbor Pharmaceuticals
Attention: Allison Lowry
Director, Quality and Regulatory Affairs
980 Hammond Drive, Suite 1250
Atlanta, GA 30328

Dear Ms. Lowry:

Please refer to your New Drug Application (NDA) dated November 18, 2011, received November 18, 2011, submitted under section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act, for Nimodipine 60 mg/ml Oral Solution.

We also refer to your amendment dated January 10, 2012.

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 **Priority**. Therefore, the user fee goal date is May 18, 2012.

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 requirement/commitment requests by April 27, 2012.

During our filing review of your application, we identified the following potential review issues:

CMC Issues:

1. With respect to (b)(4), methylparaben, you propose limits of (b)(4)% - (b)(4)% of label claim. You should provide data to support the proposed target level of methylparaben and the lower specification limit.

2. With respect to extractables and leachables, we note that you have submitted results of container extraction and migration studies. You should also monitor the primary stability batches for leachables through the proposed shelf life.
3. You propose a shelf life of (b) (4) months for product stored at room temperature. Given the instability of the product and the limited stability data provided in the application, there do not appear to be sufficient data to support the proposed shelf life.
4. With respect to the post-approval stability commitment, you propose to place the first commercial batch on stability at (b) (4) and (b) (4); however, the second and third batch would only be placed on stability at (b) (4). All three of the first commercial batches should be tested under accelerated conditions. Additionally, the post approval stability protocol should incorporate storage at (b) (4) in case of significant change at (b) (4).
5. The following files cause Global Submit and Adobe Acrobat to freeze if text is selected. This appears to be an issue with the pdf files themselves, not a software issue. We request that you correct this problem.

2.3.S Manufacture

2.3.S Characterization

2.3.S Stability

3.2.S.3.2 Impurities

3.2.S.5 Reference Standards or Materials

3.2.S.7.2 Post-approval Stability Protocol and Stability Commitment

3.2.S.7.3 Stability Data

CMC/Nonclinical Issues

1. The drug product stability specification provided in the original NDA submission provides for acceptance criteria for six specified impurities that exceed the ICH qualification threshold ((b) (4)). This issue, and potential approaches for qualifying these impurities, was discussed with you in a teleconference on December 7, 2011. With regard to qualification of impurities, we acknowledge your January 12, 2012, submission in which you provided the results of analytical comparisons of the impurity profile of your product with approved nimodipine capsules.

We have reviewed the data provided and determined that they do not demonstrate comparable impurity levels between your product and the approved capsules.

Specifically, there are three impurities ((b) (4), (b) (4) and (b) (4) (b) (4)) that are present in your product at levels higher than those in the approved capsules and for which the acceptance criteria exceed the qualification threshold. We acknowledge that you have provided published literature to document that (b) (4) (b) (4) is an *in vivo* metabolite of nimodipine; the adequacy of these data are a

matter of review. However, you have provided no data to qualify the other two impurities.

We are providing the above comments to give you preliminary notice of potential review issues. Our filing review is only a preliminary evaluation of the application and is not indicative of deficiencies that may be identified during our review. Issues may be added, deleted, expanded upon, or modified as we review the application. If you respond to these issues during this review cycle, we may not consider your response before we take an action on your application.

During our preliminary review of your submitted labeling, we have identified the following labeling format issues and you should address the following issues in your proposed nimodipine oral solution label:

Highlights

1. Consider removing the trademark symbols throughout the label.
2. Bold the entire product title line and use lowercase for the dosage form.
3. Include the correct pharmacologic class for nimodipine.
4. Do not repeat the indication under the Dosage and Administration heading.
5. Remove the word (b) (4) under the Contraindications heading.
6. Consider including “edema” and “headaches” in the Adverse Reactions list.
7. Only include clinically significant Drug Interactions.

Table of Contents

8. Remove subsections 1.1, 2.1, and 14.1 because there are no subsections 1.2, 2.2, or 14.2.

Full Prescribing Information

9. Revise the Dosage and Administration subsection to include subsections and avoid bolding and use of uppercase.
10. Use appropriate cross-referencing (see Implementation Guidance at <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm075082.pdf>).
11. Make sure that all Warnings and Precautions regarding dihydropyridine calcium channel blockers are included (e.g., edema) in the Warnings and Precautions section.
12. Do not capitalize verbiage and minimize the use of bold.
13. The title of Warnings and Precautions should be specific to the adverse reactions; it should not be “General.”
14. Include the following statement in Section 6.1: “Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice.”
15. All tables should include a title.
16. Nimotop (nimodipine) capsules have been marketed for over 20 years; spontaneous adverse reactions associated with Nimotop could be included in a Postmarketing

Experience subsection.

17. Only clinically significant Drug Interactions should be included.
18. For the Patient Counseling Information section, use command language and include all important information that a prescriber should tell a patient.

We will request that you resubmit labeling that addresses these issues in a timely manner. The resubmitted labeling will be used for further labeling discussions.

Please respond only to the above requests for information. While we anticipate that any response submitted in a timely manner will be reviewed during this review cycle, such review decisions will be made on a case-by-case basis at the time of receipt of the submission.

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(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

Because the drug product for this indication has orphan drug designation, you are exempt from this requirement.

If you have any questions, call Vandna Kishore, R.Ph., Regulatory Project Manager, at (301) 796-4193.

Sincerely,

{See appended electronic signature page}

Russell Katz, MD
Director
Division of Neurology Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

RUSSELL G KATZ
01/30/2012

ACTION PACKAGE CHECKLIST

APPLICATION INFORMATION¹

NDA # 203340 BLA #	NDA Supplement # BLA Supplement #	If NDA, Efficacy Supplement Type:
Proprietary Name: Nymalize Established/Proper Name: Nimodipine Oral Solution Dosage Form: Liquid		Applicant: Arbor Pharmaceuticals Agent for Applicant (if applicable):
RPM: Vandna Kishore		Division: DNP
<p><u>NDA and NDA Efficacy Supplements:</u></p> <p>NDA Application Type: <input type="checkbox"/> 505(b)(1) <input checked="" type="checkbox"/> 505(b)(2) Efficacy Supplement: <input type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2)</p> <p>(A supplement can be either a (b)(1) or a (b)(2) regardless of whether the original NDA was a (b)(1) or a (b)(2). Consult page 1 of the 505(b)(2) Assessment or the Appendix to this Action Package Checklist.)</p>		<p><u>505(b)(2) Original NDAs and 505(b)(2) NDA supplements:</u></p> <p>Listed drug(s) relied upon for approval (include NDA #(s) and drug name(s)): Nimotop, NDA 18-869</p> <p>Provide a brief explanation of how this product is different from the listed drug. Liquid form from the gel caps; listed drug is also discontinued</p> <p><input checked="" type="checkbox"/> This application does not rely upon a listed drug. <input type="checkbox"/> This application relies on literature. <input type="checkbox"/> This application relies on a final OTC monograph. <input checked="" type="checkbox"/> This application relies on (explain) submission relies upon previous findings of safety and effectiveness of Nimotop capsules noted above</p> <p><u>For ALL (b)(2) applications, two months prior to EVERY action, review the information in the 505(b)(2) Assessment and submit the draft² to CDER OND IO for clearance. Finalize the 505(b)(2) Assessment at the time of the approval action.</u></p> <p><u>On the day of approval, check the Orange Book again for any new patents or pediatric exclusivity.</u></p> <p><input checked="" type="checkbox"/> No changes <input type="checkbox"/> Updated Date of check: August 3, 2012</p> <p>If pediatric exclusivity has been granted or the pediatric information in the labeling of the listed drug changed, determine whether pediatric information needs to be added to or deleted from the labeling of this drug.</p>
❖ Actions		
<ul style="list-style-type: none"> • Proposed action • User Fee Goal Date is <u>05/20/13</u> 		<input checked="" type="checkbox"/> AP <input type="checkbox"/> TA <input type="checkbox"/> CR
<ul style="list-style-type: none"> • Previous actions (<i>specify type and date for each action taken</i>) 		<input type="checkbox"/> None CR 8/16/12

¹ The **Application Information** Section is (only) a checklist. The **Contents of Action Package** Section (beginning on page 5) lists the documents to be included in the Action Package.

² For resubmissions, (b)(2) applications must be cleared before the action, but it is not necessary to resubmit the draft 505(b)(2) Assessment to CDER OND IO unless the Assessment has been substantively revised (e.g., new listed drug, patent certification revised).

<p>❖ If accelerated approval or approval based on efficacy studies in animals, were promotional materials received? Note: Promotional materials to be used within 120 days after approval must have been submitted (for exceptions, see http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm069965.pdf). If not submitted, explain _____</p>	<p><input type="checkbox"/> Received</p>
<p>❖ Application Characteristics ³</p>	
<p>Review priority: <input type="checkbox"/> Standard <input checked="" type="checkbox"/> Priority Chemical classification (new NDAs only):</p> <p><input checked="" type="checkbox"/> Fast Track <input type="checkbox"/> Rx-to-OTC full switch <input type="checkbox"/> Rolling Review <input type="checkbox"/> Rx-to-OTC partial switch <input checked="" type="checkbox"/> Orphan drug designation <input type="checkbox"/> Direct-to-OTC</p> <p>NDAs: Subpart H BLAs: Subpart E <input type="checkbox"/> Accelerated approval (21 CFR 314.510) <input type="checkbox"/> Accelerated approval (21 CFR 601.41) <input type="checkbox"/> Restricted distribution (21 CFR 314.520) <input type="checkbox"/> Restricted distribution (21 CFR 601.42)</p> <p>Subpart I Subpart H <input type="checkbox"/> Approval based on animal studies <input type="checkbox"/> Approval based on animal studies</p> <p><input type="checkbox"/> Submitted in response to a PMR REMS: <input type="checkbox"/> MedGuide <input type="checkbox"/> Submitted in response to a PMC <input type="checkbox"/> Communication Plan <input type="checkbox"/> Submitted in response to a Pediatric Written Request <input type="checkbox"/> ETASU <input type="checkbox"/> MedGuide w/o REMS <input type="checkbox"/> REMS not required</p> <p>Comments:</p>	
<p>❖ BLAs only: Ensure <i>RMS-BLA Product Information Sheet for TBP</i> and <i>RMS-BLA Facility Information Sheet for TBP</i> have been completed and forwarded to OPI/OBI/DRM (Vicky Carter)</p>	<p><input type="checkbox"/> Yes, dates</p>
<p>❖ BLAs only: Is the product subject to official FDA lot release per 21 CFR 610.2 (<i>approvals only</i>)</p>	<p><input type="checkbox"/> Yes <input type="checkbox"/> No</p>
<p>❖ Public communications (<i>approvals only</i>)</p>	
<ul style="list-style-type: none"> • Office of Executive Programs (OEP) liaison has been notified of action 	<p><input checked="" type="checkbox"/> Yes <input type="checkbox"/> No</p>
<ul style="list-style-type: none"> • Press Office notified of action (by OEP) 	<p><input checked="" type="checkbox"/> Yes <input type="checkbox"/> No</p>
<ul style="list-style-type: none"> • Indicate what types (if any) of information dissemination are anticipated 	<p><input type="checkbox"/> None <input checked="" type="checkbox"/> HHS Press Release <input type="checkbox"/> FDA Talk Paper <input type="checkbox"/> CDER Q&As <input type="checkbox"/> Other</p>

³ Answer all questions in all sections in relation to the pending application, i.e., if the pending application is an NDA or BLA supplement, then the questions should be answered in relation to that supplement, not in relation to the original NDA or BLA. For example, if the application is a pending BLA supplement, then a new *RMS-BLA Product Information Sheet for TBP* must be completed.

❖ Exclusivity	
<ul style="list-style-type: none"> Is approval of this application blocked by any type of exclusivity? 	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes
<ul style="list-style-type: none"> NDA and BLA: Is there existing orphan drug exclusivity for the “same” drug or biologic for the proposed indication(s)? <i>Refer to 21 CFR 316.3(b)(13) for the definition of “same drug” for an orphan drug (i.e., active moiety). This definition is NOT the same as that used for NDA chemical classification.</i> 	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If, yes, NDA/BLA # _____ and date exclusivity expires: _____
<ul style="list-style-type: none"> (b)(2) NDAs only: Is there remaining 5-year exclusivity that would bar effective approval of a 505(b)(2) application? <i>(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)</i> 	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If yes, NDA # _____ and date exclusivity expires: _____
<ul style="list-style-type: none"> (b)(2) NDAs only: Is there remaining 3-year exclusivity that would bar effective approval of a 505(b)(2) application? <i>(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)</i> 	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If yes, NDA # _____ and date exclusivity expires: _____
<ul style="list-style-type: none"> (b)(2) NDAs only: Is there remaining 6-month pediatric exclusivity that would bar effective approval of a 505(b)(2) application? <i>(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)</i> 	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If yes, NDA # _____ and date exclusivity expires: _____
<ul style="list-style-type: none"> NDAs only: Is this a single enantiomer that falls under the 10-year approval limitation of 505(u)? <i>(Note that, even if the 10-year approval limitation period has not expired, the application may be tentatively approved if it is otherwise ready for approval.)</i> 	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If yes, NDA # _____ and date 10-year limitation expires: _____
❖ Patent Information (NDAs only)	
<ul style="list-style-type: none"> Patent Information: Verify that form FDA-3542a was submitted for patents that claim the drug for which approval is sought. If the drug is an old antibiotic, skip the Patent Certification questions. 	<input checked="" type="checkbox"/> Verified <input type="checkbox"/> Not applicable because drug is an old antibiotic.
<ul style="list-style-type: none"> Patent Certification [505(b)(2) applications]: Verify that a certification was submitted for each patent for the listed drug(s) in the Orange Book and identify the type of certification submitted for each patent. 	21 CFR 314.50(i)(1)(i)(A) <input type="checkbox"/> Verified 21 CFR 314.50(i)(1) <input type="checkbox"/> (ii) <input type="checkbox"/> (iii)
<ul style="list-style-type: none"> [505(b)(2) applications] If the application includes a paragraph III certification, it cannot be approved until the date that the patent to which the certification pertains expires (but may be tentatively approved if it is otherwise ready for approval). 	<input checked="" type="checkbox"/> No paragraph III certification Date patent will expire _____
<ul style="list-style-type: none"> [505(b)(2) applications] For each paragraph IV certification, verify that the applicant notified the NDA holder and patent owner(s) of its certification that the patent(s) is invalid, unenforceable, or will not be infringed (review documentation of notification by applicant and documentation of receipt of notice by patent owner and NDA holder). <i>(If the application does not include any paragraph IV certifications, mark “N/A” and skip to the next section below (Summary Reviews)).</i> 	<input checked="" type="checkbox"/> N/A (no paragraph IV certification) <input type="checkbox"/> Verified

- [505(b)(2) applications] For **each paragraph IV** certification, based on the questions below, determine whether a 30-month stay of approval is in effect due to patent infringement litigation.

Answer the following questions for **each** paragraph IV certification:

- (1) Have 45 days passed since the patent owner’s receipt of the applicant’s notice of certification?

Yes No

(Note: The date that the patent owner received the applicant’s notice of certification can be determined by checking the application. The applicant is required to amend its 505(b)(2) application to include documentation of this date (e.g., copy of return receipt or letter from recipient acknowledging its receipt of the notice) (see 21 CFR 314.52(e)).

If “Yes,” skip to question (4) below. If “No,” continue with question (2).

- (2) Has the patent owner (or NDA holder, if it is an exclusive patent licensee) submitted a written waiver of its right to file a legal action for patent infringement after receiving the applicant’s notice of certification, as provided for by 21 CFR 314.107(f)(3)?

Yes No

If “Yes,” there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip the rest of the patent questions.

If “No,” continue with question (3).

- (3) Has the patent owner, its representative, or the exclusive patent licensee filed a lawsuit for patent infringement against the applicant?

Yes No

(Note: This can be determined by confirming whether the Division has received a written notice from the (b)(2) applicant (or the patent owner or its representative) stating that a legal action was filed within 45 days of receipt of its notice of certification. The applicant is required to notify the Division in writing whenever an action has been filed within this 45-day period (see 21 CFR 314.107(f)(2)).

If “No,” the patent owner (or NDA holder, if it is an exclusive patent licensee) has until the expiration of the 45-day period described in question (1) to waive its right to bring a patent infringement action or to bring such an action. After the 45-day period expires, continue with question (4) below.

- (4) Did the patent owner (or NDA holder, if it is an exclusive patent licensee) submit a written waiver of its right to file a legal action for patent infringement within the 45-day period described in question (1), as provided for by 21 CFR 314.107(f)(3)?

Yes No

If “Yes,” there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next section below (Summary Reviews).

If “No,” continue with question (5).

<p>(5) Did the patent owner, its representative, or the exclusive patent licensee bring suit against the (b)(2) applicant for patent infringement within 45 days of the patent owner's receipt of the applicant's notice of certification?</p> <p>(Note: This can be determined by confirming whether the Division has received a written notice from the (b)(2) applicant (or the patent owner or its representative) stating that a legal action was filed within 45 days of receipt of its notice of certification. The applicant is required to notify the Division in writing whenever an action has been filed within this 45-day period (see 21 CFR 314.107(f)(2)). If no written notice appears in the NDA file, confirm with the applicant whether a lawsuit was commenced within the 45-day period).</p> <p><i>If "No," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next section below (Summary Reviews).</i></p> <p><i>If "Yes," a stay of approval may be in effect. To determine if a 30-month stay is in effect, consult with the OND ADRA and attach a summary of the response.</i></p>	<p><input type="checkbox"/> Yes <input type="checkbox"/> No</p>
---	--

CONTENTS OF ACTION PACKAGE

❖ Copy of this Action Package Checklist ⁴	included
--	----------

Officer/Employee List

❖ List of officers/employees who participated in the decision to approve this application and consented to be identified on this list (<i>approvals only</i>)	<input checked="" type="checkbox"/> Included
Documentation of consent/non-consent by officers/employees	<input checked="" type="checkbox"/> Included

Action Letters

❖ Copies of all action letters (<i>including approval letter with final labeling</i>)	Action(s) and date(s) CR 8/18/12; AP 5/10/13
---	--

Labeling

❖ Package Insert (<i>write submission/communication date at upper right of first page of PI</i>)	
<ul style="list-style-type: none"> • Most recent draft labeling. If it is division-proposed labeling, it should be in track-changes format. 	included
<ul style="list-style-type: none"> • Original applicant-proposed labeling 	included
<ul style="list-style-type: none"> • Example of class labeling, if applicable 	

⁴ Fill in blanks with dates of reviews, letters, etc.

Medication Guide/Patient Package Insert/Instructions for Use/Device Labeling (<i>write submission/communication date at upper right of first page of each piece</i>)	<input type="checkbox"/> Medication Guide <input type="checkbox"/> Patient Package Insert <input type="checkbox"/> Instructions for Use <input type="checkbox"/> Device Labeling <input checked="" type="checkbox"/> None
<ul style="list-style-type: none"> Most-recent draft labeling. If it is division-proposed labeling, it should be in track-changes format. 	
<ul style="list-style-type: none"> Original applicant-proposed labeling 	
<ul style="list-style-type: none"> Example of class labeling, if applicable 	
❖ Labels (full color carton and immediate-container labels) (<i>write submission/communication date on upper right of first page of each submission</i>)	
<ul style="list-style-type: none"> Most-recent draft labeling 	n/a
❖ Proprietary Name <ul style="list-style-type: none"> Acceptability/non-acceptability letter(s) (<i>indicate date(s)</i>) Review(s) (<i>indicate date(s)</i>) Ensure that both the proprietary name(s), if any, and the generic name(s) are listed in the Application Product Names section of DARRTS, and that the proprietary/trade name is checked as the 'preferred' name. 	ppn granted letter:022713;021312 6/26/12 final review 2/7/12 first review
❖ Labeling reviews (<i>indicate dates of reviews and meetings</i>)	<input checked="" type="checkbox"/> RPM 01/28/12 <input checked="" type="checkbox"/> DMEPA 3/1/12;5/16/12; 6/16/12 <input type="checkbox"/> DMPP/PLT (DRISK) <input type="checkbox"/> ODPD (DDMAC) <input checked="" type="checkbox"/> SEALD 01/28/12; 5/7/13 <input type="checkbox"/> CSS <input type="checkbox"/> Other reviews
Administrative / Regulatory Documents	
❖ Administrative Reviews (<i>e.g., RPM Filing Review⁵/Memo of Filing Meeting</i>) (<i>indicate date of each review</i>)	12/6/11
❖ All NDA (b)(2) Actions: Date each action cleared by (b)(2) Clearance Cmte	<input type="checkbox"/> Not a (b)(2)
❖ NDA (b)(2) Approvals Only: 505(b)(2) Assessment (<i>indicate date</i>)	<input type="checkbox"/> Not a (b)(2) 08/2/12; 4/26/13
❖ NDAs only: Exclusivity Summary (<i>signed by Division Director</i>)	<input type="checkbox"/> Included
❖ Application Integrity Policy (AIP) Status and Related Documents http://www.fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/default.htm	
<ul style="list-style-type: none"> Applicant is on the AIP 	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<ul style="list-style-type: none"> This application is on the AIP <ul style="list-style-type: none"> If yes, Center Director's Exception for Review memo (<i>indicate date</i>) If yes, OC clearance for approval (<i>indicate date of clearance communication</i>) 	<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Not an AP action
❖ Pediatrics (<i>approvals only</i>) <ul style="list-style-type: none"> Date reviewed by PeRC <u>n/a-Orphan Drug</u> If PeRC review not necessary, explain: <u>Orphan Drug Designation</u> Pediatric Page/Record (<i>approvals only, must be reviewed by PERC before finalized</i>) 	<input type="checkbox"/> Included

⁵ Filing reviews for scientific disciplines should be filed behind the respective discipline tab.

❖ Debarment certification (original applications only): verified that qualifying language was not used in certification and that certifications from foreign applicants are cosigned by U.S. agent <i>(include certification)</i>	<input checked="" type="checkbox"/> Verified, statement is acceptable
❖ Outgoing communications <i>(letters, including response to FDRR (do not include previous action letters in this tab), emails, faxes, telecons)</i>	
❖ Internal memoranda, telecons, etc.	
❖ Minutes of Meetings	
• Regulatory Briefing <i>(indicate date of mtg)</i>	<input type="checkbox"/> No mtg
• If not the first review cycle, any end-of-review meeting <i>(indicate date of mtg)</i>	<input type="checkbox"/> N/A or no mtg
• Pre-NDA/BLA meeting <i>(indicate date of mtg)</i>	<input type="checkbox"/> No mtg
• EOP2 meeting <i>(indicate date of mtg)</i>	<input type="checkbox"/> No mtg
• Other milestone meetings (e.g., EOP2a, CMC pilots) <i>(indicate dates of mtgs)</i>	
❖ Advisory Committee Meeting(s)	<input checked="" type="checkbox"/> No AC meeting
• Date(s) of Meeting(s)	
• 48-hour alert or minutes, if available <i>(do not include transcript)</i>	
Decisional and Summary Memos	
❖ Office Director Decisional Memo <i>(indicate date for each review)</i>	<input type="checkbox"/> None
Division Director Summary Review <i>(indicate date for each review)</i>	<input type="checkbox"/> None 051013
Cross-Discipline Team Leader Review <i>(indicate date for each review)</i>	<input type="checkbox"/> None 050913
PMR/PMC Development Templates <i>(indicate total number)</i>	<input checked="" type="checkbox"/> None
Clinical Information⁶	
❖ Clinical Reviews	
• Clinical Team Leader Review(s) <i>(indicate date for each review)</i>	see CDTL review above
• Clinical review(s) <i>(indicate date for each review)</i>	3/18/12
• Social scientist review(s) (if OTC drug) <i>(indicate date for each review)</i>	<input checked="" type="checkbox"/> None
❖ Financial Disclosure reviews(s) or location/date if addressed in another review OR If no financial disclosure information was required, check here <input type="checkbox"/> and include a review/memo explaining why not <i>(indicate date of review/memo)</i>	
❖ Clinical reviews from immunology and other clinical areas/divisions/Centers <i>(indicate date of each review)</i>	<input checked="" type="checkbox"/> None
❖ Controlled Substance Staff review(s) and Scheduling Recommendation <i>(indicate date of each review)</i>	<input checked="" type="checkbox"/> Not applicable
❖ Risk Management	
• REMS Documents and Supporting Statement <i>(indicate date(s) of submission(s))</i>	
• REMS Memo(s) and letter(s) <i>(indicate date(s))</i>	
• Risk management review(s) and recommendations (including those by OSE and CSS) <i>(indicate date of each review and indicate location/date if incorporated into another review)</i>	<input checked="" type="checkbox"/> None

⁶ Filing reviews should be filed with the discipline reviews.

❖ DSI Clinical Inspection Review Summary(ies) (include copies of DSI letters to investigators)	<input checked="" type="checkbox"/> None requested
Clinical Microbiology <input type="checkbox"/> None	
❖ Clinical Microbiology Team Leader Review(s) (indicate date for each review)	<input checked="" type="checkbox"/> None
Clinical Microbiology Review(s) (indicate date for each review)	<input type="checkbox"/> None 6/28/12
Biostatistics <input type="checkbox"/> None	
❖ Statistical Division Director Review(s) (indicate date for each review)	<input checked="" type="checkbox"/> None
Statistical Team Leader Review(s) (indicate date for each review)	<input checked="" type="checkbox"/> None
Statistical Review(s) (indicate date for each review)	<input checked="" type="checkbox"/> None
Clinical Pharmacology <input type="checkbox"/> None	
❖ Clinical Pharmacology Division Director Review(s) (indicate date for each review)	<input checked="" type="checkbox"/> None
Clinical Pharmacology Team Leader Review(s) (indicate date for each review)	<input checked="" type="checkbox"/> None
Clinical Pharmacology review(s) (indicate date for each review)	<input type="checkbox"/> None 8/10/12
❖ DSI Clinical Pharmacology Inspection Review Summary (include copies of DSI letters)	<input checked="" type="checkbox"/> None
Nonclinical <input type="checkbox"/> None	
❖ Pharmacology/Toxicology Discipline Reviews	
• ADP/T Review(s) (indicate date for each review)	<input checked="" type="checkbox"/> None
• Supervisory Review(s) (indicate date for each review)	<input type="checkbox"/> None 6/26/12
• Pharm/tox review(s), including referenced IND reviews (indicate date for each review)	<input type="checkbox"/> None 5/18/12
❖ Review(s) by other disciplines/divisions/Centers requested by P/T reviewer (indicate date for each review)	<input checked="" type="checkbox"/> None
❖ Statistical review(s) of carcinogenicity studies (indicate date for each review)	<input type="checkbox"/> No carc
❖ ECAC/CAC report/memo of meeting	<input type="checkbox"/> None Included in P/T review, page
❖ DSI Nonclinical Inspection Review Summary (include copies of DSI letters)	<input type="checkbox"/> None requested
Product Quality <input type="checkbox"/> None	
❖ Product Quality Discipline Reviews	
• ONDQA/OBP Division Director Review(s) (indicate date for each review)	<input type="checkbox"/> None
• Branch Chief/Team Leader Review(s) (indicate date for each review)	<input type="checkbox"/> None
• Product quality review(s) including ONDQA biopharmaceutics reviews (indicate date for each review)	<input type="checkbox"/> None 4/16/12;4/24/12;3/19/13
❖ Microbiology Reviews	<input type="checkbox"/> Not needed 6/28/12
<input checked="" type="checkbox"/> NDAs: Microbiology reviews (sterility & pyrogenicity) (OPS/NDMS) (indicate date of each review)	
<input type="checkbox"/> BLAs: Sterility assurance, microbiology, facilities reviews (OMPQ/MAPCB/BMT) (indicate date of each review)	
❖ Reviews by other disciplines/divisions/Centers requested by CMC/quality reviewer (indicate date of each review)	<input checked="" type="checkbox"/> None

❖ Environmental Assessment (check one) (original and supplemental applications)	
<input type="checkbox"/> Categorical Exclusion (<i>indicate review date</i>)(<i>all original applications and all efficacy supplements that could increase the patient population</i>)	
<input type="checkbox"/> Review & FONSI (<i>indicate date of review</i>)	
<input type="checkbox"/> Review & Environmental Impact Statement (<i>indicate date of each review</i>)	
❖ Facilities Review/Inspection	
<input checked="" type="checkbox"/> NDAs: Facilities inspections (include EER printout) (<i>date completed must be within 2 years of action date</i>) (<i>only original NDAs and supplements that include a new facility or a change that affects the manufacturing sites⁷</i>)	Date completed: <input checked="" type="checkbox"/> Acceptable <input type="checkbox"/> Withhold recommendation <input type="checkbox"/> Not applicable
<input type="checkbox"/> BLAs: TB-EER (<i>date of most recent TB-EER must be within 30 days of action date</i>) (<i>original and supplemental BLAs</i>)	Date completed: <input type="checkbox"/> Acceptable <input type="checkbox"/> Withhold recommendation
❖ NDAs: Methods Validation (<i>check box only, do not include documents</i>)	<input type="checkbox"/> Completed <input type="checkbox"/> Requested <input type="checkbox"/> Not yet requested <input checked="" type="checkbox"/> Not needed (per review)

⁷ I.e., a new facility or a change in the facility, or a change in the manufacturing process in a way that impacts the Quality Management Systems of the facility.

Appendix to Action Package Checklist

An NDA or NDA supplemental application is likely to be a 505(b)(2) application if:

- (1) It relies on published literature to meet any of the approval requirements, and the applicant does not have a written right of reference to the underlying data. If published literature is cited in the NDA but is not necessary for approval, the inclusion of such literature will not, in itself, make the application a 505(b)(2) application.
- (2) **Or** it relies for approval on the Agency's previous findings of safety and efficacy for a listed drug product and the applicant does not own or have right to reference the data supporting that approval.
- (3) **Or** it relies on what is "generally known" or "scientifically accepted" about a class of products to support the safety or effectiveness of the particular drug for which the applicant is seeking approval. (Note, however, that this does not mean *any* reference to general information or knowledge (e.g., about disease etiology, support for particular endpoints, methods of analysis) causes the application to be a 505(b)(2) application.)

Types of products for which 505(b)(2) applications are likely to be submitted include: fixed-dose combination drug products (e.g., heart drug and diuretic (hydrochlorothiazide) combinations); OTC monograph deviations (see 21 CFR 330.11); new dosage forms; new indications; and, new salts.

An efficacy supplement can be either a (b)(1) or a (b)(2) regardless of whether the original NDA was a (b)(1) or a (b)(2).

An efficacy supplement is a 505(b)(1) supplement if the supplement contains all of the information needed to support the approval of the change proposed in the supplement. For example, if the supplemental application is for a new indication, the supplement is a 505(b)(1) if:

- (1) The applicant has conducted its own studies to support the new indication (or otherwise owns or has right of reference to the data/studies).
- (2) **And** no additional information beyond what is included in the supplement or was embodied in the finding of safety and effectiveness for the original application or previously approved supplements is needed to support the change. For example, this would likely be the case with respect to safety considerations if the dose(s) was/were the same as (or lower than) the original application.
- (3) **And** all other "criteria" are met (e.g., the applicant owns or has right of reference to the data relied upon for approval of the supplement, the application does not rely for approval on published literature based on data to which the applicant does not have a right of reference).

An efficacy supplement is a 505(b)(2) supplement if:

- (1) Approval of the change proposed in the supplemental application would require data beyond that needed to support our previous finding of safety and efficacy in the approval of the original application (or earlier supplement), and the applicant has not conducted all of its own studies for approval of the change, or obtained a right to reference studies it does not own. For example, if the change were for a new indication AND a higher dose, we would likely require clinical efficacy data and preclinical safety data to approve the higher dose. If the applicant provided the effectiveness data, but had to rely on a different listed drug, or a new aspect of a previously cited listed drug, to support the safety of the new dose, the supplement would be a 505(b)(2).
- (2) **Or** the applicant relies for approval of the supplement on published literature that is based on data that the applicant does not own or have a right to reference. If published literature is cited in the supplement but is not necessary for approval, the inclusion of such literature will not, in itself, make the supplement a 505(b)(2) supplement.
- (3) **Or** the applicant is relying upon any data they do not own or to which they do not have right of reference.

If you have questions about whether an application is a 505(b)(1) or 505(b)(2) application, consult with your ODE's ADRA.



NDA 203340

PRIORITY REVIEW DESIGNATION

Arbor Pharmaceuticals
Attention: Allison Lowry
Director, Quality and Regulatory Affairs
980 Hammond Drive, Suite 1250
Atlanta, GA 30328

Dear Ms. Lowry:

Please refer to your New Drug Application (NDA) dated November 18, 2011, received November 18, 2011, submitted under section section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act, for Nimodipine 60 mg/ml Oral Solution.

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 **Priority**. Therefore, the user fee goal date is May 18, 2012.

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 requirement/commitment requests by April 27, 2012.

While conducting our filing review, we identified potential review issues and will communicate them to you on or before January 31, 2012.

If you have any questions, call Vandna Kishore, R.Ph., Regulatory Project Manager, at (301) 796-4193.

Sincerely,

{See appended electronic signature page}

Russell Katz, MD
Director
Division of Neurology Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

ERIC P BASTINGS
01/17/2012
Signed for Dr. Katz.



NDA 203340

NDA ACKNOWLEDGMENT

Arbor Pharmaceuticals
Attention: Allison Lowry
Director, Quality and Regulatory Affairs
980 Hammond Drive, Suite 1250
Atlanta, GA 30328

Dear Ms. Lowry:

We have received your New Drug Application (NDA) submitted under section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for the following:

Name of Drug Product: Nimodipine Oral Solution

Date of Application: November 18, 2011

Date of Receipt: November 18, 2011

Our Reference Number: NDA 203340

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 January 17, 2012, 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/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>. 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.

You are also 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).

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/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/DrugMasterFilesDMFs/ucm073080.htm>.

If you have any questions, call Vandna Kishore, R.Ph., Regulatory Project Manager, at (301) 796-4193.

Sincerely,

{See appended electronic signature page}

Vandna Kishore, R.Ph.
Regulatory Project Manager
Division of Neurology Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

VANDNA N KISHORE
12/02/2011