CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

202810Orig1s000

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

NDA 202810

PROPRIETARY NAME REQUEST
CONDITIONALLY ACCEPTABLE

Supernus Pharmaceuticals, Inc
1550 East Gude Drive
Rockville, MD 20850

ATTENTION: Tami T. Martin, RN, Esq.
Vice President, Regulatory Affairs

Dear Ms. Martin:

Please refer to your New Drug Application (NDA) dated and received December 19, 2011, submitted under section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Oxcarbazepine Extended-release Tablets, 150 mg, 300 mg, and 600 mg.

We also refer to your correspondence, dated and received August 29, 2012, requesting review of your proposed proprietary name, Oxtellar XR. We have completed our review of the proposed proprietary name, Oxtellar XR and have concluded that it is acceptable.

If **any** of the proposed product characteristics as stated in your August 29, 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, Stephanie Parncutt, at (301) 796-4098.

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

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/s/

LAURIE A KELLEY
10/12/2012

CAROL A HOLQUIST
10/15/2012

From: Tami Martin
To: Parncutt, Stephanie
Subject: RE: FDA Request for Information - NDA 202810/oxcarbazepine extended-release Tablets
Date: Wednesday, October 10, 2012 6:54:31 PM

Hello Stephanie,

Confirming receipt of this request from DMEPA as well.

We will work with the vendor doing the artwork for the labels to accommodate the requests.

Tami Martin
301-838-2607
tmartin@supernus.com

From: Parncutt, Stephanie [mailto:Stephanie.Parncutt@fda.hhs.gov]
Sent: Wednesday, October 10, 2012 5:59 PM
To: Tami Martin
Subject: FDA Request for Information - NDA 202810/oxcarbazepine extended-release Tablets
Importance: High

Below is a request from the Division of Medication Error Prevention and Analysis team related to their ongoing review of the oxcarbazepine extended-release application (N 202-810). Please submit your response to this request in electronic archival format as an amendment to the above NDA. It is acceptable for you to email your response to me in advance of a formal, archival submission as long as both communications (email & archive) contain identical information.

* Please see the comments below from the Division of Medication Error Prevention and Analysis:

A. Container Labels and Professional Sample Blister Card Labeling

1. The 150 mg statement of strength as well as other statements are in (b) (4) font on a yellow background and are difficult to read due to the lack of sufficient contrast between the two colors. We recommend replacing the (b) (4) font with a black font, outlining the (b) (4) font with black, or using other means to improve contrast.

2. Although we recognize you have attempted to better differentiate your strengths within your product line, we still believe the strengths lack sufficient differentiation. The dark yellow utilized for 150 mg looks similar to the brown color utilized for 600 mg. Additionally, the pinkish-brown utilized for 300 mg also looks similar to the brown color utilized for 600 mg. Although
the color used for the 600 mg strength is darker we believe they continue to look too similar. Consider the use of alternate colors for strength differentiation to minimize the risk of selection error.

3. Per the Office of New Drug Quality Assessment, revise the storage statement to read: "Store at 25°C (77°F); excursions 15°C to 30°C (59°F to 86°F) [See USP controlled room temperature]. Protect from light and moisture." We recommend dashes not be used in order

to provide clarity and prevent the potential for misinterpretation of the "-" symbol.

B. Container Labels

C. Professional Sample Blister Card Labeling

Please confirm receipt and respond to this request as soon as possible; if you have any questions, please contact me to discuss.

Thank you,

Stephanie N. Parncutt, MHA
Regulatory Project Manager
Division of Neurology Products
Center for Drug Evaluation and Research, FDA
10903 New Hampshire Avenue; WO22 Rm. 4355
Silver Spring, MD 20993-0002

phone: 301-796-4098
email: stephanie.parncutt@fda.hhs.gov

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/s/

STEPHANIE N PARNCUTT
10/11/2012

From:	David, Jeannie C
To:	"Tami Martin"
Cc:	Bouie, Teshara; Parncutt, Stephanie
Subject:	RE: NDA 202810 and Out of office
Date:	Monday, August 20, 2012 11:46:22 AM

Hi Tami,

Many thanks for your team's quick response. The formal submission tomorrow or Wednesday should be fine.

Best regards,

Jeannie

From: Tami Martin [mailto:tmartin@supernus.com]
Sent: Monday, August 20, 2012 11:43 AM
To: David, Jeannie C
Cc: Bouie, Teshara; Parncutt, Stephanie
Subject: RE: NDA 202810 and Out of office

Hello Ms. David,

Please find attached the Module 2 and Module 3 files that are being supplied to the publisher for submission in Sequence 0019 to NDA 202810. These are responsive to your August 16th request, below. As you can see we are happy to finalize these dissolution specifications as agreed upon by the agency.

I will be completing the cover letter and forms (Module 1 files) for the formal submission that will follow by esub gateway either tomorrow or Wednesday. I hope that is acceptable.

Tami Martin
Supernus Pharmaceuticals, Inc.
301-838-2607
Cell 202-489-4331
tmartin@supernus.com

From: David, Jeannie C [mailto:Jeannie.David@fda.hhs.gov]
Sent: Thursday, August 16, 2012 10:17 AM
To: Tami Martin
Cc: Bouie, Teshara; Parncutt, Stephanie; Kelley, Laurie
Subject: RE: NDA 202810 and Out of office

Hi Tami,

Thanks so much for your reply while OOO. An email copy by Monday, with the duplicate submitted in the final esubmssion soon afterward would be fine.

Jeannie

From: Tami Martin [mailto:tmartin@supernus.com]
Sent: Thursday, August 16, 2012 10:11 AM
To: David, Jeannie C
Subject: Re: NDA 202810 and Out of office

I am OOO but still in touch. - will forward to the team, and work for a submission as requested. We do work with an outside e sub vendor so it alSo depends on their ability to prepare the final esubmission, fyi.

From: David, Jeannie C
To: Tami Martin
Cc: Bouie, Teshara ; Parncutt, Stephanie ; Kelley, Laurie
Sent: Thu Aug 16 09:58:54 2012
Subject: RE: NDA 202810 and Out of office
Hi Tami,

May I ask who is the contact covering for you while you are away? We have the following Biopharmaceutics request and kindly request prompt response by Monday, August 20, 2012:

The following dissolution method and dissolution acceptance criteria are acceptable for Oxcarbazepine ER tablets, 150 mg, 300 mg and 600 mg:

USP Apparatus/RPM	Medium	Volume	Acceptance Criteria
II/75 rpm	De-ionized water with 1% (w/v) SLS	900 mL	2 hrs: (b) (4) 4 hrs: 8 hrs:

The dissolution acceptance criteria are based on the results of PK study 804P101 which evaluated the BA/BE of formulations with a wide range of release rate and on the performance of the pivotal clinical and stability batches (refer to submission dated August 6, 2012).

Revise the dissolutions specifications accordingly and submit the updated drug product specification which includes the agreed upon acceptance criteria.

Thank you,

Jeannie

From: Tami Martin [mailto:tmartin@supernus.com]
Sent: Wednesday, August 15, 2012 10:24 AM
To: Bouie, Teshara; David, Jeannie C; Parncutt, Stephanie; Kelley, Laurie
Subject: NDA 202810 and Out of office

NDA 202810
Oxcarbazepine extended-release tablets

Hello,

I wanted to mention that I will be out of the office for training and then vacation Aug 16-24th. I believe Supernus has responded to all outstanding requests for CMC, clinical, statistics for NDA 202810. Please let me know if you disagree. I had understood there might be one additional CMC-related comment/request forthcoming?

I am aware of the DMEPA comments on the bottle label and edits to the PI (like mg/day changing to "mg per day"), as you know we are still in discussions about a tradename and so we were considering making all of those edits at once when a conditionally accepted tradename is identified if that sounds reasonable to you. I anticipate having new tradenames for submission after Aug 24th as we are working with a vendor now to identify and do preliminary testing on new names. Of course, assuming the review is proceeding as we hope, we also understand that it is highly likely that there will be content discussions about the draft labeling as well. Please let me know if this is not a satisfactory plan.

I will be monitoring my e mail Aug 16-24th and will not be so far away but what I can't come back to the office if it becomes necessary.

Tami Martin, RN, Esq.
Vice President, Regulatory Affairs
Supernus Pharmaceuticals, Inc.
Ph: 301-838-2607
mailto:tmartin@supernus.com

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/s/

STEPHANIE N PARNCUTT
08/20/2012

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Silver Spring, MD 20993

NDA 202810

PROPRIETARY NAME REQUEST WITHDRAWN

Supernus Pharmaceuticals, Inc
1550 East Gude Drive
Rockville, MD 20850

ATTENTION: Tami T. Martin, RN, Esq.
Vice President, Regulatory Affairs

Dear Ms. Martin:

Please refer to your New Drug Application (NDA) dated and received December 19, 2012, submitted under section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Oxcarbazepine Extended-release Tablets, 150 mg, 300 mg, and 600 mg.

We also refer to your correspondence, dated and received August 9, 2012, notifying us that you are withdrawing your request for a review of the proposed proprietary name, (b) (4). This proposed proprietary name request is considered withdrawn as of August 9, 2012

We note that you have not proposed an alternate proprietary name for review at this time and that it is your intention to submit a new proposed proprietary name in future. In order to initiate review of any proprietary name, a new request for a proposed proprietary name review should be submitted as soon as possible. (See the Guidance for Industry, Contents of a Complete Submission for the Evaluation of Proprietary Names, http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM075068.pdf and "PDUFA Reauthorization Performance Goals and Procedures Fiscal Years 2008 through 2012".)

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, Stephanie Parncutt at (301) 796-4098.

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

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/s/

LAURIE A KELLEY
08/17/2012

CAROL A HOLQUIST
08/17/2012

From: Tami Martin
To: Parncutt, Stephanie
Subject: RE: FDA Request for Information - NDA 202810/oxcarbazepine extended-release Tablets
Date: Monday, July 09, 2012 4:31:27 PM

Stephanie,

I notice that the comments received today speak about a Medication Guides statement "dependent upon whether the Medication Guide accompanies the product". Trileptal® was released from the requirement that they have a Medication Guide as a REMS requirement: based on letters on the Drugs@FDA website, it appears that the Medication Guide is considered to be part of Trileptal's package insert. I would like some clarification about the rules for distribution of a Medication Guide that is not part of a REMS program, but is part of the product label.

Tami Martin
Supernus Pharmaceuticals, Inc.
301-838-2607
tmartin@supernus.com

From: Tami Martin
Sent: Monday, July 09, 2012 3:13 PM
To: 'Parncutt, Stephanie'
Cc: 'Bouie, Teshara'
Subject: RE: FDA Request for Information - NDA 202810/oxcarbazepine extended-release Tablets

Hello Stephanie and Teshara,

Stephanie, I am acknowledging receipt of today's e mail, below. I will get back to you about timing of response on these labeling items.

Teshara, concerning timing for the remaining CMC responses, we are working with our DS vendor to complete the tasks needed to generate a technical report and validation report. Based on current expectations, I think that we will be responding to the remaining items in late July-early August timeframe. We are trying to beat those dates, but as we are reliant on activities at our DS vendor, the timing is not completely under our control.

Thank you.

Tami Martin
Supernus Pharmaceuticals, Inc.
301-838-2607
tmartin@supernus.com

From: Parncutt, Stephanie [mailto:Stephanie.Parncutt@fda.hhs.gov]
Sent: Monday, July 09, 2012 2:16 PM
To: Tami Martin
Subject: FDA Request for Information - NDA 202810/oxcarbazepine extended-release Tablets
Importance: High

Below is a request from the Division of Medication Error Prevention and Analysis team related to their ongoing review of the oxcarbazepine extended-release application (N 202-810). Please submit your response to this request in electronic archival format as an amendment to the above NDA. It is acceptable for you to email your response to me in advance of a formal, archival submission as long as both communications (email & archive) contain identical information.

* Please see the comments below from the Division of Medication Error Prevention and Analysis:

A. General Comments for all labels and labeling (150 mg, 300 mg, and 600 mg)

1. (b) (4)

2. Ensure the established name has a prominence commensurate with the proprietary name, taking into account all pertinent factors, including typography, layout, contrast, and other printing features [21 CFR 201.10(g)(2)].
3. The numerical strength is above its corresponding unit of measure. Relocate the unit of measure so that it is beside the numerical strength (i.e., 150 mg, 300 mg, and 600 mg).
4. The net quantity and "Rx only" statements are too prominent due to the bold font. Debold the font for these statements.
5. The "EXTENDED-RELEASE" in the dosage form is in all uppercase letters, which decreases the readability of the statement. Revise the presentation from upper case to title case (i.e., Extended-release).
6. The 300 mg strength is printed on a (b) (4) background with a brownish font. The 600 mg strength appears to reverse the presentation of the 300 mg strength, leading to the 300 mg and 600 mg strengths having similar colors that are not well differentiated from one another. Additionally, the yellow background color of the 150 mg strength and the (b) (4) background of the 300 mg strength are not sufficiently distinct due to minimal contrast. We recommend choosing different colors for strength differentiation that are distinct within the product line and ensure that they do not overlap with the colors already utilized for strength differentiation within the Trileptal product line.
7. The extended-release tablets overlap in strength with the currently marketed immediate-release strengths. In order to help differentiate the two formulations, place the statement "Once-a-day" or a similar statement on the principle display panel. Additionally, add the statement "Swallow whole, do not cut, crush or chew" to the principle display panel as well.
8. The NDC numbers only contain the first five numbers (i.e., 17772-XXXXX) and are, therefore, not complete. Include the entire NDC number on all container labels and blister card labeling.
9. The Supernus logo is too prominent as compared to the proprietary name, established name and product strength. Decrease the size of the logo.
10. The storage and handling information states "Store in well-closed container" at XX temperature and "Protect from moisture". These two statements are not in the insert labeling.

Ensure the storage statements are consistent between all labels and labeling.

B. Container Labels

C. Professional Sample Blister Card Labeling

D. Insert Labeling

1. Section 2: Dosage and Administration

a. The dangerous symbol "/" is used when expressing the daily dose (e.g., 300 mg/day or 600 mg/day). Replace the symbol "/" with the word "per" when referring to the total daily dose (e.g., 600 mg per day). Additionally, remove the symbol "-" and insert the intended meaning. For example, revise "1200-2400 mg/day" to read 1200 mg to 2400 mg per day".

b. In the section *Patients with Renal Impairment*, the symbol "<" is used (i.e., "<30 mL/min"). Remove the symbol "<" and revise the statement to read "less than 30 mL/min".

c. The dosage information states "Tradename is administered as a single daily dose taken before food." This statement is confusing and should be clarified because is it not clear whether the product should be taken with meals or on an empty stomach.

2. Section 16: How Supplied/Storage and Handling

The professional sample blister cards are listed in this section. Professional samples are

not for commercial distribution and, therefore, should not be listed. Delete the professional sample blister card information.

Please confirm receipt and respond to this request within 7 to 10 business days; if you are unable to meet this timeframe, please contact me to discuss.

Thank you,

~~~~~~~~~~~~~~~~~~~~~~~~~~

Stephanie N. Parncutt
Regulatory Project Manager
Division of Neurology Products
Center for Drug Evaluation and Research, FDA
10903 New Hampshire Avenue; WO22 Rm. 4355
Silver Spring, MD 20993-0002

phone: 301-796-4098
email: stephanie.parncutt@fda.hhs.gov
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/s/

STEPHANIE N PARNCUTT
07/12/2012

From:	Tami Martin
To:	Parncutt, Stephanie
Subject:	RE: FDA Request for Information - NDA 202810/oxcarbazepine extended-release Tablets
Date:	Tuesday, June 19, 2012 1:16:21 PM

Hello Stephanie,

Acknowledging receipt.

Thank you!

Tami Martin
Supernus Pharmaceuticals, Inc.
301-838-2607

From: Parncutt, Stephanie [mailto:Stephanie.Parncutt@fda.hhs.gov]
Sent: Tuesday, June 19, 2012 12:57 PM
To: Tami Martin
Subject: FDA Request for Information - NDA 202810/oxcarbazepine extended-release Tablets

Below is a request from the Clinical Pharmacology team related to their ongoing review of the oxcarbazepine extended-release application (N 202-810). Please submit your response to this request in electronic archival format as an amendment to the above NDA. It is acceptable for you to email your response to me in advance of a formal, archival submission as long as both communications (email & archive) contain identical information.
* Please see the comment below from the Clinical Pharmacology team reviewer:

Was any of the formulations used in the pilot Study 804P101 used in Study 804P103 and/or the pivotal safety and efficacy study (Study 804P301).

Please respond to this request in the next 7-10 days; if you are unable to meet this timeframe, please contact me to discuss.

~~~~~~~~~~~~~~~~~~~~~~~~~~~

Stephanie N. Parncutt
Regulatory Project Manager
Division of Neurology Products
Center for Drug Evaluation and Research, FDA
10903 New Hampshire Avenue; WO22 Rm. 4355
Silver Spring, MD 20993-0002

phone: 301-796-4098
email: stephanie.parncutt@fda.hhs.gov
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/s/

STEPHANIE N PARNCUTT
06/19/2012

Bouie, Teshara
From: Bouie, Teshara
Sent: Wednesday, June 06, 2012 6:31 PM
To: 'Tami Martin'
Cc: Parncutt, Stephanie
Subject: NDA 202810 - Dissolution Acceptance Criteria

Hi Tami,

1. The following dissolution acceptance criteria are recommended for your proposed product:

Recommended Dissolution Acceptance Criteria for all Strengths (% Dissolved)	
2 hrs:	(b) (4)
4 hrs:	
8 hrs	

This recommendation is based on the results of Pharmacokinetic study 804P101. Revise the dissolution acceptance criteria accordingly and submit an updated sheet of specifications.

2. Your proposed dissolution method is acceptable. However, you should consider revising it for the following reasons:
   - The proposed dissolution method is over-discriminating for formulations with faster *in vitro* dissolution rates and under-discriminating for formulations with slower *in vitro* dissolution rates.
   - This may cause a problem when implementing this method for post-approval changes which rely on f2 testing, especially for those formulations with slower release rates.

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

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/s/

TESHARA G BOUIE
06/06/2012

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 202810

PROPRIETARY NAME REQUEST
UNACCEPTABLE

Supernus Pharmaceuticals, Inc.
1550 East Gude Drive
Rockville, MD 20850

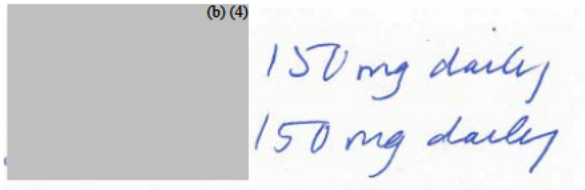
Attention: Tami T. Martin, RN, Esq.
Vice President, Regulatory Affairs

Dear Ms. Martin:

Please refer to your New Drug Application (NDA) dated and received December 19, 2011, submitted under section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for oxcarbazepine extended-release tablets, 150 mg, 300 mg, and 600 mg.

We also refer to your correspondence, dated and received February 8, 2012, requesting review of your proposed proprietary name, [redacted]. We have completed our review of [redacted] and have concluded that this name is unacceptable for the following reasons:

The proposed name [redacted], is orthographically similar to and shares overlapping product characteristics with the currently marketed product [redacted] which is an [redacted]. The orthographic similarities of this name pair stem from the similar length, shape of the names, and similarity of the letters comprising each name when scripted. The beginning letter string [redacted]" looks similar to [redacted]" especially when the "a" in [redacted] is not closed as the sample below demonstrates. Additionally, the suffixes "[redacted]" and "[redacted]" look similar when scripted. We recognize this name has a modifier; however, postmarketing evidence indicates that modifiers have been omitted or overlooked in practice. Additionally, since the root name [redacted]" does not currently exist in the market, prescribers may not include the modifier when writing a prescription because there is no product differentiation required.



In addition to the orthographic similarities, [redacted] and [redacted] share similar product characteristics that increase the likelihood of a medication error to occur in the usual practice setting. These overlapping product characteristics include strength (150 mg), dose (150 mg), route of administration (oral), frequency of administration (once daily), and dosage form

(tablets). Thus, a prescription for "[redacted] (b) (4) (with the modifier dropped) 150 mg po daily" could be misinterpreted as "[redacted] (b) (4) 150 mg po daily".

Our findings differ from the conclusion reached in the external name study conducted by Addison Whitney. However, Tarceva was not among the look-alike or sound-alike names evaluated in the external name study.

We note that you have proposed an alternate proprietary name, [redacted] (b) (4), for review. However, based on our decision concerning [redacted] (b) (4) would not be an acceptable alternative. If you intend to have a proprietary name for this product, we recommend that you submit a new name and a new request for a proposed proprietary name review (See the Guidance for Industry, *Contents of a Complete Submission for the Evaluation of Proprietary Names,* http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM075068.pdf and "PDUFA Reauthorization Performance Goals and Procedures Fiscal Years 2008 through 2012")..

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, Stephanie Parncutt at (301) 796-4098.

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

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/s/

LAURIE A KELLEY
05/04/2012

CAROL A HOLQUIST
05/04/2012

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 202810 **INFORMATION REQUEST**

Supernus Pharmaceuticals, Inc.
Attention: Tami T. Martin, RN, Esq., VP, Regulatory Affairs
1550 East Gude Drive
Rockville, MD 20833

Dear Ms. Martin:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Oxcarbazepine Extended-Release Tablets.

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

S.2.2 Description of Manufacturing Process and Process Controls

1. As stated in the NDA, the drug substance is [redacted] (b) (4) to obtain the desired particle size distribution. Provide data to confirm that [redacted] (b) (4) does not adversely affect drug substance characteristics, e.g. polymorphic transformation, impurity profile, etc.

S.4.3 Validation of Analytical Procedures

Method Validation for the estimation of Particle Size Distribution of Oxacarbazepine using Laser Diffraction

2. The validation data does not include the accuracy element of the analytical procedure, as stipulated and defined in ICH Q2 (R1). Provide data to demonstrate the accuracy of the analytical method based on data from standard samples..

Validation of the determination of identification, assay and related substances content in oxacarbazepine drug substance by HPLC – TR-1-031-00.

3. In this section you state that method accuracy was inferred when suitable precision, linearity and specificity were demonstrated. However, 'accuracy' is considered as an independent validation characteristic as per ICH Q2 (R1); accordingly, provide data on this validation element.

4. Additionally, you have not provided any data on the robustness of this procedure. ICH Q2 (R1) states that this validation characteristic should be considered at an appropriate stage in the development of the analytical procedure. Provide validation data for this element.

P.2.3 Manufacturing Process Development

5. As stated in the NDA, (b) (4)

P.3.3 Description of Manufacturing Process and Process Controls

6. Particle size analysis is inscribed in the box shown in the manufacturing flow diagram; clarify where in the process this test is conducted and provide the related in-process specification for this test.

P.5.1 Specification(s)

7. Include a test and acceptance criteria for residual solvents to conform to USP<467>; (b) (4)

8. You have justified deletion of the microbial limits test (b) (4)

P.5.3 Validation of Analytical Procedures - Validation of Method, TM-801-102

9. Section 2.3.4 Limit of Quantitation (LOQ) in the validation of analytical method for the determination of the non-parent peaks (TR-08-014.00) states "The signal to noise ratio for oxcarbazepine and each related compound was reported"; provide this ratio and confirm that it is greater than or equal to 10 according to the ICH Q2B guideline.

P.7 Container Closure System [name, dosage form]

10. Provide a statement regarding conformity of the container/closure systems and desiccant to appropriate food contact CFR regulations.

P.8.1 Stability Summary and Conclusion – Photostability

11. Your photostability study indicated that unprotected product fails the dissolution test. Since the product is packaged in a bottle (multiple dose container) where there can be potential for removal from the container, provide a precautionary statement on the bottle label to 'Protect from Light'.

P.8.3 Stability Data

12. Dissolution Stability Data for 150 mg Batch C8K02732 (SS09R), 12 months at 25ºC/60% RH-5 tablet blister pack: The average of the percent dissolved is incorrectly stated as (b) (4) for individual values of (b) (4) the average value should be (b) (4) Provide revised table.

Review of Common Technical Document-Quality (Ctd-Q) Module 1 Labeling & Package Insert

13. Colloidal silicon dioxide is included as an inactive ingredient of the tablet; (b) (4) remove it from Section 11 of the package insert.

14. Provide the NDC code numbers for the bottle and unit dose blister for each strength.

Additional Comments:

Additionally, we are awaiting your response to the following CMC request in the Filing Communication Letter, which you have acknowledged in the NDA Sequence # 0005:

"With respect to the drug substance specification we note inconsistencies with the current USP requirement for Oxacarbazepine. You propose use of an HPLC assay method that differs from the USP assay method. Additionally, the USP monograph (b) (4) Please acknowledge the USP methods as regulatory methods and provide justification for use of the proposed alternative methods."

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

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/s/

RAMESH K SOOD
05/04/2012

From:	Tami Martin
To:	Parncutt, Stephanie
Subject:	RE: FDA Request for Information - NDA 202810/ (b) (4) (oxcarbazepine extended-release) Tablets
Date:	Monday, May 21, 2012 2:17:52 PM

Thank you very much for this welcome news.

Tami Martin
Supernus Pharmaceuticals, Inc.
301-838-2607

From: Parncutt, Stephanie [mailto:Stephanie.Parncutt@fda.hhs.gov]
Sent: Monday, May 21, 2012 2:11 PM
To: Tami Martin
Subject: RE: FDA Request for Information - NDA 202810/ (b) (4) (oxcarbazepine extended-release) Tablets

Tami,

Please refer to the Clinical Information Request sent on May 11, 2012, regarding justification of why a thorough QT study was not included in your development program. We have determined that such information is not necessary for labeling. We would like to rescind this Information Request and ask that you please disregard this request completely. We apologize for the inconvenience this may have caused members of your review team.

Thank you,

Stephanie

From: Tami Martin [mailto:tmartin@supernus.com]
Sent: Friday, May 11, 2012 2:33 PM
To: Parncutt, Stephanie
Cc: Bouie, Teshara
Subject: RE: FDA Request for Information - NDA 202810/ (b) (4) (oxcarbazepine extended-release) Tablets

Thank you Stephanie, acknowledging receipt of your request for an explanation concerning definitive QT effect evaluation. I will speak to the team about our ability to meet your action date.

Other key outstanding matters for this NDA: I am trying hard to progress the EXCEL spreadsheet presentation of 804P302 exposure data so that we can complete the safety update and file. As we have explained, this is a manual process and so it is taking us longer than even we expected. As of about an hour ago, I am expecting receipt in my department of the final "piece" late on Tuesday May 15th, so barring any additional obstacles I would hope to submit by the end of next week.

The statistician has indicated that he can provide the reprogrammed SAS codes mid week next week, so by the time we receive and process it is most likely going to be approx. May 21st before we can complete that response.

We also received a set of CMC queries from Ms. Bouie. We plan to respond in two parts: some points we can address immediately, two points are going to require some additional work on our part before we can answer fully.

Tami Martin
Supernus Pharmaceuticals, Inc.
301-838-2607
tmartin@supernus.com

From: Parncutt, Stephanie [mailto:Stephanie.Parncutt@fda.hhs.gov]
Sent: Friday, May 11, 2012 2:15 PM
To: Tami Martin
Subject: FDA Request for Information - NDA 202810/ (b) (4) (oxcarbazepine extended-release) Tablets
Importance: High

Below is a request from the Clinical team related to their ongoing review of the (b) (4) application (N 202-810). Please submit your response to this request in electronic archival format as an amendment to the above NDA. It is acceptable for you to email your response to me in advance of a formal, archival submission as long as both communications (email & archive) contain identical information.
* Please see the comment below from the Clinical team reviewer:

The review process has revealed that Trileptal label indicates there has been no definitive evaluation of QT effect. Your development program has not included a thorough QT study. We request that you justify why a thorough QT study is unnecessary. Information available from your study or in the public domain may be utilized. If this is unsatisfactory then a formal evaluation of oxcarbazepine extended release formulation on the QT interval may be requested through a post marketing requirement or commitment.

Please respond to this request by July 6, 2012; if you are unable to meet this timeframe, please contact me to discuss.

~~~~~~~~~~~~~~~~~~~~~~~~~~

Stephanie N. Parncutt
Regulatory Project Manager
Division of Neurology Products
Center for Drug Evaluation and Research, FDA
10903 New Hampshire Avenue; WO22 Rm. 4355
Silver Spring, MD 20993-0002

phone: 301-796-4098
email: stephanie.parncutt@fda.hhs.gov
~~~~~~~~~~~~~~~~~~~~~~~~~~

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/s/

STEPHANIE N PARNCUTT
05/31/2012

From:	Tami Martin
To:	Parncutt, Stephanie
Cc:	Bouie, Teshara
Subject:	RE: FDA Request for Information - NDA 202810/ (b) (4) (oxcarbazepine extended-release) Tablets
Date:	Friday, May 11, 2012 2:32:25 PM

Thank you Stephanie, acknowledging receipt of your request for an explanation concerning definitive QT effect evaluation. I will speak to the team about our ability to meet your action date.

Other key outstanding matters for this NDA: I am trying hard to progress the EXCEL spreadsheet presentation of 804P302 exposure data so that we can complete the safety update and file. As we have explained, this is a manual process and so it is taking us longer than even we expected. As of about an hour ago, I am expecting receipt in my department of the final "piece" late on Tuesday May 15th, so barring any additional obstacles I would hope to submit by the end of next week.

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We also received a set of CMC queries from Ms. Bouie. We plan to respond in two parts: some points we can address immediately, two points are going to require some additional work on our part before we can answer fully.

Tami Martin
Supernus Pharmaceuticals, Inc.
301-838-2607
tmartin@supernus.com

From: Parncutt, Stephanie [mailto:Stephanie.Parncutt@fda.hhs.gov]
Sent: Friday, May 11, 2012 2:15 PM
To: Tami Martin
Subject: FDA Request for Information - NDA 202810/ (b) (4) (oxcarbazepine extended-release) Tablets
Importance: High

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* Please see the comment below from the Clinical team reviewer:

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utilized. If this is unsatisfactory then a formal evaluation of oxcarbazepine extended release formulation on the QT interval may be requested through a post marketing requirement or commitment.

Please respond to this request by July 6, 2012; if you are unable to meet this timeframe, please contact me to discuss.

~~~~~~~~~~~~~~~~~~~~~~~~~~

Stephanie N. Parncutt
Regulatory Project Manager
Division of Neurology Products
Center for Drug Evaluation and Research, FDA
10903 New Hampshire Avenue; WO22 Rm. 4355
Silver Spring, MD 20993-0002

phone: 301-796-4098
email: stephanie.parncutt@fda.hhs.gov
~~~~~~~~~~~~~~~~~~~~~~~~~~

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/s/

STEPHANIE N PARNCUTT
05/15/2012

From:	Tami Martin
To:	Parncutt, Stephanie
Cc:	Jocelyn McQueen
Subject:	RE: FDA Request for Information - NDA 202810/ (b) (4) (oxcarbazepine extended-release) Tablets
Date:	Thursday, March 29, 2012 5:14:30 PM

Hello Stephanie,

We have forwarded this request to our vendor. The statistician who is expected to prepare the response has not yet replied about the date by which he can provide the requested information.

Since I am going to be out of the office tomorrow, and Monday April 2nd, I wanted to at least reply and let you know we are working on this request. By the way, if you have any urgent requests for Supernus before next Tuesday, please send me an e mail as usual but please copy Jocelyn McQueen, RA Associate, at jmcqueen@supernus.com. Jocelyn's direct dial phone number is 301-838-2570.

Hopefully, upon my return on Tuesday, we'll have a better idea of when the response will be available.

Tami Martin
Supernus Pharmaceuticals, Inc.
301-838-2607
tmartin@supernus.com

From: Parncutt, Stephanie [mailto:Stephanie.Parncutt@fda.hhs.gov]
Sent: Tuesday, March 27, 2012 11:50 AM
To: Tami Martin
Subject: FDA Request for Information - NDA 202810/ (b) (4) (oxcarbazepine extended-release) Tablets
Importance: High

Attached is a request from the Statistical team related to their ongoing review of the (b) (4) application (N 202-810). Please submit your response to this request in electronic archival format as an amendment to the above NDA. It is acceptable for you to email your response to me in advance of a formal, archival submission as long as both communications (email & archive) contain identical information.
* Please see the attachment below from the Statistical team reviewer:

Please respond to this request in 7-10 days; if you are unable to meet this timeframe, please contact me to discuss.

Thank you,

~~~~~~~~~~~~~~~~~~~~~~~~~~

Stephanie N. Parncutt
Regulatory Project Manager
Division of Neurology Products
Center for Drug Evaluation and Research, FDA
10903 New Hampshire Avenue; WO22 Rm. 4355
Silver Spring, MD 20993-0002
~~~~~~~~~~~~~~~~~~~~~~~~~~

phone: 301-796-4098
email: stephanie.parncutt@fda.hhs.gov

A Stat request to Sponsor.

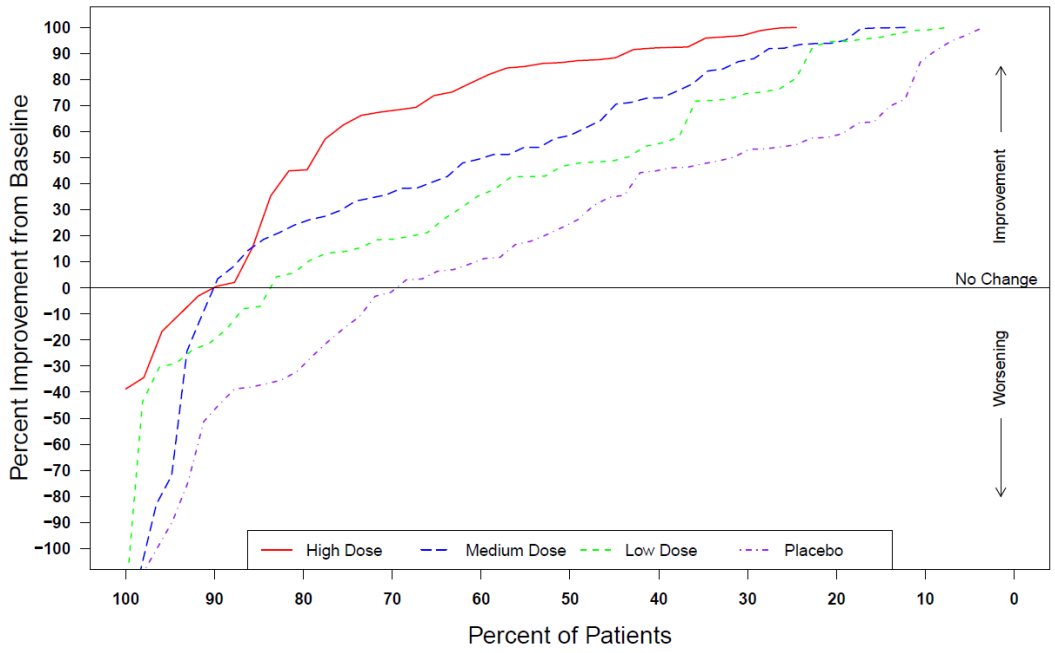
Please send us SAScodes for following tables and figure.

1. Table 12, Table 14, Table 5.6.1.1 & Table 5.6.2.1 (Study report)

SAScodes for additional analyses

2. Model Rank (PCH_T) =Rank (Baseline partial SZ/28days) + Country+ Treatment Group. (Please report P-values for LSMEAN comparison of Treatment groups)
3. Log (PCH_T) =Log (Baseline partial SZ /28 days) +country+Treatment Group (Please report P-values for LSMEAN comparison of Treatment groups)
4. Continuous Responder Curves Based on Percent Reduction From Baseline in PCH_T for the ITT Population

Figure 1. Continuous Responder Curves Based on Percent Reduction From Baseline in PCH_T – TT Population



5. A table for Subgroup analyses on the PCH_T on categories of the following measures:
_ Gender
_ Race
_ Seizure types: simple partial seizures, complex partial seizures, simple and complex partial seizures, secondarily generalized seizures.

Please provide the tables and figures along with the SASCODEs . Please don’t use SAS Macro.

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/s/

STEPHANIE N PARNCUTT
04/10/2012

Parncutt, Stephanie

From: Tami Martin [tmartin@supernus.com]
Sent: Tuesday, March 27, 2012 2:00 PM
To: Parncutt, Stephanie
Subject: RE: FDA Request for Information - NDA 202810/ (b) (4) (oxcarbazepine extended-release) Tablets

Hello Stephanie,

I want to acknowledge receipt of your three e mails. The first, responsive to our query about package insert items in the Filing Communication letter, the second, a request from the statistical reviewer, and the third, the request, below, from the clinical team.

I am conferring with team members and will get back to you concerning any timing issues. Thank you for your response to our questions concerning the package insert.

Tami Martin
Supernus Pharmaceuticals, Inc.
301-838-2607

From: Parncutt, Stephanie [mailto:Stephanie.Parncutt@fda.hhs.gov]
Sent: Tuesday, March 27, 2012 11:54 AM
To: Tami Martin
Subject: FDA Request for Information - NDA 202810/ (b) (4) (oxcarbazepine extended-release) Tablets
Importance: High

Attached is a request from the Clinical team related to their ongoing review of the (b) (4) application (N 202-810). Please submit your response to this request in electronic archival format as an amendment to the above NDA. It is acceptable for you to email your response to me in advance of a formal, archival submission as long as both communications (email & archive) contain identical information.

* Please see the comments below from the Clinical team reviewer:

Request for additional exposure data:

1. Please provide the number of all patients in the development program who received at least one dose of SPN-804O
2. Clinical pharmacology studies: Please provide the mean and median exposure of the following phase 1 studies (combined): 804P101, 804P102, 804P103, 804P104, 804P104.5, 804P105.
3. study 804P107: Please provide a table of exposure duration and dose by number of patients and a mean / median exposure of total patients.
4. In order to obtain the most complete safety and exposure data available for SPN-8040 we are requesting that you include study 804P302 in the 120 day safety update. To fulfill this request please provide all exposure and safety data from study 804P302 up to safety data cut off for the 120 update (no exposure data for 804P302 is present in the initial submission). Please pool the exposure data from studies 804P301 and 804P302 and provide a table of exposure in the following format: a) patient number exposed -at time intervals, any dose (table 1), b). Patient number exposed by time interval and dose (table 2). Also, pool all adverse event data from studies 804P301 and 804P302 for the 120 day update.

Table 1 Patient study drug exposure by time interval (and dose)- studies 804P301 & 804P302

Total n	
Total time on Drug	Number of Patients

≤ 1 week	n
week to 1 month	n
1 month to 3 months	n
3 months to 6 months	n
6 month to 9 months	n
9 months to 12 months	n
12 months to 18 months	n
18 months to 24 months	n
24 months to 36 months	n
36 months	n
Total Time on Drug, Days	
Mean ± SD	
Median	
Range	
Total patient-days	
Total patient-years	

Table 2 Patient number on study drug by time interval and dose- studies 804P301 & 804P302

Total n			
Total time on drug	**600mg**	**1200mg**	**2400mg**
≤ 1 week	n	n	n
week to 1 month	n	n	n
1 month to 3 months	n	n	n
3 months to 6 months	n	n	n
6 month to 9 months	n	n	n
9 months to 12 months	n	n	n
12 months to 18 months	n	n	n
18 months to 24 months	n	n	n
24 months to 36 months	n	n	n
36 months	n	n	n
Total patient days			
Mean ± SD			
Median			
Range			
Total patients years			

Please respond to this request in 7-10 days; if you are unable to meet this timeframe, please contact me to discuss.

Thank you,

~~~~~~~~~~~~~~~~~~~~~~~~~~~~

Stephanie N. Parncutt
Regulatory Project Manager
Division of Neurology Products
Center for Drug Evaluation and Research, FDA
10903 New Hampshire Avenue; WO22 Rm. 4355
Silver Spring, MD 20993-0002
~~~~~~~~~~~~~~~~~~~~~~~~~~~~

phone: 301-796-4098
email: stephanie.parncutt@fda.hhs.gov

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/s/

STEPHANIE N PARNCUTT
04/10/2012

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 202810

FILING COMMUNICATION

Supernus Pharmaceuticals, Inc.
Attention: Tami Martin, RN, Esq.
Vice President, Regulatory Affairs
1550 East Gude Drive
Rockville, MD 20850

Dear Ms. Martin:

Please refer to your New Drug Application (NDA) dated December 19, 2011, received December 19, 2011, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act, for oxcarbazepine extended-release tablets 150mg, 300mg, and 600mg.

We also refer to your amendments dated December 21, 2011; February 8, 2012 and February 24, 2012.

We have completed our filing review and have determined that your application is sufficiently complete to permit a substantive review. Therefore, in accordance with 21 CFR 314.101(a), this application is considered filed 60 days after the date we received your application. The review classification for this application is **Standard**. Therefore, the user fee goal date is October 19, 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, midcycle, team and wrap-up meetings). Please be aware that the timelines described in the guidance are flexible and subject to change based on workload and other potential review issues (e.g., submission of amendments). We will inform you of any necessary information requests or status updates following the milestone meetings or at other times, as needed, during the process. If major deficiencies are not identified during the review, we plan to communicate proposed labeling and, if necessary, any postmarketing commitment requests by September 19, 2012.

We request that you submit the following information:

Chemistry, Manufacturing & Controls

1. With respect to the drug substance specification we note inconsistencies with the current USP requirements for Oxcarbazepine. You propose use of an HPLC assay method that differs from the USP assay method. Additionally, the USP monograph requires water determination according to <921> Method 1a. Please acknowledge the USP methods as regulatory methods and provide justification for use of the proposed alternative methods.

ONDQA Biopharmaceutics

2. It was noted that the provided information on the *in vitro* alcohol interaction study for Oxcarbazepine ER tablets was obtained using only the HCl medium. Therefore, in order to rule out a possible dose-dumping (DD) effect in the presence of alcohol, we recommend that you conduct an *in vitro* drug-alcohol interaction study with your ER product using the proposed QC medium. The following alcohol concentrations for the in vitro dissolution studies (using 12 units each) are recommended: 0 %, 4 %, 10 %, 20 %, and 40 %. Please also include the following information as part of your report:
    a. f2 values to assess the similarity (or lack thereof) in the dissolution profiles.
    b. Compare the shape of the dissolution profile to see if the modified release characteristics are maintained, especially in the first 2 hours.

During our preliminary review of your submitted labeling, we have identified the following labeling format issues:

Under **Highlights (HL)** section of Labeling

1. HL must be in two-column format, with ½ inch margins on all sides and between columns, and in a minimum of 8-point font. HL does not have ½ inch margins on all size and is not in 8 point font.
2. HL is limited in length to one-half page. It is difficult to determine if the HL meets the ½ page requirement because it is not in the correct format.
3. The Highlights Limitation Statement must be placed at the beginning of HL in **bolded font** and read as follows: "**These highlights do not include all the information needed to use (insert name of drug product in UPPER CASE) safely and effectively. See full prescribing information for (insert name of drug product in UPPER CASE)**."
4. The Product Title must be **bolded** and note the proprietary and established drug names, followed by the dosage form, route of administration (ROA), and, if applicable, controlled substance symbol.
5. The verbatim statement "Initial U.S. Approval" followed by the 4-digit year in which the FDA initially approved the new molecular entity (NME), new biological product, or new combination of active ingredients, must be placed immediately beneath the product title line. If this is an NME, the year must correspond to the current approval action. You should not include the month; "January" should be removed.
6. Recent Major Changes (RMC) applies only to supplements and is limited to substantive changes in five sections: Boxed Warning, Indications and Usage, Dosage and Administration, Contraindications, and Warnings and Precautions.

7. Only "adverse reactions" as defined in 21 CFR 201.57(a)(11) are included in HL. Other terms, such as "adverse events" or "treatment-emergent adverse events," should be avoided. Note the criteria used to determine their inclusion (e.g., incidence rate greater than X%). Instead of "adverse experiences" insert "adverse reactions."
8. HL must include the verbatim statement: "**See 17 for Patient Counseling Information**" or if the product has FDA-approved patient labeling: "**See 17 for Patient Counseling Information and (insert either "FDA-approved patient labeling" or "Medication Guide")**. Remove "FDA-Approved."

Under **Table of Contents (TOC)** section of Labeling

9. All section headings must be in **bold** type, and subsection headings must be indented and not bolded. The subsections in the TOC are not indented.

Under **Full Prescribing Information (FPI)** section of Labeling

10. A horizontal line must separate the TOC and FPI. No horizontal line is present between these two parts.
11. The heading – **FULL PRESCRIBING INFORMATION** – must appear at the beginning in UPPER CASE and **bold** type. This needs to be added.
12. The section and subsection headings must be named and numbered in accordance with 21 CFR 201.56(d)(1). All section and subsection numbers should not have a trailing period.
13. Only "adverse reactions" as defined in 21 CFR 201.57(c)(7) should be included in labeling. Other terms, such as "adverse events" or "treatment-emergent adverse events," should be avoided. Multiple places do not use the term adverse reaction.
14. For the "Clinical Trials Experience" subsection, the following verbatim statement or appropriate modification should precede the presentation of adverse reactions:

    "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." **This statement should be in 6.1; not after 6.**
15. For the "Postmarketing Experience" subsection, the listing of post-approval adverse reactions must be separate from the listing of adverse reactions identified in clinical trials. Include the following verbatim statement or appropriate modification:

    "The following adverse reactions have been identified during post-approval use of (insert drug name). Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure." **This statement should be in 6.2. Note, it was slightly modified to be consistent with the reactions listed in this section.**
16. FPI must reference any FDA-approved patient labeling, including the type of patient labeling. The statement "See FDA-approved patient labeling (insert type of patient labeling)." should appear at the beginning of Section 17 for prominence. For example:
    - "See FDA-approved patient labeling (Medication Guide)"
    - "See FDA-approved patient labeling (Medication Guide and Instructions for Use)"

- "See FDA-approved patient labeling (Patient Information)"
- "See FDA-approved patient labeling (Instructions for Use)"
- "See FDA-approved patient labeling (Patient Information and Instructions for Use)"

The identical words are not in your proposed label.

17. The Patient Counseling Information does not have command language. Instead of "patients should be advised", one can state "Advise patients."

We request that you resubmit labeling that addresses these issues by March 23, 2012. 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.

PROMOTIONAL MATERIAL

You may request advisory comments on proposed introductory advertising and promotional labeling. Please submit, in triplicate, a detailed cover letter requesting advisory comments (list each proposed promotional piece in the cover letter along with the material type and material identification code, if applicable), the proposed promotional materials in draft or mock-up form with annotated references, and the proposed package insert (PI) and Medication Guide. Submit consumer-directed, professional-directed, and television advertisement materials separately and send each submission to:

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion (OPDP)
5901-B Ammendale Road
Beltsville, MD 20705-1266

Do not submit launch materials until you have received our proposed revisions to the package insert (PI) and Medication Guide, and you believe the labeling is close to the final version.

For more information regarding OPDP submissions, please see http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm. If you have any questions, call OPDP at 301-796-1200.

REQUIRED PEDIATRIC ASSESSMENTS

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

We acknowledge receipt of your request for a partial waiver of pediatric studies for pediatric patients from birth to less than four years of age and for pediatric patients 17 years of age in this application. Once we have reviewed your request, we will notify you if the partial waiver request is denied. Please note that a deferral for patients over the age of 16 is not required.

We note that you have submitted pediatric studies with this application for pediatric patients 4 to 16 years of age. Once the review of this application is complete we will notify you whether you have fulfilled the pediatric study requirement for this age group.

If you have any questions, contact Stephanie N. Parncutt, Regulatory Health Project Manager, at (301) 796-4098.

Sincerely,

{See appended electronic signature page}

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

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/s/

RUSSELL G KATZ
03/01/2012

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 202810

NDA ACKNOWLEDGMENT

Supernus Pharmaceuticals, Inc.
Attention: Tami Martin, RN, Esq.
Vice President, Regulatory Affairs
1550 East Gude Drive
Rockville, MD 20833

Dear Ms. Martin:

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

Name of Drug Product: oxcarbazepine extended-release tablets 150mg, 300mg, and 600mg

Date of Application: December 19, 2012

Date of Receipt: December 19, 2012

Our Reference Number: NDA 202810

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 February 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 me at (301) 796-4098.

Sincerely,

{See appended electronic signature page}

Stephanie N. Parncutt
Regulatory Health Project Manager
Division of Neurology Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

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/s/

STEPHANIE N PARNCUTT
01/05/2012