

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:
200603

ADMINISTRATIVE and CORRESPONDENCE
DOCUMENTS

EXCLUSIVITY SUMMARY

NDA # 200603

SUPPL #

HFD # 130

Trade Name Latuda

Generic Name lurasidone hydrochloride

Applicant Name Sunovion Pharmaceuticals, Inc. (formerly Sepracor, Inc. and Dainippon Sumitomo Pharma America)

Approval Date, If Known October 28, 2010

PART I IS AN EXCLUSIVITY DETERMINATION NEEDED?

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

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

YES NO

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

505(b)(1)

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

YES NO

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

N/A

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

N/A

d) Did the applicant request exclusivity?

YES NO

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

5 years

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

YES NO

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

N/A

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

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

YES NO

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

PART II FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES

(Answer either #1 or #2 as appropriate)

1. Single active ingredient product.

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

YES NO

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

NDA# N/A

NDA#

NDA#

2. Combination product.

If the product contains more than one active moiety(as defined in Part II, #1), has FDA previously approved an application under section 505 containing any one of the active moieties in the drug product? If, for example, the combination contains one never-before-approved active moiety and one previously approved active moiety, answer "yes." (An active moiety that is marketed under an OTC monograph, but that was never approved under an NDA, is considered not previously approved.)

YES NO

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

NDA# N/A

NDA#

NDA#

IF THE ANSWER TO QUESTION 1 OR 2 UNDER PART II IS "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8. (Caution: The questions in part II of the summary should only be answered "NO" for original approvals of new molecular entities.)
IF "YES," GO TO PART III.

PART III THREE-YEAR EXCLUSIVITY FOR NDAs AND SUPPLEMENTS

To qualify for three years of exclusivity, an application or supplement must contain "reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant." This section should be completed only if the answer to PART II, Question 1 or 2 was "yes."

1. Does the application contain reports of clinical investigations? (The Agency interprets "clinical investigations" to mean investigations conducted on humans other than bioavailability studies.) If the application contains clinical investigations only by virtue of a right of reference to clinical investigations in another application, answer "yes," then skip to question 3(a). If the answer to 3(a)

is "yes" for any investigation referred to in another application, do not complete remainder of summary for that investigation.

YES NO

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

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

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

YES NO

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

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

YES NO

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

YES NO

If yes, explain:

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

YES NO

If yes, explain:

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

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

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

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

Investigation #1 YES NO

Investigation #2 YES NO

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

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

Investigation #1 YES NO

Investigation #2 YES NO

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

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

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

YES NO

If yes, explain:

=====
Name of person completing form: Ann Sohn
Title: Regulatory Project Manager
Date: 10/28/10

Name of Office/Division Director signing form: Thomas Laughren, M.D.
Title: Division Director

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

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/s/

ANN J SOHN
10/28/2010

THOMAS P LAUGHREN
10/29/2010

From: [Sohn, Ann J](#)
To: ["Walton, Bridget";](#)
Subject: NDA 200603 lurasidone carton and container labels
Date: Wednesday, October 27, 2010 12:29:16 PM

Hi Bridget,

We acknowledge your submission of carton and container labels dated October 26, 2010. We agree to your changes in carton and container labels. Please let me know if you have any questions.

Best Regards,

*Ann Sohn, Pharm.D., LT USPHS
Regulatory Project Manager
Division of Psychiatry Products
Center For Drug Evaluation and Research, FDA
Office of Drug Evaluation I
Email: ann.sohn@fda.hhs.gov*

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/s/

ANN J SOHN
10/27/2010

From: [Walton, Bridget](#)
To: [Sohn, Ann J;](#)
Subject: NDA 200603
Date: Tuesday, October 26, 2010 10:26:55 AM

Hi Ann,

I am confirming with this e-mail that Sunovion Pharmaceuticals Inc. agrees to submit 15-day safety reports for angioedema post-approval for Latuda.

Best regards,
Bridget

Bridget Walton

Director, Regulatory Affairs
Sunovion Pharmaceuticals Inc.
One Bridge Plaza, Suite 510
Fort Lee, NJ 07024
Direct: 201-228-8333 | Cell:201-310-0156
Bridget.Walton@sunovion.com

THE INFORMATION CONTAINED IN THIS COMMUNICATION AND ANY ATTACHMENTS HERETO IS CONFIDENTIAL, MAY BE ATTORNEY-CLIENT PRIVILEGED, AND IS INTENDED ONLY FOR THE PERSONAL AND CONFIDENTIAL USE OF THE ADDRESSEE(S). IF THE READER OF THIS MESSAGE IS NOT AN INTENDED RECIPIENT, OR AN AGENT THEREOF, YOU ARE HEREBY NOTIFIED THAT ANY REVIEW, USE, DISSEMINATION, DISTRIBUTION, OR COPYING OF THIS COMMUNICATION OR ANY ATTACHMENT HERETO IS STRICTLY PROHIBITED. IF YOU HAVE RECEIVED THIS MESSAGE IN ERROR, PLEASE NOTIFY US IMMEDIATELY BY E-MAIL, AND DELETE THE ORIGINAL MESSAGE.

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/s/

ANN J SOHN
10/26/2010

From: [Sohn, Ann J](#)
To: ["Walton, Bridget";](#)
Subject: Lurasidone Carton and Container Labels
Date: Thursday, October 21, 2010 1:47:25 PM

Hi Bridget,

I have the following comments/requests from the Division of Medication Error Prevention and Analysis (DMEPA) regarding carton and container labels for lurasidone:

1. Revise the presentation of the established name on the container labels, carton labeling, and blistercard so that the established name is printed in letters that are at least half as large as the letters comprising the proprietary name or designation with which it is joined, and the established name shall have a prominence commensurate with the prominence with which such proprietary name or designation appears, taking into account all pertinent factors, including typography, layout, contrast, and other printing features, per 21 CFR 201.10(g) (2).
2. Revise the color used in the presentation of the proprietary name to one that is not used in the strength differentiation color scheme (i.e., no blue, green, or yellow).

Please let me know if you have any questions.

Thank you,

*Ann Sohn, Pharm.D., LT USPHS
Regulatory Project Manager
Division of Psychiatry Products
Center For Drug Evaluation and Research, FDA
Office of Drug Evaluation I
Email: ann.sohn@fda.hhs.gov*

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/s/

ANN J SOHN
10/21/2010



NDA 200603

**PROPRIETARY NAME REQUEST
CONDITIONALLY ACCEPTABLE**

Sepracor, Inc.
One Bridge Plaza, Suite 510
Fort Lee, New Jersey, 07024

ATTENTION: Bridget Walton, MS, RAC
Director, Regulatory Affairs

Dear Ms. Walton:

Please refer to your New Drug Application (NDA) dated December 30, 2009, received December 30, 2009, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Lurasidone Hydrochloride Tablets, 40 mg, 80 mg, and 120 mg.

We also refer to your October 7, 2010, correspondence, received October 8, 2010, requesting review of your proposed proprietary name, Latuda. We have completed our review of the proposed proprietary name, Latuda, and have concluded that it is acceptable.

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

If **any** of the proposed product characteristics as stated in your October 7, 2010 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 Sandra Griffith, Safety Regulatory Project Manager in the Office of Surveillance and Epidemiology, at (301) 796-2445. For any other information regarding this application contact the Office of New Drugs (OND) Regulatory Project Manager, Ann Sohn at (301) 796-2232.

Sincerely,

{See appended electronic signature page}

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

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/s/

CAROL A HOLQUIST
10/21/2010

From: [Sohn, Ann J](#)
To: ["Walton, Bridget";](#)
Subject: Lurasidone Information Request
Date: Wednesday, September 22, 2010 12:02:05 PM

Hi Bridget,

I have the following request from our review team:

In your NDA submission, we note you reported a SAE case of angioedema (leading to respiratory failure) in a 50 yr old black male on Day 2 of lurasidone 80 mg treatment. We are aware of AE reports of “swollen face, eyelid swelling, swollen tongue, thick tongue, lip swelling, edema, etc.” It is unclear if some of these events were EPS-related events or part of hypersensitivity reaction to drug product. We would like you to look for any relevant clinical information in the case reports of these patients who were involved in phase 2/3 placebo-controlled studies in order to further clarify or to determine which of these events were either EPS-related events or hypersensitivity reaction. In your response, please provide your search methodology and a descriptive summary of your findings. Please also provide a detailed line listing of these adverse events by patient including patient identification, study number, treatment assignment/dosing, day on study drug when the event occurred, event end date, severity and any intervention given to resolve the event.

Upon your completion of this evaluation to ensure that these events are reclassified appropriately, please determine the frequency of hypersensitivity or EPS-related adverse events. Please include as the risk for all terms under the general heading “All EPS events”; then include the risks for each EPS related event individually. You should, however, combine the preferred terms such as oculogyric crisis, torticollis and oromandibular dystonia under the rate of dystonia; and tremor, cogwheel rigidity, bradykinesia, drooling etc., under Parkinsonian-related adverse events.

Please revise and resubmit the incidence of treatment emergent adverse reactions reported in $\geq 2\%$ of lurasidone treated subjects the phase 2/3 placebo-controlled clinical trials for the treatment of schizophrenia (2% table) with above changes. You should also combine certain adverse terms, for example, somnolence and sedation; and provide the percentage. You may insert a foot note stating what AE terms were combined with the individual incidences.

In your proposed labeling, we note in section 6.5 that in the short-term, placebo-controlled studies for lurasidone treated patients, the incidence of reported EPS-related events, excluding akathisia was 16.7% vs. 6.6% for placebo-treated patients; and the incidence of akathisia for lurasidone treated patients was 15% vs. 3.3% for placebo-treated patients. Please identify the adverse event terms included in your calculation. Please indicate if there is any significant change in the numbers or percentage based on your recalculation.

We also note that in your proposed labeling, [REDACTED] (b) (4)
[REDACTED]
[REDACTED] Please clarify your basis of this proposal.

We request that you provide your response by COB, October 5, 2010.

Best Regards,

*Ann Sohn, Pharm.D., LT USPHS
Regulatory Project Manager
Division of Psychiatry Products
Center For Drug Evaluation and Research, FDA
Office of Drug Evaluation I
Email: ann.sohn@fda.hhs.gov*

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/s/

ANN J SOHN
09/22/2010

REQUEST FOR DDMAC LABELING REVIEW CONSULTATION

****Please send immediately following the Filing/Planning meeting****

TO:

CDER-DDMAC-RPM:
Attention: Amy Toscano

FROM: (Name/Title, Office/Division/Phone number of requestor)

Ann Sohn, RPM, Division of Psychiatry Products

REQUEST DATE
August 24, 2010

IND NO.

NDA/BLA NO.
NDA 200603

TYPE OF DOCUMENTS
Labeling

NAME OF DRUG

Lurasidone HCl

PRIORITY CONSIDERATION

Standard

CLASSIFICATION OF DRUG

Antipsychotic

DESIRED COMPLETION DATE

October 1, 2010

NAME OF FIRM:

Sepracor, Inc. (formerly Dainippon Sumitomo Pharma America Inc.)

PDUFA Date: October 30, 2010

TYPE OF LABEL TO REVIEW

TYPE OF LABELING:

(Check all that apply)

- PACKAGE INSERT (PI)
- PATIENT PACKAGE INSERT (PPI)
- CARTON/CONTAINER LABELING
- MEDICATION GUIDE
- INSTRUCTIONS FOR USE(IFU)

TYPE OF APPLICATION/SUBMISSION

- ORIGINAL NDA/BLA
- IND
- EFFICACY SUPPLEMENT
- SAFETY SUPPLEMENT
- LABELING SUPPLEMENT
- PLR CONVERSION

REASON FOR LABELING CONSULT

- INITIAL PROPOSED LABELING
- LABELING REVISION

EDR link to submission:

<\\CDSESUB1\EVSPROD\NDA200603\200603.ENX>

Please Note: There is no need to send labeling at this time. DDMAC reviews substantially complete labeling, which has already been marked up by the CDER Review Team. The DDMAC reviewer will contact you at a later date to obtain the substantially complete labeling for review.

COMMENTS/SPECIAL INSTRUCTIONS:

Mid-Cycle Meeting: 5/17/10

Labeling Meetings: 10/4/10

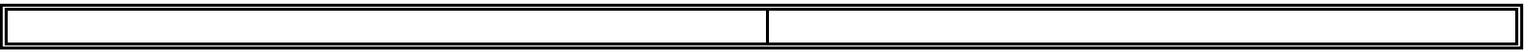
Wrap-Up Meeting: 9/7/10

SIGNATURE OF REQUESTER
Ann Sohn, RPM, HRF-130, DPP

SIGNATURE OF RECEIVER

METHOD OF DELIVERY (Check one)
 eMAIL

HAND



Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-200603	ORIG-1	DAINIPPON SUMITOMO PHARMA AMERICA INC	Lurasidone HCl

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/s/

ANN J SOHN
08/24/2010

THOMAS P LAUGHREN
08/24/2010



NDA 200603

INFORMATION REQUEST

Sepracor, Inc.
Attention: Bridget Walton, MS, RAC
Associate Director, Regulatory Affairs
1 Bridge Plaza, Suite 510
Fort Lee, NJ 07024

Dear Ms. Walton:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Lurasidone Hydrochloride Tablets, 40mg, 80mg, and 120mg.

We also refer to your December 30, 2009 and March 4, 2010 submissions, containing information supporting lurasidone indicated for the acute treatment of adult patients with schizophrenia.

We are reviewing the Chemistry, Manufacturing and Control 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. Provide all available dissolution data (release and stability) obtained for Lurasidone drug product tablets of 40, 80 and 120 mg strength obtained at time intervals earlier than 30 min with the current dissolution method for evaluation.
2. Provide comparative dissolution data for Group C formulations (b) (4) relative to Group B formulations (b) (4) in the dissolution medium of diluted McIlvaine's buffer (pH 4.0).
3. Provide physical dimensions for each tablet strength of Group C formulations (not included in Drug Product description and composition).
4. In Section 3.P.2.3.4.6.1 (b) (4), the batch numbers cited in Table 26 are not consistent with those cited in Section 3.P.2.3.4.6.2 as well as Figures 12 and 13. Provide clarification as to the origin of batches employed in evaluating tablet properties and dissolution.
5. Based on the proposed expiration dating of 30 months for the drug product shelf-life, please revise and submit the current stability protocols to include a 30 month interval for confirmation of drug product expiration dating period.

6. Provide missing data elements in SPL for Lurasidone Hydrochloride tablets for each strength. Information considered missing for 40 mg strength were listed here: Inactive ingredients, drug product size, NDC product number(s), manufacturer address and ID/FEI number(s) . Please correct the duplication of 10 blister pack in 1 box in lieu of 7 blister pack in 1 box , unit dose.

If you have any questions, call Teshara Bouie, Product Quality Regulatory Project Manager, at (301) 796-1649.

Sincerely,

{See appended electronic signature page}

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

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-200603	ORIG-1	DAINIPPON SUMITOMO PHARMA AMERICA INC	Lurasidone HCl

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/s/

RAMESH K SOOD
08/20/2010



NDA 200603

GENERAL ADVICE

Sepracor, Inc.
Attention: Bridget Walton, Director
Regulatory Affairs
1 Bridge Plaza, Suite 510
Fort Lee, NJ 07024

Dear Ms. Walton:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for lurasidone HCl 40 mg, 80 mg, and 120 mg tablets.

We also refer to your December 30, 2009 submission, containing draft carton and container labeling and to your June 11, 2010 submission, containing draft hospital unit-dose blister labels. We have reviewed the referenced material and have the following comments and recommendations.

A. Carton Labeling, Container labels and Professional Sample Blistercards (All strengths and quantities)

1. Revise the presentation of the established name on the container labels, carton labeling and blistercard so that the established name is printed in letters that are at least half as large as the letters comprising the proprietary name or designation with which it is joined, and the established name shall have a prominence commensurate with the prominence with which such proprietary name or designation appears, taking into account all pertinent factors, including typography, layout, contrast, and other printing features, per 21 CFR 201.10(g)(2).
2. Relocate the strength presentation to appear directly below the established name and above the bar graphic on the principle display panel.
3. Relocate the "each tablet contains" statement to appear below the bar graphic or on the side panel. See below.

(b) (4)



B. Carton Labeling for professional samples (10 x 7 tablet blistercards)

The proprietary and established names appear on the portion of the carton that is intended to be removed upon opening. Revise the presentation of the proprietary and established names in conjunction with the strength to provide this information on the carton before and after the carton is opened.

C. Professional sample Blistercards (7 tablets)

Relocate the “each tablet contains” statement to the inside center panel of the blistercard, panel containing the tablets. Inclusion of this statement on the inside center panel provides the patient with the amount of lurasidone HCl each tablet contains on the panel holding the tablets.

D. Hospital Unit-Dose Blister Labels (10 tablets)

1. Revise the strength presentation to provide additional methods to differentiate the strengths (e.g. color, shapes, or outlining).
2. Increase the prominence of the strength presentation to improve identification.
3. Relocate the dosage form, tablet, to appear below the established name.

If you have any questions, email Ann Sohn, Regulatory Project Manager, at ann.sohn@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Thomas Laughren, M.D.
Director
Division of Psychiatry Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

Application
Type/Number

Submission
Type/Number

Submitter Name

Product Name

NDA-200603

ORIG-1

DAINIPPON
SUMITOMO
PHARMA AMERICA
INC

Lurasidone HCl

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/s/

THOMAS P LAUGHREN
07/07/2010

From: [Sohn, Ann J](#)
To: ["Walton, Bridget";](#)
Subject: NDA 200603 lurasidone Clinical Requests
Date: Wednesday, June 30, 2010 10:51:04 AM

Hi Bridget,

I have the following requests from our clinical review team:

Perform an analysis for prolactin change from baseline to LOCF endpoint for P23STC studies (e.g. Table 85 in I SS), but include only those patients with a baseline prolactin within the normal range.

Provide a line listing of all subjects with prolactin levels meeting criteria for MAPLV and list all prolactin levels for these patients by visit.

Provide details regarding the patient receiving lurasidone who gained > 25 to 30 kg in the P23STC group (Table 107, I SS).

Please provide details for the P1NON subjects receiving lurasidone 40 mg/day who experienced an increase in QTcB of 164 msec and QTcF of 166 msec (same or different subjects?) [Table 10.1.1.1 in I SS].

The urinalysis laboratory data for the P23STC population [Table 7.5.1.3 in the I SS] show that 4.2% of patients receiving placebo had ketones present at LOCF endpoint compared to 2 - 2.2% of patients receiving lurasidone. Is there an explanation for the increase in ketones in the placebo group?

Please verify the number (%) of patients with $\geq 7\%$ weight gain in the P23STC studies. Table 7.5.1.3 (I SS) and Table 9.2.1.3 (I SS) have different numbers. For example, in the All Lurasidone group, Table 9.2.1.3 indicates that 65/999 (6.5%) of patients had this weight change whereas Table 9.3.2.1 indicates that 56/999 (5.6%) of patients had this weight change. It appears to be more than a transcription error (56/65) since the numbers in the olanzapine group are also different between the two tables.

For P23STC and P1SCH populations, perform an analysis for patients meeting criteria for changes in vital signs consistent with orthostatic hypotension - e.g. ≥ 20 mmHg decrease in SBP (sitting to standing or supine to standing) and ≥ 10 bpm increase in pulse (same positions).

Please let me know if you have any questions.

Thank you,

*Ann Sohn, Pharm.D., LT USPHS
Regulatory Project Manager
Division of Psychiatry Products
Center For Drug Evaluation and Research, FDA
Office of Drug Evaluation I
Email: ann.sohn@fda.hhs.gov*

Application
Type/Number

Submission
Type/Number

Submitter Name

Product Name

NDA-200603

ORIG-1

DAINIPPON
SUMITOMO
PHARMA AMERICA
INC

Lurasidone HCl

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/s/

ANN J SOHN
06/30/2010

From: [Sohn, Ann J](#)
To: ["Walton, Bridget";](#)
Subject: NDA 200603 lurasidone request
Date: Tuesday, June 22, 2010 10:15:30 AM

Hi Bridget,

I have the following requests from our review team:

1. Please determine the menopausal status for the following subjects.

Subject #	Postmenopausal?
0011-00001	
0011-00018	
0014-00018	
0024-00004	
0024-00005	
0024-00034	
0032-00001	
0053-00001	
0055-00003	
0018-00008	
0028-00001	
0046-00012	

2. Using available unblinded data from study D1050237:
 - Provide individual line listings and summary tables for CTx, NTx, BSAP, osteocalcin and PTH. Data should be summarized by treatment group and include the following timepoints: Baseline, Month 3, Month 6, and Month 12. These tables can be limited to subjects with post-baseline values.
 - Provide individual line listings and summary tables for the mean change from baseline in calcium, phosphorus, vitamin D, prolactin, 25-hydroxyvitamin D3, and free and total testosterone, by treatment group.

3. Provide clarification on your method of BMD correction.

Thank you,

*Ann Sohn, Pharm.D., LT USPHS
Regulatory Project Manager
Division of Psychiatry Products
Center For Drug Evaluation and Research, FDA
Office of Drug Evaluation I
Email: ann.sohn@fda.hhs.gov*

Application
Type/Number

Submission
Type/Number

Submitter Name

Product Name

NDA-200603

ORIG-1

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INC

Lurasidone HCl

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/s/

ANN J SOHN
06/22/2010

REQUEST FOR CONSULTATION

TO (Office/Division): ODEII/Division of Metabolism and Endocrinology Products/ Enid Galliers

FROM (Name, Office/Division, and Phone Number of Requestor): Cara Alfaro, MO, ODEI/Division of Psychiatry Products, 301-796-1033

DATE
May 10, 2010

IND NO.

NDA NO.
200603

TYPE OF DOCUMENT
120-Day Safety Update

DATE OF DOCUMENT
April 29, 2010

NAME OF DRUG
lurasidone HCl

PRIORITY CONSIDERATION

CLASSIFICATION OF DRUG
antipsychotic

DESIRED COMPLETION DATE
July 15, 2010

NAME OF FIRM: Sepracor, Inc.

REASON FOR REQUEST

I. GENERAL

- | | | |
|--|--|--|
| <input type="checkbox"/> NEW PROTOCOL | <input type="checkbox"/> PRE-NDA MEETING | <input type="checkbox"/> RESPONSE TO DEFICIENCY LETTER |
| <input type="checkbox"/> PROGRESS REPORT | <input type="checkbox"/> END-OF-PHASE 2a MEETING | <input type="checkbox"/> FINAL PRINTED LABELING |
| <input type="checkbox"/> NEW CORRESPONDENCE | <input type="checkbox"/> END-OF-PHASE 2 MEETING | <input type="checkbox"/> LABELING REVISION |
| <input type="checkbox"/> DRUG ADVERTISING | <input type="checkbox"/> RESUBMISSION | <input type="checkbox"/> ORIGINAL NEW CORRESPONDENCE |
| <input type="checkbox"/> ADVERSE REACTION REPORT | <input type="checkbox"/> SAFETY / EFFICACY | <input type="checkbox"/> FORMULATIVE REVIEW |
| <input type="checkbox"/> MANUFACTURING CHANGE / ADDITION | <input type="checkbox"/> PAPER NDA | <input type="checkbox"/> OTHER (SPECIFY BELOW): |
| <input type="checkbox"/> MEETING PLANNED BY | <input type="checkbox"/> CONTROL SUPPLEMENT | |

II. BIOMETRICS

- | | |
|---|---|
| <input type="checkbox"/> PRIORITY P NDA REVIEW | <input type="checkbox"/> CHEMISTRY REVIEW |
| <input type="checkbox"/> END-OF-PHASE 2 MEETING | <input type="checkbox"/> PHARMACOLOGY |
| <input type="checkbox"/> CONTROLLED STUDIES | <input type="checkbox"/> BIOPHARMACEUTICS |
| <input type="checkbox"/> PROTOCOL REVIEW | <input type="checkbox"/> OTHER (SPECIFY BELOW): |
| <input type="checkbox"/> OTHER (SPECIFY BELOW): | |

III. BIOPHARMACEUTICS

- | | |
|--|--|
| <input type="checkbox"/> DISSOLUTION | <input type="checkbox"/> DEFICIENCY LETTER RESPONSE |
| <input type="checkbox"/> BIOAVAILABILITY STUDIES | <input type="checkbox"/> PROTOCOL - BIOPHARMACEUTICS |
| <input type="checkbox"/> PHASE 4 STUDIES | <input type="checkbox"/> IN-VIVO WAIVER REQUEST |

IV. DRUG SAFETY

- | | |
|--|--|
| <input type="checkbox"/> PHASE 4 SURVEILLANCE/EPIDEMIOLOGY PROTOCOL | <input type="checkbox"/> REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY |
| <input type="checkbox"/> DRUG USE, e.g., POPULATION EXPOSURE, ASSOCIATED DIAGNOSES | <input type="checkbox"/> SUMMARY OF ADVERSE EXPERIENCE |
| <input type="checkbox"/> CASE REPORTS OF SPECIFIC REACTIONS (List below) | <input type="checkbox"/> POISON RISK ANALYSIS |
| <input type="checkbox"/> COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP | |

V. SCIENTIFIC INVESTIGATIONS

- | | |
|--|--------------------------------------|
| <input checked="" type="checkbox"/> CLINICAL | <input type="checkbox"/> NONCLINICAL |
|--|--------------------------------------|

COMMENTS / SPECIAL INSTRUCTIONS: In 2003, we requested consultation from your division regarding protocols submitted under IND 61,292 for lurasidone (then SM-13496) an antipsychotic with high affinity for D2 and 5HT2 receptors. The protocols were proposing to monitor several biochemical bone turnover markers as surrogates for bone mineral density. The consult was completed 9/3/2003 with the suggestion that DEXA scans be obtained at discrete timepoints in these studies (baseline, 6 months) as the bone turnover markers cannot be used as surrogates for BMD (other recommendations were included in the consult).

The Sponsor incorporated DEXA scans at specific timepoints (screening, 6 months, 12 months and 18 months) in study D1050237 and D1050237E. Study D1050237 was a randomized, double-blind, 12 month study evaluating the safety of lurasidone (flexible dose) and risperidone (flexible dose) and Study D1050237E was a 6-month open-label extension to the double-blind study (lurasidone flexible dose). A subset of subjects in this study (~100 per group) were to undergo DEXA scans.

The NDA for lurasidone was submitted in December 2009 (N200603) and the 120-day safety update (which was to include more available DEXA data) was submitted on April 29, 2010. The EDR link for the 120-day safety update: \\CDSESUB1\EVSPROD\NDA200603\0008

Please evaluate the DEXA findings in this study with regard to the overall risk of BMD changes with lurasidone. It

is understood that overall conclusions may be hampered by lack of a placebo group, though risperidone was a treatment group and comparisons to risperidone could be done.

SIGNATURE OF REQUESTOR

Ann Sohn, Pharm.D., Regulatory Project Manager
301-796-2232
Ann.sohn@fda.hhs.gov

METHOD OF DELIVERY (Check one)

DFS EMAIL MAIL HAND

PRINTED NAME AND SIGNATURE OF RECEIVER

PRINTED NAME AND SIGNATURE OF DELIVERER

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-200603	ORIG-1	DAINIPPON SUMITOMO PHARMA AMERICA INC	Lurasidone HCl

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

/s/

ANN J SOHN
05/10/2010

THOMAS P LAUGHREN
05/11/2010

REQUEST FOR CONSULTATION

TO (Office/Division): OAP/ Division of Anti-Infective and
Ophthalmology Products/Frances LeSane

FROM (Name, Office/Division, and Phone Number of Requestor): Cara Alfaro,
MO, ODEI/Division of Psychiatry Products, 301-796-
1033

DATE
May 10, 2010

IND NO.

NDA NO.
200603

TYPE OF DOCUMENT
120-Day Safety Update

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April 29, 2010

NAME OF DRUG
lurasidone HCl

PRIORITY CONSIDERATION

CLASSIFICATION OF DRUG
antipsychotic

DESIRED COMPLETION DATE
July 15, 2010

NAME OF FIRM: Sepracor, Inc.

REASON FOR REQUEST

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| <input type="checkbox"/> MANUFACTURING CHANGE / ADDITION | <input type="checkbox"/> PAPER NDA | <input type="checkbox"/> OTHER (SPECIFY BELOW): |
| <input type="checkbox"/> MEETING PLANNED BY | <input type="checkbox"/> CONTROL SUPPLEMENT | |

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| <input type="checkbox"/> END-OF-PHASE 2 MEETING | <input type="checkbox"/> PHARMACOLOGY |
| <input type="checkbox"/> CONTROLLED STUDIES | <input type="checkbox"/> BIOPHARMACEUTICS |
| <input type="checkbox"/> PROTOCOL REVIEW | <input type="checkbox"/> OTHER (SPECIFY BELOW): |
| <input type="checkbox"/> OTHER (SPECIFY BELOW): | |

III. BIOPHARMACEUTICS

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|--|--|
| <input type="checkbox"/> DISSOLUTION | <input type="checkbox"/> DEFICIENCY LETTER RESPONSE |
| <input type="checkbox"/> BIOAVAILABILITY STUDIES | <input type="checkbox"/> PROTOCOL - BIOPHARMACEUTICS |
| <input type="checkbox"/> PHASE 4 STUDIES | <input type="checkbox"/> IN-VIVO WAIVER REQUEST |

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| <input type="checkbox"/> CASE REPORTS OF SPECIFIC REACTIONS (List below) | <input type="checkbox"/> POISON RISK ANALYSIS |
| <input type="checkbox"/> COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP | |

V. SCIENTIFIC INVESTIGATIONS

- | | |
|--|--------------------------------------|
| <input checked="" type="checkbox"/> CLINICAL | <input type="checkbox"/> NONCLINICAL |
|--|--------------------------------------|

COMMENTS / SPECIAL INSTRUCTIONS: The NDA for lurasidone was submitted to our Division (NDA 200603 [IND 61,292]) in December 2009 and the 120-day safety update submitted April 29, 2010. Lurasidone is an antipsychotic agent with high affinities to D2 and 5HT2 receptors as well as melanin-binding properties. Due to the melanin-binding, the Sponsor was advised to obtain ophthalmologic examinations in one of their long-term clinical trials. The Sponsor incorporated ophthalmologic examinations at specific timepoints (baseline, 6 months, 12 months, 18+ months) in study D1050237 and D1050237E. Study D1050237 was a randomized, double-blind, 12 month study evaluating the safety of lurasidone (flexible dose) and risperidone (flexible dose) and Study D1050237E was a 6-month open-label extension to the double-blind study (lurasidone flexible dose). A subset of subjects were to undergo ophthalmologic examinations including visual acuity, dilated fundusoscopic examination, slit-lamp examination and external eye examination. In the NDA, the Sponsor had reported these findings as either "normal" or "abnormal" and the Division requested that more information regarding abnormal findings be submitted. The 120-day safety update includes additional clinical data for these ophthalmologic findings.

Please evaluate the ophthalmologic examination findings with regard to overall risk of ophthalmologic adverse events with lurasidone.

It is understood that conclusions may be hampered by lack of a placebo group and by the low numbers of available assessments - ~38 lurasidone-treated patients had baseline and post-baseline assessments and data for 85 patients with baseline and post-baseline assessments are still blinded at this time.

The EDR link for the 120-day safety update: \\CDSesub1\EVSPROD\NDA200603\0008

SIGNATURE OF REQUESTOR

Ann Sohn, Pharm.D., Regulatory Project Manager
301-796-2232
Ann.sohn@fda.hhs.gov

METHOD OF DELIVERY (Check one)

DFS EMAIL MAIL HAND

PRINTED NAME AND SIGNATURE OF RECEIVER

PRINTED NAME AND SIGNATURE OF DELIVERER

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-200603	ORIG-1	DAINIPPON SUMITOMO PHARMA AMERICA INC	Lurasidone HCl

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/s/

ANN J SOHN
05/10/2010

THOMAS P LAUGHREN
05/11/2010

From: [Sohn, Ann J](#)
To: ["Bridget Walton"](#)
Subject: NDA 200603 lurasidone
Date: Thursday, January 28, 2010 10:52:05 AM

Hi Bridget,

I have the following request from our statistical review team:

For studies D1050006 and D1050196, please provide extended versions of the primary analyses data sets (scales.xpt for study D1050006 and panslocf.xpt for D1050196) that contain variables for baseline BPRS total score.

For studies D1050229 and D1050231, please provide extended versions of the primary analyses data sets (cvpanss.xpt for study D1050229 and cvpanss.xpt for D1050231) that contain variables for pooled site.

Please provide a response by COB Thursday, Feb. 4 at the latest.

Thank you,

*Ann Sohn, Pharm.D., LT USPHS
Regulatory Project Manager
Division of Psychiatry Products
Center For Drug Evaluation and Research, FDA
Office of Drug Evaluation I
Email: ann.sohn@fda.hhs.gov*

Application
Type/Number

Submission
Type/Number

Submitter Name

Product Name

NDA-200603

ORIG-1

DAINIPPON
SUMITOMO
PHARMA AMERICA
INC

Lurasidone HCl

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/s/

ANN J SOHN
01/28/2010

DSI Consult for Biostudy in NDA200603

Request for Biopharmaceutical Inspections

Subject: Request for Biopharmaceutical Inspections

NDA: 200603

(b) (4) (Lurasidone HCl) Tablets

Indication: Treatment of Schizophrenia

Study/Site Identification:

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

Study number: D1001053

Title: An Open-Label, Randomized, Single-Dose, 2-Period, Crossover Study to Determine the Bioequivalence of Two Different SM-13496 Formulations of 40 mg tablet (b) (4) and 20 mg tablet (b) (4) in Healthy Young Adult Subjects

The study will officially be submitted by the 120 day safety update for the NDA which is April 30, 2010. However, a draft copy has been e-mailed by the sponsor to the reviewer.

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

Clinical site: Kitasato University East Hospital, The Kitasato Institute

2-1-1 Asamizodai, Sagamihara, Kanagawa 228-8520, Japan

Phone: 042-748-9111; Fax: 042-741-1743

Principal Investigator: Yasuhiko Ikeda

(b) (4)

The NDA is an electronic submission and can be found in EDR. The necessary information can be found in the network location as follows:

<http://CDSESUB1\EVSPROD\NDA200603.ENX>

OCP requests that the inspection report be sent by **August 31, 2010**. The clinical division intends to issue an action letter on this application by **October 30, 2010**.

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-200603	ORIG-1	DAINIPPON SUMITOMO PHARMA AMERICA INC	Lurasidone HCl

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/s/

ANN J SOHN
04/08/2010

THOMAS P LAUGHREN
04/08/2010

From: [Sohn, Ann J](#)
To: ["Bridget Walton"](#)
Subject: NDA 200603 lurasidone Request
Date: Thursday, March 04, 2010 10:39:37 AM

Hi Bridget,

Our review team is requesting datasets for study D1020549, please submit the following:

- Annotated CRF
- A Define file which describes the contents of the electronic data sets
- Electronic data sets as SAS transport files
- Please make sure that the ECG raw data set includes at least the followings: subject ID, treatment, period, ECG date, ECG time (up to second), nominal day, nominal time, replicate number, intervals (QT, RR, PR, QRS), HR, QTc [all corrected QT as end points, e.g. QTcF, QTcI (including individual correction factor), QTcB, or QTcN], Lead, ECG ID (link to waveform files if applicable).

- SAS code for the primary statistical analysis
- Data set whose QT/QTc values are the average of the replicates
- Statistical programs with analysis datasets that were used to analyze the study endpoints as well as to perform exposure-response analysis

- Submission of the related ECG waveforms to the ECG warehouse (www.ecgwarehouse.com)
- A completed Highlights of Clinical Pharmacology Table (attached)

Thank you,

*Ann Sohn, Pharm.D., LT USPHS
Regulatory Project Manager
Division of Psychiatry Products
Center For Drug Evaluation and Research, FDA
Office of Drug Evaluation I
Email: ann.sohn@fda.hhs.gov*

Application
Type/Number

Submission
Type/Number

Submitter Name

Product Name

NDA-200603

ORIG-1

DAINIPPON
SUMITOMO
PHARMA AMERICA
INC

Lurasidone HCl

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/s/

ANN J SOHN
03/04/2010



NDA 200603

FILING COMMUNICATION

Dainippon Sumitomo Pharma America, Inc.
Attention: Bridget Walton, Associate Director
Regulatory Affairs
One Bridge Plaza, Suite 510
Fort Lee, NJ 07024

Dear Ms. Walton:

Please refer to your new drug application (NDA) dated December 30, 2009, received December 30, 2009, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act, for lurasidone hydrochloride 40mg, 80mg, and 120mg tablets. We also refer to your submission dated January 26, 2010.

We have completed our filing review and have determined that your application is sufficiently complete to permit a substantive review. Therefore, this application is considered filed 60 days after the date we received your application in accordance with 21 CFR 314.101(a). The review classification for this application is **Standard**. Therefore, the user fee goal date is October 30, 2010.

We are reviewing your application according to the processes described in the Guidance for Review Staff and Industry: Good Review Management Principles and Practices for PDUFA Products. Therefore, we have established internal review timelines as described in the guidance, which includes the timeframes for FDA internal milestone meetings (e.g., filing, planning, mid-cycle, team and wrap-up meetings). Please be aware that the timelines described in the guidance are flexible and subject to change based on workload and other potential review issues (e.g., submission of amendments). We will inform you of any necessary information requests or status updates following the milestone meetings or at other times, as needed, during the process. If major deficiencies are not identified during the review, we plan to communicate proposed labeling and, if necessary, any postmarketing requirement/commitment requests by October 8, 2010.

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

Clinical:

1. Please include a more detailed description of “abnormal” findings on ophthalmologic examinations. State what the abnormalities were and, for subjects with abnormal baseline and abnormal end-of-study examinations, if those abnormalities were unchanged. Since the majority of the ophthalmologic examination data will be provided in the 120-day update, it is

acceptable to include this information for all data at that time (e.g. you do not need to provide these data at this time for the few subjects for which data have already been submitted).

2. For all deaths, please provide comprehensive narratives that include relevant clinical details including laboratory assessments, ECG data and vital signs.
3. Please provide the autopsy report and any other relevant clinical details for patient #23701730. The event “sudden death – hypertensive heart disease” is noted, however, the information provided in the narrative does not indicate a prior history of hypertension. Please clarify.
4. Please provide an updated narrative for patient D1050231-0011-00001 who died due to “accidental (heroin) overdose”. The current narrative only provides information relevant to ALT changes (the AE that led to discontinuation from study).
5. Please indicate whether an application for lurasidone for any indication has been submitted to any foreign country.
6. On page 410 of the ISS, it appears that a literature search was performed, but there is little information regarding the clinical findings of this search. Please provide a summary of worldwide experience on the safety of this drug. We will need your warrant that you have reviewed this literature systematically, and in detail, and that you have discovered no finding that would adversely affect conclusions about the safety of lurasidone. The report should also detail whether it relied on abstracts or full texts (including translations) of articles. The report should emphasize clinical data, but new findings in preclinical reports of potential significance should also be described. Should any report or finding be judged important, a copy (translated as required) should be submitted for our review.

Statistical:

1. For all 4 efficacy studies, for each treatment group please provide a response profile plot in the primary endpoint for dropouts at each visit and for completers. That is, for each treatment group, provide response profile curves up to visit i for each cohort of patients who drop out between visits i and $i+1$, where $i = 1, 2, 3, \dots$
2. Please include in your submission a list of serial numbers/submission dates for all protocol/SAP submissions pertaining to studies D1050006 and D1050196.
3. For studies D1050006 and D1050196, please provide subgroup analyses by race and gender.

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.

REQUIRED PEDIATRIC ASSESSMENTS

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

Pediatric studies conducted under the terms of section 505B of the Federal Food, Drug, and Cosmetic Act (the Act) may also qualify for pediatric exclusivity under the terms of section 505A of the Act. Please note that satisfaction of the requirements in section 505B of the Act alone may not qualify you for pediatric exclusivity under 505A of the Act.

We acknowledge receipt of your request for a partial waiver of pediatric studies for this application. Once we have reviewed your request, we will notify you if the partial waiver request is denied.

We acknowledge receipt of your request for a partial deferral of pediatric studies for this application. Once we have reviewed your request, we will notify you if the partial deferral request is denied.

If you have any questions, please email Ann Sohn, Pharm.D., Regulatory Project Manager, at ann.sohn@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Thomas Laughren, M.D.
Director
Division of Psychiatry Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

Application
Type/Number

Submission
Type/Number

Submitter Name

Product Name

NDA-200603

ORIG-1

DAINIPPON
SUMITOMO
PHARMA AMERICA
INC

Lurasidone HCl

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/s/

THOMAS P LAUGHREN
03/04/2010

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-200603	ORIG-1	DAINIPPON SUMITOMO PHARMA AMERICA INC	Lurasidone HCl

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/s/

ANN J SOHN
03/02/2010

THOMAS P LAUGHREN
03/02/2010

REQUEST FOR CONSULTATION

TO (Office/Division): **Patrick Marroum, Biopharmaceutics, ONDQA**

FROM (Name, Office/Division, and Phone Number of Requestor):
Don Henry Project Manager, ONDQA, 301-796-4227 on behalf of S. Bhmaidpati/T. Oliver

DATE
2/25/2010

IND NO.

NDA NO.
200603

TYPE OF DOCUMENT
NDA submission

DATE OF DOCUMENT
December 30, 2009

NAME OF DRUG
lurasidone

PRIORITY CONSIDERATION
standard

CLASSIFICATION OF DRUG
psychiatry

DESIRED COMPLETION DATE
May 30, 2010

NAME OF FIRM: **Dainippon Sumitomo Pharma America, Inc.**

REASON FOR REQUEST

I. GENERAL

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| <input type="checkbox"/> COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP | |

V. SCIENTIFIC INVESTIGATIONS

- | | |
|-----------------------------------|--------------------------------------|
| <input type="checkbox"/> CLINICAL | <input type="checkbox"/> NONCLINICAL |
|-----------------------------------|--------------------------------------|

COMMENTS / SPECIAL INSTRUCTIONS: This application is completely electronic and can be accessed via Global Submit Review. The applicant has provided dissolution data for clinical and commercial formulations. Review of the data is requested to determine the appropriateness of the dissolution specifications. The applicant has not requested a waiver but referred to bioequivalence studies. Review of this information may be necessary.

SIGNATURE OF REQUESTOR
{See appended electronic signature page}

METHOD OF DELIVERY (Check one)
 DFS EMAIL MAIL HAND

PRINTED NAME AND SIGNATURE OF RECEIVER

PRINTED NAME AND SIGNATURE OF DELIVERER

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-200603	ORIG-1	DAINIPPON SUMITOMO PHARMA AMERICA INC	Lurasidone HCl

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/s/

DON L HENRY
02/26/2010

RAMESH K SOOD
03/01/2010

REQUEST FOR CONSULTATION

TO (Office/Division): Div. of Cardiovascular & Renal Products;
QT Interdisciplinary Review Team

FROM (Name, Office/Division, and Phone Number of Requestor): HFD-130/Division of Psychiatry Products/ Ann Sohn

DATE
February 24, 2010

IND NO.

NDA NO.
200603

TYPE OF DOCUMENT
Original NDA

DATE OF DOCUMENT
December 30, 2009

NAME OF DRUG
lurasidone hydrochloride

PRIORITY CONSIDERATION

CLASSIFICATION OF DRUG
antipsychotic/ treatment
of schizophrenia

DESIRED COMPLETION DATE
June 15, 2010

NAME OF FIRM: Dainippon Sumitomo Pharma America, Inc.

REASON FOR REQUEST

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| <input type="checkbox"/> DRUG ADVERTISING | <input type="checkbox"/> RESUBMISSION | <input type="checkbox"/> ORIGINAL NEW CORRESPONDENCE |
| <input type="checkbox"/> ADVERSE REACTION REPORT | <input type="checkbox"/> SAFETY / EFFICACY | <input type="checkbox"/> FORMULATIVE REVIEW |
| <input type="checkbox"/> MANUFACTURING CHANGE / ADDITION | <input type="checkbox"/> PAPER NDA | <input type="checkbox"/> OTHER (SPECIFY BELOW): |
| <input type="checkbox"/> MEETING PLANNED BY | <input type="checkbox"/> CONTROL SUPPLEMENT | |

II. BIOMETRICS

- | | |
|---|---|
| <input type="checkbox"/> PRIORITY P NDA REVIEW | <input type="checkbox"/> CHEMISTRY REVIEW |
| <input type="checkbox"/> END-OF-PHASE 2 MEETING | <input type="checkbox"/> PHARMACOLOGY |
| <input type="checkbox"/> CONTROLLED STUDIES | <input type="checkbox"/> BIOPHARMACEUTICS |
| <input type="checkbox"/> PROTOCOL REVIEW | <input type="checkbox"/> OTHER (SPECIFY BELOW): |
| <input type="checkbox"/> OTHER (SPECIFY BELOW): | |

III. BIOPHARMACEUTICS

- | | |
|---|--|
| <input type="checkbox"/> DISSOLUTION | <input type="checkbox"/> DEFICIENCY LETTER RESPONSE |
| <input type="checkbox"/> BIOAVAILABILTY STUDIES | <input type="checkbox"/> PROTOCOL - BIOPHARMACEUTICS |
| <input type="checkbox"/> PHASE 4 STUDIES | <input type="checkbox"/> IN-VIVO WAIVER REQUEST |

IV. DRUG SAFETY

- | | |
|--|--|
| <input type="checkbox"/> PHASE 4 SURVEILLANCE/EPIDEMIOLOGY PROTOCOL | <input type="checkbox"/> REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY |
| <input type="checkbox"/> DRUG USE, e.g., POPULATION EXPOSURE, ASSOCIATED DIAGNOSES | <input type="checkbox"/> SUMMARY OF ADVERSE EXPERIENCE |
| <input type="checkbox"/> CASE REPORTS OF SPECIFIC REACTIONS (List below) | <input type="checkbox"/> POISON RISK ANALYSIS |
| <input type="checkbox"/> COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP | |

V. SCIENTIFIC INVESTIGATIONS

- | | |
|--|--------------------------------------|
| <input checked="" type="checkbox"/> CLINICAL | <input type="checkbox"/> NONCLINICAL |
|--|--------------------------------------|

COMMENTS / SPECIAL INSTRUCTIONS: The sponsor has submitted an original NDA for marketing approval of lurasidone in the treatment of schizophrenia. The target dose is 40-80 mg once daily. In this NDA submission, the sponsor has included proposed labeling regarding the effect of lurasidone on the QT interval based on results of a QTc exposure-response study (protocol D1050249). The Division of Psychiatry Products (DPP/HFD-130) would like to have the IRT's input and recommendations on QT findings and the sponsor's proposed labeling language in the

(b) (4)

. Of note, a metabolic inhibitor approach in this study was not used due to tolerability issues, however, lurasidone is primarily metabolized by CYP3A4 with significant increases in Cmax and AUC when coadministered with potent inhibitors (e.g. ketoconazole). The Sponsor was asked to provide an assessment of expected effects on the QT interval if lurasidone was coadministered with a CYP3A4 inhibitor - this analysis (exposure-response modeling) is also provided in the submission (M1050004). The QT study report, the ECG findings in clinical trials and the sponsor's labeling proposal can be found in the EDR <EDR link: \\CDSESUB1\EVSPROD\NDA200603\200603.ENX >. The clinical reviewer is Cara Alfaro. Please let me know who the assigned reviewer is for this consult. If you have any further questions you can contact me.

SIGNATURE OF REQUESTOR Ann Sohn, Pharm.D., Regulatory Project Manager 301-796-2232 Ann.sohn@fda.hhs.gov		METHOD OF DELIVERY (Check one) <input type="checkbox"/> DFS <input type="checkbox"/> EMAIL <input type="checkbox"/> MAIL <input type="checkbox"/> HAND	
PRINTED NAME AND SIGNATURE OF RECEIVER		PRINTED NAME AND SIGNATURE OF DELIVERER	

Application
Type/Number

Submission
Type/Number

Submitter Name

Product Name

NDA-200603

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/s/

ANN J SOHN
02/26/2010

THOMAS P LAUGHREN
02/26/2010

From: [Bridget Walton](#)
To: [Sohn, Ann J;](#)
Subject: NDA200603
Date: Tuesday, February 23, 2010 3:33:23 PM
Attachments: [emfalert.txt](#)

Hi Ann,

I wanted to let you know DSPA had a teleconference requested by the Clinical Pharmacology reviewers last Friday, February 19th at 5PM. I indicated I would send you a summary.

FDA participants: Kofi Kumi
Raman Baweja
DSPA participants: Bridget Walton
James Rawls
Donald Sarubbi

The reviewers had some questions regarding the design of the clinical pharmacology studies to be submitted in the 120-day safety update (D1050267 and D1001053) and Study D1050263, which was submitted in the original NDA.

DSPA stated that Study D1050267 (food effect) included both fed and fasted arms with increasing caloric intake (300, 500 or 1000 kcal) and one arm included the standard FDA high-fat breakfast.

DSPA indicated that the Japanese food effect (FE) study, D1001053 was performed under fed conditions. FDA asked why 40 mg was selected as the dose for the Japanese FE study. DSPA indicated that drug tolerability is an important factor when Japanese physicians prescribe a medication. Therefore, Japanese physicians tend to prescribe certain medications at the low to mid range of the pharmacological dose range.

FDA noted that in Study D1050263 (BE) the clinical trial material was used as a reference and compared to commercial drug. They asked if a solution or IV comparison was also included in the study or if a relative bioavailability (BA) study was performed. DSPA indicated that Study D1050263 did not include either of these formulations and that a separate BA study was not performed.

FDA also asked if the label would indicate lurasidone should be given with food. It was confirmed that it would.

Please let me know if you have any questions.

Thanks and best regards,
Bridget

Bridget Walton, MS, RAC

Associate Director, Regulatory Affairs
Dainippon Sumitomo Pharma America, Inc.
One Bridge Plaza
Suite 510
Fort Lee, NJ 07024
Office: (201) 228-8333
Mobile:(201) 310-0156

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/s/

ANN J SOHN
02/23/2010

From: [Bridget Walton](#)
To: [Sohn, Ann J](#);
Subject: RE: NDA200603
Date: Tuesday, February 23, 2010 8:16:43 PM
Attachments: [emfinfo.txt](#)

Hi Ann,

We checked and can confirm that Study D1001053 was performed under fed conditions only. I have included a post meeting note in the summary below.

Best regards,
Bridget

Bridget Walton, MS, RAC

Associate Director, Regulatory Affairs
Dainippon Sumitomo Pharma America, Inc.
One Bridge Plaza
Suite 510
Fort Lee, NJ 07024
Office: (201) 228-8333
Mobile:(201) 310-0156

From: Sohn, Ann J [mailto:Ann.Sohn@fda.hhs.gov]
Sent: Tuesday, February 23, 2010 6:05 PM
To: Bridget Walton
Subject: RE: NDA200603

Hi Bridget,

Our Clin Pharm reviewers mentioned that DSPA was going to check whether the study D1001053 (BE between DSP Formulation B and C in Japanese subjects) has a fasted arm in the study. Please include this in the notes.

Thanks,
Ann

From: Bridget Walton [mailto:bwalton@dsp-a.com]
Sent: Tuesday, February 23, 2010 3:31 PM
To: Sohn, Ann J
Subject: NDA200603

Hi Ann,

I wanted to let you know DSPA had a teleconference requested by the Clinical Pharmacology reviewers last Friday, February 19th at 5PM. I indicated I would send you a summary.

FDA participants: Kofi Kumi
Raman Baweja

DSPA participants: Bridget Walton
James Rawls
Donald Sarubbi

The reviewers had some questions regarding the design of the clinical pharmacology studies to be submitted in the 120-day safety update (D1050267 and D1001053) and Study D1050263, which was submitted in the original NDA.

DSPA stated that Study D1050267 (food effect) included both fed and fasted arms with increasing caloric intake (300, 500 or 1000 kcal) and one arm included the standard FDA high-fat breakfast.

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FDA noted that in Study D1050263 (BE) the clinical trial material was used as a reference and compared to commercial drug. They asked if a solution or IV comparison was also included in the study or if a relative bioavailability (BA) study was performed. DSPA indicated that Study D1050263 did not include either of these formulations and that a separate BA study was not performed.

FDA also asked if the label would indicate lurasidone should be given with food. It was confirmed that it would.

Post meeting note: FDA had asked that DSPA confirm if Study D1001053 had a fasting arm in the study. DSPA can confirm that

Study D1001053 was performed under fed conditions only.

Please let me know if you have any questions.

Thanks and best regards,
Bridget

Bridget Walton, MS, RAC

Associate Director, Regulatory Affairs
Dainippon Sumitomo Pharma America, Inc.
One Bridge Plaza
Suite 510
Fort Lee, NJ 07024
Office: (201) 228-8333
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/s/

ANN J SOHN
02/24/2010



NDA 200603

NDA ACKNOWLEDGMENT

Dainippon Sumitomo Pharma America, Inc.
Attention: Bridget Walton, MS, RAC
Associate Director, Regulatory Affairs
1 Bridge Plaza, Suite 510
Fort Lee, NJ 07024

Dear Ms. Walton:

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

Name of Drug Product: lurasidone hydrochloride tablets 40mg, 80mg, and 120mg

Date of Application: December 30, 2009

Date of Receipt: December 30, 2009

Our Reference Number: NDA 200603

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 28, 2010 in accordance with 21 CFR 314.101(a).

Please note that you are responsible for complying with the applicable provisions of sections 402(i) and 402(j) of the Public Health Service Act (PHS Act) (42 USC §§ 282(i) and (j)), which was amended by Title VIII of the Food and Drug Administration Amendments Act of 2007 (FDAAA) (Public Law No. 110-85, 121 Stat. 904). Title VIII of FDAAA amended the PHS Act by adding new section 402(j) (42 USC § 282(j)), which expanded the current database known as ClinicalTrials.gov to include mandatory registration and reporting of results for applicable clinical trials of human drugs (including biological products) and devices. FDAAA requires that, at the time of submission of an application under section 505 of the FDCA, the application must be accompanied by a certification that all applicable requirements of 42 USC § 282(j) have been met. Where available, the certification must include the appropriate National Clinical Trial (NCT) control numbers. 42 USC 282(j)(5)(B). You did not include such certification when you submitted this application. You may use Form FDA 3674, *Certification of Compliance, under 42 U.S.C. § 282(j)(5)(B), with Requirements of ClinicalTrials.gov Data Bank*, to comply with the certification requirement. The form may be found at <http://www.fda.gov/opacom/morechoices/fdaforms/default.html>.

In completing Form FDA 3674, you should review 42 USC § 282(j) to determine whether the requirements of FDAAA apply to any clinical trials referenced in this application. Additional information regarding the certification form is available at:

<http://www.fda.gov/RegulatoryInformation/Legislation/FederalFoodDrugandCosmeticActFDCAct/SignificantAmendmentstotheFDCAct/FoodandDrugAdministrationAmendmentsActof2007/ucm095442.htm>. Additional information regarding Title VIII of FDAAA is available at: <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-08-014.html>. Additional information on registering your clinical trials is available at the Protocol Registration System website <http://prsinfo.clinicaltrials.gov/>.

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

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Psychiatry 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, email Ann Sohn, Regulatory Project Manager, at ann.sohn@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

LT Ann Sohn, Pharm.D.
Regulatory Project Manager
Division of Psychiatry Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

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/s/

ANN J SOHN
01/05/2010