

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

21-875

**ADMINISTRATIVE and CORRESPONDENCE
DOCUMENTS**

EXCLUSIVITY SUMMARY

NDA # 21-875

SUPPL #

HFD # 120

Trade Name: Nuvigil

Generic Name: armodafinil

Applicant Name: Cephalon

Approval Date, If Known: 6/15/07

PART I IS AN EXCLUSIVITY DETERMINATION NEEDED?

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

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

YES

NO

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

505(b)(1)

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

YES

NO

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

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

d) Did the applicant request exclusivity?

YES

NO

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

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

YES

NO

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

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

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

YES

NO

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

PART II FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES

(Answer either #1 or #2 as appropriate)

1. Single active ingredient product.

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

YES

NO

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

NDA# 20-717

Provigil (modafinil) Tablets

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#

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:

There were three indications for which Nuvigil gained approval. The three indications as well as the studies essential to the approval are following:

- 1.) Obstructive Sleep Apnea Hypopnea Syndrome (OSAHS): Study 3021 and Study 3025
- 2.) Shift Work Sleep Disorder (SWSD): Study 3022
- 3.) Narcolepsy: Study 3020

4.) To be eligible for exclusivity, a new investigation that is essential to approval must also have been conducted or sponsored by the applicant. An investigation was "conducted or sponsored by" the applicant if, before or during the conduct of the investigation, 1) the applicant was the sponsor of the IND named in the form FDA 1571 filed with the Agency, or 2) the applicant (or its predecessor in interest) provided substantial support for the study. Ordinarily, substantial support will mean providing 50 percent or more of the cost of the study.

a) For each investigation identified in response to question 3(c): if the investigation was carried out under an IND, was the applicant identified on the FDA 1571 as the sponsor?

Investigation #1	Study 3021	!
IND # 68,517	YES <input checked="" type="checkbox"/>	! NO
	! Explain:	
Investigation #2	Study 3025	!
IND # 68,517	YES <input checked="" type="checkbox"/>	! NO
	! Explain:	
Investigation #3	Study 3022	!
IND # 68,517	YES <input checked="" type="checkbox"/>	! NO
	! Explain:	
Investigation #4	Study 3020	!
IND # 68,517	YES <input checked="" type="checkbox"/>	! NO
	! Explain:	

(b) For each investigation not carried out under an IND or for which the applicant was not identified as the sponsor, did the applicant certify that it or the applicant's predecessor in interest provided substantial support for the study?

Investigation #1	Not applicable	
IND #	YES	! NO
	! Explain:	
Investigation #2	Not applicable	
IND #	YES	! NO
	! 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: Tamy Kim, PharmD
Title: Regulatory Project Manager
Date: 8/3/07

Name of Office/Division Director signing form: Division of Neurology Products/Russell Katz, MD
Title: Division Director

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

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/s/

Russell Katz

10/30/2007 01:26:26 PM

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MEMORANDUM

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

DATE: May 25, 2007

TO: Russell Katz, M.D., Director
Division of Neurology Products

VIA: Tamy Kim, Pharm.D., Regulatory Project Manager
Division of Neurology Products

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

Toni Piazza-Hepp, Pharm.D., Deputy Director
Division of Surveillance, Research, and Communication Support

SUBJECT: OSE/DSRCS Review of Patient Labeling for Nuvigil (armodafinil)
Tablets, NDA 21-875

Background and Summary

Cephalon, Inc. submitted a complete response for Nuvigil (armodafinil) Tablets, NDA 21-875 on April 16, 2007, in response to an Approvable letter dated March 28, 2007.

Identical Patient Labeling in the form of a Patient Package Insert (PPI) were submitted with the complete response and consulted to DSRCS for review.

b(4)

The review division plans to notify the sponsor that a product cannot have two separate forms of Patient Labeling and that the

b(5)

Comments and Recommendations

1. See the attached documents (marked and clean copies) for our recommended revisions to the draft PPI. We have ensured the information is consistent with the information in the prescribing information (PI) and removed unnecessary information. Our revisions have kept the reading level at an 8th grade level (Flesh-Kincaid).
2. There are no distribution requirements for PPIs. It is unlikely that a patient will receive Nuvigil PPI unless it is packaged with the product in unit-of-use packaging.

Comments to the review division in the attached documents are **bolded, underlined and italicized**. Please call us if you have any questions.

12 Page(s) Withheld

 Trade Secret / Confidential (b4)

✓ Draft Labeling (b4)

 Draft Labeling (b5)

 Deliberative Process (b5)

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/s/

Jeanine Best
5/25/2007 02:38:38 PM
DRUG SAFETY OFFICE REVIEWER

Toni Piazza Hepp
5/25/2007 06:23:21 PM
DRUG SAFETY OFFICE REVIEWER

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Kim, Tamy

From: Kim, Tamy
Sent: Monday, May 07, 2007 12:15 PM
To: Kirsch, Paul
Cc: 'Murray, Colleen'
Subject: NDA 21-875

Dear Mr. Kirsch,

Please refer to your Complete Response to Approvable Letter for Nuvigil (NDA 21-875) dated, April 16, 2007. We consider this a Class I Resubmission, with an Action date of June 16, 2007.

Best regards,
Tamy

Tamy Kim, PharmD
Regulatory Project Manager
Division of Neurology Products
Food and Drug Administration
Phone: 301-796-1125
Email: tamy.kim@fda.hhs.gov

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/s/

Tamy E. Kim
5/7/2007 12:17:42 PM
CSO

Tamy E. Kim
5/7/2007 12:18:16 PM
CSO

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Kim, Tamy

From: Kim, Tamy
Sent: Tuesday, May 01, 2007 12:26 PM
To: 'Murray, Colleen'
Subject: NDA 21-875 - Request for information and comment

Dear Colleen,

We have the following requests and comments about your April 16, 2007 response to the March 28, 2007 Approvable Letter for NDA 21-875.

Requests:

Clinical

1. Please send the actual materials and components of your educational program for items 4, 5, 7 and 8 under Table 1: *Educational Program for PROVIGIL and NUVIGIL* of your CLINICAL FDA QUESTION section as soon as possible.
2. The annual report for IND 59,661, dated April 2, 2007, includes case 034015/ →, a case of severe rash that led to discontinuation of modafinil. Please clarify whether trial C1538/3044/AD/US was one of the trials included in the denominator used in the Nuvigil/Provigil labeling (N= 1622) and whether this case has been previously submitted to the Agency. If this case was previously submitted, please provide the date of submission. If this case was not previously submitted, please provide all available information regarding this case (e.g. medical records, biopsy, photographs).
3. As discussed in a telephone conversation on April 3, 2007, please confirm that you plan to submit a CBE labeling supplement for Provigil as soon as agreement on the Provigil labeling is reached, which will hopefully happen in close proximity to the June 16, 2007 action date for Nuvigil.

b(6)

Comments:

Clinical Pharmacology

1. The in vitro and in vivo results have indicated that armodafinil is a CYP3A4 inducer. Because of the shared mechanism of regulation, co-induction of P-gp and CYP3A is likely, and that formed the basis for our previous recommendation for the evaluation for the P-gp inducibility. However, based on current understanding, methods for in vitro evaluation for P-gp induction are not well understood and P-gp induction potential of an investigational drug can only be more reliably evaluated in vivo. Therefore, our original intent was for you to conduct a literature search for any available information on the induction potential. In our view, the in-vitro investigation for the potential P-gp induction is not necessary at this point. However, a thorough literature search should be undertaken to see if there is any information on the P-gp induction potential of modafinil in vivo. We ask that you provide this literature search as a post-marketing commitment. This can form the basis for discussion and to see if any future in vivo P-gp induction study is necessary.

Please submit your responses to the above requests and comments to the NDA, and please e-mail me a copy of your submission, if possible. Please confirm receipt of this e-mail.

Best regards,
Tamy

Tamy Kim, PharmD
Regulatory Project Manager
Division of Neurology Products
Food and Drug Administration
Phone: 301-796-1125
Email: tamy.kim@fda.hhs.gov

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/s/

Tamy E. Kim
5/1/2007 12:29:50 PM
CSO

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(2) PPI: Please review the Nuvigil PPI, which has **slight** modifications to the Provigil PPI.

We request that this review be completed by 5/28/07. However, if you complete this review before the requested date, please let me know so that I can incorporate you into DNP meetings to discuss your review.

Submission:

The Nuvigil PPI can be found in the EDR at: http://cdemet/edr/loadfile.asp?PATH=FILE://\CDSESUB1\N21875\N_000\2007-04-

A review by DSRCS for the approved Provigil PPI was dated 1/14/04 for comparison to the Nuvigil PPI. The Approved Provigil PPI can be found in the Approval Letter dated 1/23/04.

Please call me if you have any questions. Thank you.

SIGNATURE OF REQUESTER Tamy Kim, PharmD, Regulatory Project Manager, DNP Food and Drug Administration Phone: 301-796-1125 Email: tamy.kim@fda.hhs.gov	METHOD OF DELIVERY (Check one) <input checked="" type="checkbox"/> DFS <input type="checkbox"/> E-MAIL <input type="checkbox"/> MAIL <input type="checkbox"/> HAND
SIGNATURE OF RECEIVER	SIGNATURE OF DELIVERER

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b(4)

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Tamy E. Kim

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MEMORANDUM

Division of Medication Errors and Technical Support
Office of Surveillance and Epidemiology
HFD-420; WO22, Mail Stop 4447
Center for Drug Evaluation and Research

To: Russell Katz, MD
Director, Division of Neurology Products
HFD-120

Through: Linda Y. Kim-Jung, PharmD, Team Leader
Denise P. Toyer, PharmD, Deputy Director
Carol A. Holquist, RPh, Director
Division of Medication Errors and Technical Support, HFD-420

From: Loretta Holmes, PharmD, Safety Evaluator
Division of Medication Errors and Technical Support, HFD-420

Date: March 13, 2007

Subject: **DMETS Proprietary Name, Label, and Labeling Review**
Drug: Nuvigil (Armodafinil) Tablets; 50 mg, 150 mg, and 250 mg
NDA#: 21-875
Sponsor: Cephalon, Inc.

Review #: 2007-524

This review is in response to a request from the Division of Neurology Products (HFD-120) for a re-review of the proposed proprietary name, Nuvigil (NDA 21-875). Additionally, revised container labels, carton and package insert labeling were provided for review and comment.

The proposed proprietary name, Nuvigil, was found unacceptable by DMETS in our previous review of the name (OSE Review 05-0091, dated August 5, 2005) because of concerns with potential look-alike similarities to Norinyl. DMETS label and labeling recommendations were also included in that review. Subsequently, the Division determined that the proposed proprietary name is acceptable, but asked that the sponsor submit any medication error reports associated with Nuvigil as 15-day reports. Additionally, the sponsor agreed to include a statement about potential name confusion between Nuvigil and Norinyl in their promotional material as per recommendations from the Division.

Since our previous review of Nuvigil, we have not identified any additional names of concern. Additionally, the sponsor has decided not to market the 100 mg strength. However, this decision has not impacted our previous recommendation not to recommend the name based on similarities to Norinyl.

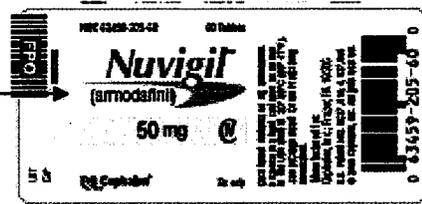
In reviewing the revised container labels, carton and package insert labeling of Nuvigil, DMETS has focused on safety issues relating to possible medication errors. We have the following additional recommendations for the revised container labels, carton and package insert labeling.

A. GENERAL COMMENTS

1. Use the same type and font size for the dosage form statement ("tablets") and the established name. Additionally, there is an orange graphic on the principal display panel that is superimposed over the word "tablets". In its current position, the graphic is distracting and more prominent than the established name. Please delete it or relocate it so that it is not superimposed over any of the wording on the principal display panel.

2. Precede the usual dosage statement with the wording "Usual Dosage" so that the statement is easily identified.

1. Use the same type and font size for the established name and the word "tablets".
2. Delete or relocate the orange graphic.
3. Precede the usual dosage statement with the wording "Usual Dosage".



3. Since the sponsor has decided not to market the 100 mg strength, DMETS suggests considering the use of the trade dress that was considered for the 100 mg strength for use with one of the other strengths. The colors used to differentiate the 50 mg and 250 mg strengths are somewhat similar (yellow and light orange) while that used for the 100 mg strength is green. Use of the green color for either the 50 mg or 250 mg strength may provide improved color differentiation between the marketed strengths.

B. CONTAINER LABELS (60-count bottles)

See General Comments.

C. ✓

b(4)

b(5)

D. ✓

b(4)

b(5)

✓ E. PACKAGE INSERT LABELING

DOSAGE AND ADMINISTRATION Section

We recommend separation of the indications and doses into two sections as follows for better clarity. As it appears now, the information is abbreviated and could lead to error. For example:

Obstructive Sleep Apnea/Hypopnea Syndrome (OSAHS) and Narcolepsy

The recommended dose of Nuvigil for patients with OSAHS or narcolepsy is 150 mg or 250 mg given as a single dose in the morning. In patients with OSAHS, doses up to 250 mg/day, given as a single dose, have been well tolerated, but there is no consistent evidence that this dose confers additional benefit beyond that of the 150 mg/day dose.

Shift Work Sleep Disorder (SWSD)

The recommended dose of Nuvigil for patients with SWSD is 150 mg given daily approximately 1 hour prior to the start of their work shift

In summary, DMETS continues to not recommend the use of the proposed proprietary name, Nuvigil, because of its visual similarities to Norinyl. DMETS recommends implementation of the label and labeling recommendations as outlined above. Additionally, the Division of Drug Marketing, Advertising, and Communications (DDMAC) finds the proprietary name, Nuvigil, acceptable from a promotional perspective. If you have any questions or need clarification, please contact Diane Smith, Project Manager, at 301-796-0538.

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/s/

Loretta Holmes
4/6/2007 09:52:19 AM
DRUG SAFETY OFFICE REVIEWER

Linda Kim-Jung
4/6/2007 10:01:54 AM
DRUG SAFETY OFFICE REVIEWER

Denise Toyer
4/6/2007 12:15:18 PM
DRUG SAFETY OFFICE REVIEWER

Carol Holquist
4/6/2007 12:24:11 PM
DRUG SAFETY OFFICE REVIEWER

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REQUEST FOR CONSULTATION

TO (Office/Division): HFD-420/Director, Division of Medication Errors and Technical Support (DMETS)

FROM (Name, Office/Division, and Phone Number of Requestor): HFD-120/Division of Neurology Products

DATE
3/5/07

IND NO.

NDA NO.
21-875

TYPE OF DOCUMENT

DATE OF DOCUMENT
3/31/05 original NDA submission; 6/30/06 response to approvable ltr

NAME OF DRUG
Nuvigil

PRIORITY CONSIDERATION
Standard

CLASSIFICATION OF DRUG

DESIRED COMPLETION DATE
Action date 3/31/07

NAME OF FIRM: Cephalon

REASON FOR REQUEST

I. GENERAL

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

II. BIOMETRICS

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

III. BIOPHARMACEUTICS

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

IV. DRUG SAFETY

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

V. SCIENTIFIC INVESTIGATIONS

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

COMMENTS / SPECIAL INSTRUCTIONS: Please review the tradename for Nuvigil. This tradename was already reviewed in the 1st cycle and the sponsor was notified on 4/13/06 about tradename concerns.

The following are R. Katz' comments regarding the tradename from 1st cycle memo: "Finally, DMETS has determined that the similarity between Nuvigil 150 mg and Norinyl 1/50 when written is so great that errors are likely to occur, and that, therefore, the name NUVIGIL should not be permitted. I have discussed this with the team. I believe that the marked differences in packaging between the products (and the public's general knowledge of the unique packaging for oral contraceptives), as well as the fact that Norinyl is very rarely prescribed, mitigate these concerns. However, we will ask the sponsor to report any real or potential medication errors as 15 day reports, and to include the possibility of this error in its promotional materials."

We are now in the 2nd review cycle and the tradename needs to be re-evaluated (action date of March 31, 2007). Please contact me if you have any questions. Following is the link to the 3/31/05 original NDA submission: \\CDSesub1\N21875\N 000\2005-03-31. The link for the response to the Approvable Letter is:

\\CDSESUB1\N21875\N_000\2006-06-30. Thanks.

<p>SIGNATURE OF REQUESTOR Tamy Kim, PharmD, Regulatory Project Manager, DNP Food and Drug Administration Phone: 301-796-1125 Email: tamy.kim@fda.hhs.gov</p>	<p>METHOD OF DELIVERY (Check one) <input type="checkbox"/> DFS <input checked="" type="checkbox"/> EMAIL <input type="checkbox"/> MAIL <input type="checkbox"/> HAND</p>
<p>PRINTED NAME AND SIGNATURE OF RECEIVER</p>	<p>PRINTED NAME AND SIGNATURE OF DELIVERER</p>

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Tamy E. Kim
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REQUEST FOR CONSULTATION

TO (Office/Division): Office of Surveillance and Epidemiology,
DDRE

FROM (Name, Office/Division, and Phone Number of Requestor):
Lourdes Villalba (ext 6-1303), HFD-130

DATE
3/1/07

IND NO.

NDA NO.
20-717

TYPE OF DOCUMENT

DATE OF DOCUMENT

NAME OF DRUG
Provigil

PRIORITY CONSIDERATION
Medium

CLASSIFICATION OF DRUG
Wakefulness-promoting
agent

DESIRED COMPLETION DATE
4/15/07

NAME OF FIRM: Cephalon

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

COMMENTS / SPECIAL INSTRUCTIONS: Two potential cases of angioneurotic edema have been identified in the pre-approval database for Nuvigil (armodafinil), suggesting that this adverse reaction could be a problem for modafinil as well. The current Provigil labeling mentions angioedema under the section. Please conduct a search of the AERS database, to identify any cases of angioedema or anaphylaxis that may have occurred with the use of Provigil (modafinil) from approval through present. Please contact Dr. Villalba (6-1303) if you have any questions. (4)

SIGNATURE OF REQUESTOR
Tamy Kim, PharmD, Regulatory Project Manager, DNP
Food and Drug Administration
Phone: 301-796-1125
Email: tamy.kim@fda.hhs.gov

METHOD OF DELIVERY (Check one)
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PRINTED NAME AND SIGNATURE OF DELIVERER

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/s/

Tamy E. Kim

3/2/2007 12:01:09 PM

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Kim, Tamy

From: Kim, Tamy
Sent: Tuesday, January 30, 2007 10:15 AM
To: 'cmurray@cephalon.com'
Subject: RE: NDA 20-717/S-019 & 21-875 Request for Information

Hi Colleen,

As discussed during our telephone conversation today, I am e-mailing you about 2 issues:

1. Drug Interaction Studies:

The drug interaction potential study results between armodafinil and substrates of P-glycoprotein can be submitted now; however, they will not be reviewed until after an action letter is issued. Alternatively, the studies can be submitted after an action letter is issued.

2. Severe Cutaneous Adverse Reactions (SCARs):

As discussed, you will not be able to submit all cases of SCARs observed with modafinil by our requested date of January 31, 2007. Please submit these cases by the end-of-business day February 7, 2007.

Best regards,
Tamy

From: Kim, Tamy
Sent: Friday, January 19, 2007 2:16 PM
To: 'pkirsch@cephalon.com'
Cc: 'cmurray@cephalon.com'
Subject: NDA 20-717/S-019 & 21-875 Request for Information

Dear Paul,

We have the following requests regarding your December 19, 2006 submissions to NDA 20-717/S-019 and NDA 21-875:

Request:

Please submit a listing of all cases of Severe Cutaneous Adverse Reactions observed with modafinil in the EuroSCAR study and the German SCAR registry, regardless of time of onset, including those cases that were not considered to be definitive or probable cases. Include age, gender, day of onset relative to initiation of therapy, duration of cutaneous adverse reaction, treatment received, and outcome.

Please also provide the narratives of these cases, including those that were not considered to be definitive or probable cases.

Please submit this information to both NDAs and email me this information by end-of-business day Wednesday, January 31, 2007. Also, please confirm receipt of this e-mail.

Best regards,
Tamy

Tamy Kim, PharmD
Regulatory Project Manager
Division of Neurology Products
Food and Drug Administration
Phone: 301-796-1125
Email: tamy.kim@fda.hhs.gov

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/s/

Tamy E. Kim

1/30/2007 10:27:35 AM

CSO

Katz concurrence regarding submission of PK studies on 1/29/07.

A. Hughs concurrence of submitting SCARs cases on

1/30/07.

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REQUEST FOR CONSULTATION

TO (Office/Division): Office of Surveillance and Epidemiology

FROM (Name, Office/Division, and Phone Number of Requestor): Tamy Kim,
Division of Neurology Products, x61125

DATE
1/18/07

IND NO.

NDA NO.
21-875

TYPE OF DOCUMENT
Amendment to Pending
Application - Response to
Request for Information

DATE OF DOCUMENT
12/19/06

NAME OF DRUG
armodafinil

PRIORITY CONSIDERATION
high

CLASSIFICATION OF DRUG

DESIRED COMPLETION DATE
Mtg scheduled for 2/20/07

NAME OF FIRM: Cephalon

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 checked="" 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

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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 |

IV. DRUG SAFETY

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|---|--|
| <input type="checkbox"/> PHASE 4 SURVEILLANCE/EPIDEMIOLOGY PROTOCOL | <input type="checkbox"/> REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY |
| <input checked="" 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 type="checkbox"/> CLINICAL | <input type="checkbox"/> NONCLINICAL |
|-----------------------------------|--------------------------------------|

COMMENTS / SPECIAL INSTRUCTIONS: Please review and comment on the information and arguments presented in sections 4, 5, 6, 7 as it relates to modafinil and the risk of SJS. Please also review and comment on any conclusions, appendices, and references that are associated with these sections. In addition, please provide an update on the AERs search for serious skins reactions (last review dated May 9, 2006) and provide modafinil usage data by age. Note: The 12/19/06 submission has already been provided to OSE reviewers (Flowers and LaGrenada) during a meeting dated 1/10/07. Thanks.

SIGNATURE OF REQUESTOR
Tamy Kim, PharmD, Regulatory Project Manager, DNP
Food and Drug Administration
Phone: 301-796-1125
Email: tamy.kim@fda.hhs.gov

METHOD OF DELIVERY (Check one)
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/s/

Tamy E. Kim
1/18/2007 02:20:36 PM

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REQUEST FOR CONSULTATION

TO (Office/Division): **DIVISION OF DERMATOLOGY AND DENTAL PRODUCTS - Specific request for Dermatology consultation**

FROM (Name, Office/Division, and Phone Number of Requestor): **Tamy Kim, Division of Neurology Products, x61125**

DATE
1/18/07

IND NO.

NDA NO.
21-875

TYPE OF DOCUMENT
Amendment to Pending Application - Response to Request for Information

DATE OF DOCUMENT
12/19/06

NAME OF DRUG
armodafinil

PRIORITY CONSIDERATION
high

CLASSIFICATION OF DRUG

DESIRED COMPLETION DATE
Mtg Scheduled for 2/27/07

NAME OF FIRM: **Cephalon**

REASON FOR REQUEST

I. GENERAL

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

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

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

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

- | | |
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| <input type="checkbox"/> CLINICAL | <input type="checkbox"/> NONCLINICAL |
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COMMENTS / SPECIAL INSTRUCTIONS: Please review and comment on the information and arguments presented in sections 2.1 (Expert Case Review and Discussion) and 3.2 (Chemical Rationale Disassociating Modafinil From Sulfonamides/Sulfonylanilines...) as it relates to modafinil and the risk of SJS. Please also review and comment on any conclusions, appendices, and references that are associated with these sections. Note: The 12/19/06 submission has already been provided to DDDP (Dr. Luke) during a meeting dated 1/10/07. Thanks.

SIGNATURE OF REQUESTOR
Tamy Kim, PharmD, Regulatory Project Manager, DNP
Phone: 301-796-1125
Email: tamy.kim@fda.hhs.gov

METHOD OF DELIVERY (Check one)
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/s/

Tamy E. Kim
1/18/2007 02:02:32 PM

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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-875

Cephalon, Inc.
Attention: Paul M. Kirsch
Senior Director, Regulatory Affairs
41 Moores Road
P.O. Box 4011
Frazer, PA 19355

Dear Mr. Kirsch:

Please refer to your New Drug Application (NDA) dated March 31, 2005, received March 31, 2005, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Nuvigil™ (armodafinil) Tablets 50 mg, 100 mg, 150 mg, and 250 mg.

We acknowledge receipt of your submission dated June 30, 2006, and received June 30, 2006.

We consider your June 30, 2006 submission to be a complete, class 2 response to our April 28, 2006 action letter. Therefore, the user fee goal date is December 31, 2006.

If you have any questions, please call me at (301) 796-1160.

Sincerely,

{See appended electronic signature page}

Jacqueline H. Ware, Pharm.D., CDR USPHS
Division of Neurology Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

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/s/

Jackie Ware

8/9/2006 04:32:02 PM

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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-875

Cephalon, Inc.
Attention: Paul M. Kirsch
Senior Director, Regulatory Affairs
41 Moores Road
P.O. Box 4011
Frazer, PA 19355

Dear Mr. Kirsch:

Please refer to your March 31, 2005 New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Nuvigil (armodafinil) Tablets, 50 mg, 100 mg, 150 mg, and 250 mg.

On October 31, 2005, we received your October 31, 2005 major amendment to this application. The receipt date is within 3 months of the user fee goal date. Therefore, we are extending the goal date by three months to provide time for a full review of the submission. The extended user fee goal date is April 30, 2006.

If you have any questions, please call me at (301) 796-1160.

Sincerely,

{See appended electronic signature page}

Jacqueline H. Ware, Pharm.D., CDR-USPHS
Senior Regulatory Project Manager
Division of Neurology Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

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/s/

Jackie Ware

1/30/2006 03:41:50 PM

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Ware, Jacqueline H

From: Ware, Jacqueline H
Sent: Tuesday, December 27, 2005 1:06 PM
To: 'Murray, Colleen'; 'Kirsch, Paul'
Cc: Ware, Jacqueline H
Subject: FDA Request for Information re: NDA 21-875

Dear Paul and Colleen,

Below and attached are requests from the Division's CMC and pharmacology/toxicology groups related to their ongoing review of the above Nuvigil application. Please submit your responses to these requests in electronic archival format as an amendment to NDA 21-875. 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.

CMC

b(4)

Pharmacology/Toxicology

- The pharmacology/toxicology statistical reviewer responsible for the carcinogenicity-study review of your TgAC transgenic mice study requests that you recreate the weekly count data of skin papillomas of individual animals as a SAS dataset in the format described in the attached WORD file. If you have questions regarding this format, please contact the reviewer, Karl Lin (link@cder.fda.gov; 301-796-0943), directly.



TgAC Data
Format.doc (1 MB)

Thank you,

Jackie Ware

*Jacqueline H. Ware, Pharm.D., CDR-USPHS
Senior Regulatory Project Manager
Division of Neurology Products, WO22 Rm. 4350
Center for Drug Evaluation and Research, FDA
301-796-1160 (phone)
301-796-9842 (fax)
warej@cder.fda.gov (email)*

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/s/

Jackie Ware
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CSO

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REQUEST FOR CONSULTATION

TO (Division/Office):

**Director, Division of Medication Errors and
Technical Support (DMETS), HFD-420
WO 22 Rm. 4421**

FROM:

**Division of Neurology Products (DNP), HFD-120
WO 22 Rm. 4350**

DATE
November 29, 2005

IND NO.

NDA NO.
21-875

TYPE OF DOCUMENT
NDA Amendment-proprietary
name reconsideration request

DATE OF DOCUMENT
October 28, 2005

NAME OF DRUG
Nuvigil (armodafinil) tablets

PRIORITY CONSIDERATION
Standard

CLASSIFICATION OF DRUG
1

DESIRED COMPLETION DATE
March 1, 2006
PDUFA goal date: April 20, 2006

NAME OF FIRM: Cephalon

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

II. BIOMETRICS

STATISTICAL EVALUATION BRANCH

STATISTICAL APPLICATION BRANCH

- TYPE A OR B NDA REVIEW
- END OF PHASE II MEETING
- CONTROLLED STUDIES
- PROTOCOL REVIEW
- OTHER (SPECIFY BELOW):

- CHEMISTRY REVIEW
- PHARMACOLOGY
- BIOPHARMACEUTICS
- OTHER (SPECIFY BELOW):

III. BIOPHARMACEUTICS

- DISSOLUTION
- BIOAVAILABILITY STUDIES
- PHASE IV STUDIES

- DEFICIENCY LETTER RESPONSE
- PROTOCOL-BIOPHARMACEUTICS
- IN-VIVO WAIVER REQUEST

IV. DRUG EXPERIENCE

- PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL
- DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES
- CASE REPORTS OF SPECIFIC REACTIONS (List below)
- COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP

- REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY
- SUMMARY OF ADVERSE EXPERIENCE
- POISON RISK ANALYSIS

V. SCIENTIFIC INVESTIGATIONS

CLINICAL

PRECLINICAL

COMMENTS, CONCERNS, and/or SPECIAL INSTRUCTIONS: Please review and comment on Cephalon's 10/28/05 request for the Agency to reconsider their proposed tradename, Nuvigil, for armodafinil tablets (paper copy will be delivered). On August 5, 2005, DMETS issued a review stating that DMETS did not recommend the use of the proprietary name, Nuvigil. The Division conveyed this recommendation to the firm via phone on August 24, 2005. As such, the firm has submitted this request for reconsideration.

If additional information regarding this consult request is needed, please contact Jackie Ware, Project Manager, at 301-796-1160 or warej@cder.fda.gov.

SIGNATURE OF REQUESTER
Jackie Ware, Pharm.D., Regulatory Project Manager

METHOD OF DELIVERY (Check one)
 MAIL HAND

SIGNATURE OF RECEIVER

SIGNATURE OF DELIVERER

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/s/

Jackie Ware

11/29/2005 06:20:00 PM

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MEMORANDUM

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

DATE: August 23, 2005

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

VIA: Courtney Calder, Pharm.D., Regulatory Project Manager
Division of Neuropharmacological Drug Products
HFD-120

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

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

SUBJECT: DSRCs Review of Patient Labeling for Nuvigil (armodafinil)
Tablets, NDA 21-875

Background and Summary

The attached patient labeling reflect our recommended revisions for Nuvigil (armodafinil) Tablets, NDA 21-875. We have simplified the wording, made it consistent with the PI, and removed unnecessary information. These revisions are based on draft labeling submitted by the sponsor on March 31, 2005. Patient information should always be consistent with the prescribing information. All future changes to the PI should also be reflected in the PPI.

Comments and Recommendations

1. The submitted PPI is identical to that of the approved PPI for Provigil (monofadil), with exception to the product name. PPIs should be consistent with the information contained in their individual PIs, not another product's PPI, unless of course the products present identical information in their PIs.
2. The PI, PRECAUTIONS section, Information for Patients subsection, states, "Patients should be informed of the availability of a patient information leaflet, and they should be instructed to read the leaflet prior to taking NUVIGIL." The PPI for Nuvigil is voluntary and is not

required to be distributed with prescriptions and refills. A patient is unlikely to receive the Nuvigil PPI unless it is packaged with the product in unit-of-use packaging. The sponsor should explain how a patient is to obtain the PPI or delete the statement from the PI.

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

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 Trade Secret / Confidential (b4)

✓ Draft Labeling (b4)

 Draft Labeling (b5)

 Deliberative Process (b5)

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/s/

Jeanine Best
8/23/2005 10:22:09 AM
DRUG SAFETY OFFICE REVIEWER

Toni Piazza Hepp
8/24/2005 09:00:56 AM
DRUG SAFETY OFFICE REVIEWER
for Gerald Dal Pan

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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

FILING COMMUNICATION

NDA 21-875

Cephalon, Inc
Attention: Paul M. Kirsch
Senior Director, Regulatory Affairs
41 Moores Road
P.O. Box 4011
Frazer, PA 19355

Dear Mr. Kirsch:

Please refer to your March 31, 2005 new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Nuvigil (armodafinil) tablets.

We have completed our filing review and have determined that your application is sufficiently complete to permit a substantive review. Therefore, this application will be filed under section 505(b) of the Act on May 30, 2005 in accordance with 21 CFR 314.101(a).

In our filing review, we have identified the following potential review issues:

1. As relayed in our teleconference on May 23, 2005 there is insufficient information regarding Nuvigil's drug abuse potential. The review division has determined that this is not a filing issue for Nuvigil (armodafinil) tablets. However, this information is still required and should be submitted in a timely manner. Please submit information pertinent to drug abuse liability and an argument for the proposed scheduling. You should be aware that we do not consider the assessment of abuse potential of the racemate, which by definition is a mixture of two components, to be completely transferable to individual enantiomers. You were also informed that you may need to conduct additional studies, depending on what information already exists. The Controlled Substance Staff would be happy to discuss this further with you. The below points are comments from the Controlled Substance Staff. Hopefully, this will guide you in submitting the amendment.
 - NDA 21-875 submitted on March 31, 2005 lacks information on the topics of abuse liability studies and a proposal for Scheduling under the Controlled Substances Act (CSA). Such requirements by the Agency for a drug that has a potential for abuse are not discretionary and clearly stated in 21 CFR, Section 314.50 (d)(5)(vii). In addition, the information must be submitted in a comprehensive and organized fashion so that it can be reviewed.

- We are unable to locate in this NDA submission information on the descriptions of any studies related to overdose which is required by the Agency for a drug, such as armodafinil, that has a potential for abuse [Also stated in 21CFR, Section 314.50 (d)(5)(vii)].
- You have not provided any information regarding the comparison of the pharmacological effects/potencies of modafinil and armodafinil since differences in pharmacological activities of racemic isomers may exist. For example, each isomer of the enantiomeric pairs of dextropropoxyphene and levopropoxyphene, and levorphanol and dextrorphan, are pharmacologically different with regard to abuse potential.
- In addition, studies specifically evaluating overdose, dependence, rebound phenomena, withdrawal and abuse may need to be conducted with armodafinil since these adverse effects are known to be associated with the racemic compound modafinil. You have stated in the Clinical Overview that such studies have not been conducted for armodafinil. You should submit a proposal whereby the relative risks and benefits of Nuvigil can be assessed.

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.

We also request that you submit the following information:

Biopharmaceutics:

1. Please provide comparative dissolution for 50 mg capsule vs. 50 mg clinical formulation to bridge these two formulations. This is important since capsule formulation was used in Studies 101, 102, and 103, and data from these three studies were used for determining the dosing regimen for the pivotal Phase 3 trials. Individual data needs to be submitted.
2. Please provide individual data for dissolution profiles of each TBM strength in all the media tested.
3. Please specify the content of high-fat food for the food-effect study.
4. Please provide electronically NONMEM control streams, output files, and datasets to support the population PK and PK/PD analysis. If S-Plus was used, please submit S-Plus scripts and datasets.
5. Please provide electronic datasets as SAS transport files (.XPT) for two Phase 1 PK studies (101,102), and three Phase 1 DDI studies (1021, 1022, 1025).

Please respond to the above requests for additional 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.

If you have any questions, call Courtney Calder, Pharm.D., Regulatory Project Manager, at (301) 594-5528.

Sincerely,

{See appended electronic signature page}

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

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/s/

Russell Katz
6/1/05 12:51:34 PM

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MEMORANDUM OF TELECON

DATE: May 23, 2005

APPLICATION NUMBER: NDA 21-875, Nuvigil (armodafinil) tablets

BETWEEN:

Name: Colleen Murray, Senior Manager, Regulatory Affairs, Cephaon, Inc.
Paul Kirsch, Senior Director, Regulatory Affaris, Cephalon, Inc.
Phone: 610-738-6122
Representing: Cephalon, Inc.

AND

Name: Courtney Calder, Pharm.D., Project Manager
John Feeney, III, MD, Team Leader
Norm Hershkowitz, MD, Medical Officer
Division of Neuropharmacological Drug Products, HFD-120

SUBJECT: NDA review issues

There is insufficient information regarding **Nuvigil's drug abuse potential**. This is not a filing issue for Nuvigil. However, this information is still required and should be submitted in timely manner. Information pertinent to drug abuse and overdose and an argument for the proposed scheduling should be submitted as an amendment to the NDA. The assessment of abuse potential of the racemate is not completely transferable to individual enantiomers. Additional studies may need to be conducted, depending on what information already exists. The Controlled Substance Staff will be happy to discuss this further with the sponsor.

John Feeney, III, MD
Team Leader

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/s/

Courtney Calder
5/25/05 01:25:12 PM
CSO

John Feeney
5/25/05 03:26:44 PM
MEDICAL OFFICER
concur

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MEMORANDUM**DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH**

Date: May 16, 2005

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

Through: Deborah B. Leiderman, M.D., Director
Michael Klein, Ph.D., Team Leader
Controlled Substance Staff (HFD-009)

From: Lin-Whei Chuang, M.S.
Pharmacologist, Controlled Substance Staff (HFD-009)

Subject: Fileability Determination of NDA 21-875
Nuvigil (Armodafinil, R-enantiomer of modafinil),
50, 100, 150, 250 mg Tablets
Sponsor: Cephalon

Comments and Recommendation:

The Controlled Substance Staff identifies the following major filing deficiencies in NDA 21-875 for Nuvugil sponsored by Cephalon:

1. NDA 21-875 submitted on March 31, 2005 lacks information on the topics of abuse liability studies and a proposal for Scheduling under the Controlled Substances Act (CSA). Such requirements by the Agency for a drug that has a potential for abuse are clearly stated in 21 CFR, Section 314.50 (d)(5)(vii). In addition, the information must be submitted in a comprehensive and organized fashion so that it can be reviewed.
2. The CSS reviewer is unable to locate in this NDA submission information on the descriptions of any studies related to overdose which is required by the Agency for a drug, such as armodafinil, that has a potential for abuse [Also stated in 21 CFR, Section 314.50 (d)(5)(vii)].
3. The Sponsor has not provided any information regarding the comparison of the pharmacological effects/potencies of modafinil and armodafinil since differences in pharmacological activities of racemic isomers may exist. For example, each isomer of the enantiomeric pairs of dextropropoxyphene and levopropoxyphene,

and levorphanol and dextrorphan, are pharmacologically different with regard to abuse potential.

4. In addition, studies specifically evaluating overdose, dependence, rebound phenomena, withdrawal and abuse should be conducted with armodafinil since these adverse effects are known to be associated with the racemic compound modafinil. The Sponsor has stated in its Clinical Overview that such studies have not been conducted for armodafinil. Therefore, the relative risks and benefits of Nuvigil can not be assessed.

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/s/

Lin Whei L. Chuang
5/17/05 10:19:48 AM
BIOPHARMACEUTICS

Michael Klein
5/17/05 10:23:20 AM
CHEMIST

Deborah Leiderman
5/17/05 12:33:16 PM
MEDICAL OFFICER

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REQUEST FOR CONSULTATION

TO (Division/Office):
**Director, Division of Surveillance, Research and
Communication Support (DSRCS), HFD-410, PKLN Rm. 15B-23**

FROM: **John Feeney III, MD, Team Leader
Director, Division of Neuropharmacological Drug Products (DNDP),
HFD-120, WQGN Rm. 4028**

DATE April 5, 2005	IND NO.	NDA NO. 21-875	TYPE OF DOCUMENT PI	DATE OF DOCUMENT March 31, 2005
NAME OF DRUG Nuvigil (armodafinil)		PRIORITY CONSIDERATION	CLASSIFICATION OF DRUG	DESIRED COMPLETION DATE Primary reviewer due date is 11/22/05 (PDUFA due date: January 31, 2006)

NAME OF FIRM:

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 II MEETING | <input type="checkbox"/> FINAL PRINTED LABELING |
| <input type="checkbox"/> NEW CORRESPONDENCE | <input type="checkbox"/> RESUBMISSION | <input type="checkbox"/> LABELING REVISION |
| <input type="checkbox"/> DRUG ADVERTISING | <input type="checkbox"/> SAFETY/EFFICACY | <input type="checkbox"/> ORIGINAL NEW CORRESPONDENCE |
| <input type="checkbox"/> ADVERSE REACTION REPORT | <input type="checkbox"/> PAPER NDA | <input type="checkbox"/> FORMULATIVE REVIEW |
| <input type="checkbox"/> MANUFACTURING CHANGE/ADDITION | <input type="checkbox"/> CONTROL SUPPLEMENT | <input checked="" type="checkbox"/> OTHER (SPECIFY BELOW): Pharmacy & Caregiver
Instruction Review |
| <input type="checkbox"/> MEETING PLANNED BY | | |

II. BIOMETRICS

STATISTICAL EVALUATION BRANCH	STATISTICAL APPLICATION BRANCH
<input type="checkbox"/> TYPE A OR B NDA REVIEW <input type="checkbox"/> END OF PHASE II MEETING <input type="checkbox"/> CONTROLLED STUDIES <input type="checkbox"/> PROTOCOL REVIEW <input type="checkbox"/> OTHER (SPECIFY BELOW):	<input type="checkbox"/> CHEMISTRY REVIEW <input type="checkbox"/> PHARMACOLOGY <input type="checkbox"/> BIOPHARMACEUTICS <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 IV STUDIES | <input type="checkbox"/> IN-VIVO WAIVER REQUEST |

IV. DRUG EXPERIENCE

- | | |
|--|--|
| <input type="checkbox"/> PHASE IV 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 type="checkbox"/> CLINICAL | <input type="checkbox"/> PRECLINICAL |
|-----------------------------------|--------------------------------------|

COMMENTS, CONCERNS, and/or SPECIAL INSTRUCTIONS: This NDA for Nuvigil is located in the EDR:

\\CDSESUB1\N21875\N_000\2005-03-31

Please review the Patient Information leaflet. Let me know if you have any questions.

Thank you, Courtney

SIGNATURE OF REQUESTER Courtney Calder, Pharm.D. Regulatory Project Manager 301-594-5315 calderc@cdcr.fda.gov	METHOD OF DELIVERY (Check one) <input type="checkbox"/> MAIL <input type="checkbox"/> HAND
SIGNATURE OF RECEIVER	SIGNATURE OF DELIVERER

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/s/

Courtney Calder
4/5/05 05:23:51 PM
signed for Russell Katz, MD

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REQUEST FOR CONSULTATION

TO (Division/Office):

**Director, Division of Medication Errors and
Technical Support (DMETS), HFD-420
PKLN Rm. 6-34**

FROM:

HFD-120/ Division of Neuropharmacological Drug Products

DATE
April 5, 2005

IND NO.

NDA NO.
21-875

TYPE OF DOCUMENT

DATE OF DOCUMENT
March 31, 2005

NAME OF DRUG

Nuvigil (armodafinil)

PRIORITY CONSIDERATION

standard

CLASSIFICATION OF DRUG

DESIRED COMPLETION DATE

The Goal date is January 31, 2006.
The Primary Reviewer Duedate is 11/22/05

NAME OF FIRM:

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

II. BIOMETRICS

STATISTICAL EVALUATION BRANCH

STATISTICAL APPLICATION BRANCH

- TYPE A OR B NDA REVIEW
- END OF PHASE II MEETING
- CONTROLLED STUDIES
- PROTOCOL REVIEW
- OTHER (SPECIFY BELOW):

- CHEMISTRY REVIEW
- PHARMACOLOGY
- BIOPHARMACEUTICS
- OTHER (SPECIFY BELOW):

III. BIOPHARMACEUTICS

- DISSOLUTION
- BIOAVAILABILITY STUDIES
- PHASE IV STUDIES

- DEFICIENCY LETTER RESPONSE
- PROTOCOL-BIOPHARMACEUTICS
- IN-VIVO WAIVER REQUEST

IV. DRUG EXPERIENCE

- PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL
- DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES
- CASE REPORTS OF SPECIFIC REACTIONS (List below)
- COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP

- REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY
- SUMMARY OF ADVERSE EXPERIENCE
- POISON RISK ANALYSIS

V. SCIENTIFIC INVESTIGATIONS

CLINICAL

PRECLINICAL

COMMENTS, CONCERNS, and/or SPECIAL INSTRUCTIONS:

This NDA for Nuvigil is located in the EDR:

\\CDSESUB1\N21875\N_000\2005-03-31

Please review the trade name. The NDA includes a proprietary name assessment and labeling. Thank you, Courtney

PDUFA DATE: January 31, 2005

SIGNATURE OF REQUESTER
Courtney Calder, Pharm.D.
Regulatory Project Manager
301-594-5315
calderc@cdcr.fda.gov

METHOD OF DELIVERY (Check one)
 MAIL HAND

SIGNATURE OF RECEIVER

SIGNATURE OF DELIVERER

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/s/

Courtney Calder
4/5/05 05:14:30 PM
signed for Russell Katz, MD

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REQUEST FOR CONSULTATION

TO (Division/Office): Deborah Liederman, M.D., Director
HFD-009/Controlled Substances Staff
Attention: Corinne Moody

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

DATE:
April 5, 2005

IND NO.:

NDA NO.:
21-875

TYPE OF DOCUMENT :

Date of Submission:
March 31, 2005

NAME OF DRUG:
Nuvigil (armodafinil)

PRIORITY CONSIDERATION:

CLASSIFICATION OF DRUG:

DESIRED COMPLETION DATE:
The filing mtg. is May 18,
from 3:30-4:30. The goal
date is Jan. 31, 2006.

COMMENTS/SPECIAL INSTRUCTIONS:

Please review this NDA for Nuvigil, and provide an abuse liability assessment. It is located in the EDR:

\\CDSESUB1\N21875\N_000\2005-03-31

Thank you, Courtney

SIGNATURE OF REQUESTER:

Courtney Calder, Pharm.D.
Regulatory Project Manager
301-594-5315
calderc@cdcr.fda.gov

METHOD OF DELIVERY (Check one):

MAIL

HAND

SIGNATURE OF RECEIVER:

SIGNATURE OF DELIVERER:

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/s/

Courtney Calder
4/5/05 04:43:47 PM
signed for Russell Katz, MD

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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-875

Cephalon, Inc.
Attention: Paul M. Kirsch
Senior Director, Regulatory Affairs
145 Brandywine Parkway
West Chester, PA 19380

Dear Mr. Kirsch:

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

Name of Drug Product: Nuvigil (armodafinil) 50mg, 100mg, 150mg, and 250mg tablets

Review Priority Classification: Standard (S)

Date of Application: March 31, 2005

Date of Receipt: March 31, 2005

Our Reference Number: NDA 21-875

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 May 30, 2005 in accordance with 21 CFR 314.101(a). If the application is filed, the user fee goal date will be January 31, 2006.

Under 21 CFR 314.102(c), you may request a meeting with this Division (to be held approximately 90 days from the above receipt date) for a brief report on the status of the review but not on the ultimate approvability of the application. Alternatively, you may choose to receive a report by telephone.

All applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred. We note that you have not fulfilled the requirement. We acknowledge receipt of your request for waivers and a deferral of pediatric studies for this application. Once the application has been filed, we will notify you whether we have deferred and/or waived the pediatric study requirement for this application.

NDA 21-875

Page 2

Please cite the NDA number listed above at the top of the first page of any communications concerning this application. Address all communications concerning this NDA as follows:

U.S. Postal Service:

Center for Drug Evaluation and Research
Division of Neuropharmacological Drug Products, HFD-120
Attention: Division Document Room, 4008
5600 Fishers Lane
Rockville, Maryland 20857

Courier/Overnight Mail:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Neuropharmacological, HFD-120
Attention: Document Room 4008
1451 Rockville Pike
Rockville, Maryland 20852

If you have any questions, call Courtney Calder, Pharm.D., Regulatory Project Manager, at (301) 594-5528.

Sincerely,

{See appended electronic signature page}

Robbin Nighswander, RPh, MS
Project Manager Team Leader
Division of Neuropharmacological Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

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/s/

Paul David

4/5/05 01:47:11 PM

Signed for Robbin Nighswander

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REQUEST FOR CONSULTATION

TO (Division/Office):

**Director, Division of Medication Errors and
Technical Support (DMETS), HFD-420
PKLN Rm. 6-34**

FROM:

HFD-120/ Division of Neuropharmacological Drug Products

DATE
April 5, 2005

IND NO.

NDA NO.
21-875

TYPE OF DOCUMENT

DATE OF DOCUMENT
March 31, 2005

NAME OF DRUG

Nuvigil (armodafinil)

PRIORITY CONSIDERATION

standard

CLASSIFICATION OF DRUG

DESIRED COMPLETION DATE

The Goal date is January 31, 2005.
The Primary Reviewer Duedate is 11/22/04

NAME OF FIRM:

REASON FOR REQUEST

I. GENERAL

- | | | |
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| <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 II MEETING | <input type="checkbox"/> FINAL PRINTED LABELING |
| <input type="checkbox"/> NEW CORRESPONDENCE | <input type="checkbox"/> RESUBMISSION | <input type="checkbox"/> LABELING REVISION |
| <input type="checkbox"/> DRUG ADVERTISING | <input type="checkbox"/> SAFETY/EFFICACY | <input type="checkbox"/> ORIGINAL NEW CORRESPONDENCE |
| <input type="checkbox"/> ADVERSE REACTION REPORT | <input type="checkbox"/> PAPER NDA | <input type="checkbox"/> FORMULATIVE REVIEW |
| <input type="checkbox"/> MANUFACTURING CHANGE/ADDITION | <input type="checkbox"/> CONTROL SUPPLEMENT | <input checked="" type="checkbox"/> OTHER (SPECIFY BELOW): Trade name review |
| <input type="checkbox"/> MEETING PLANNED BY | | |

II. BIOMETRICS

STATISTICAL EVALUATION BRANCH

STATISTICAL APPLICATION BRANCH

- TYPE A OR B NDA REVIEW
 END OF PHASE II MEETING
 CONTROLLED STUDIES
 PROTOCOL REVIEW
 OTHER (SPECIFY BELOW):

- CHEMISTRY REVIEW
 PHARMACOLOGY
 BIOPHARMACEUTICS
 OTHER (SPECIFY BELOW):

III. BIOPHARMACEUTICS

- DISSOLUTION
 BIOAVAILABILITY STUDIES
 PHASE IV STUDIES

- DEFICIENCY LETTER RESPONSE
 PROTOCOL-BIOPHARMACEUTICS
 IN-VIVO WAIVER REQUEST

IV. DRUG EXPERIENCE

- PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL
 DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES
 CASE REPORTS OF SPECIFIC REACTIONS (List below)
 COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP

- REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY
 SUMMARY OF ADVERSE EXPERIENCE
 POISON RISK ANALYSIS

V. SCIENTIFIC INVESTIGATIONS

CLINICAL

PRECLINICAL

COMMENTS, CONCERNS, and/or SPECIAL INSTRUCTIONS:

This NDA for Nuvigil is located in the EDR:

\\CDSESUB1\N21875\N_000\2005-03-31

Please review the trade name. The NDA includes a proprietary name assessment and labeling. Thank you, Courtney

PDUFA DATE: January 31, 2005

SIGNATURE OF REQUESTER
Courtney Calder, Pharm.D.
Regulatory Project Manager
301-594-5315
calderc@cder.fda.gov

METHOD OF DELIVERY (Check one)
 MAIL HAND

SIGNATURE OF RECEIVER

SIGNATURE OF DELIVERER

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Courtney Calder
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