

CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:
NDA 20-717/S-006

Name: Provigil Tablets

Generic Name: modafinil

Sponsor: Cephalon, Inc.

Approval Date: 04/16/2003

CENTER FOR DRUG EVALUATION AND RESEARCH

**APPLICATION NUMBER:
NDA 20-717/S-006**

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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:
NDA 20-717/S-006

APPROVAL LETTER



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20-717/S-006

Cephalon, Inc.
Attention: Kenneth L. White, Pharm.D.
Vice President, Regulatory Affairs
145 Brandywine Parkway
West Chester, PA 19380-4245

Dear Dr. White:

Please refer to your supplemental new drug application dated March 21, 2003, received March 24, 2003, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Provigil (modafinil), 100 and 200 mg tablets.

We acknowledge receipt of your submission dated March 21, 2003.

Your submission of March 21, 2003 constituted a complete response to our February 21, 2003 action letter.

This supplemental new drug application provides for revision of the blister unit and carton labeling.

We completed our review of this application, as amended. This application is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text.

The final printed labeling (FPL) must be identical to the submitted labeling (immediate container and carton labels submitted March 21, 2003).

Please submit the FPL electronically according to the guidance for industry titled Providing Regulatory Submissions in Electronic Format – NDA. Alternatively, you may submit 20 paper copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FPL for approved supplement NDA 20717/s-006." Approval of this submission by FDA is not required before the labeling is used.

If you issue a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20857

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

NDA 20-717/S-006
Page 2

If you have any questions, call Anna Homonnay, Regulatory Project Manager, at (301) 594-5535.

Sincerely,

{See appended electronic signature page}

Maryla Guzewska, Ph.D.
Chemistry Team Leader, Neurology Drugs for the
Division of Neuropharmacological Drug Products,
(HFD-120)
DNDC I, Office of New Drug Chemistry
Center for Drug Evaluation and Research

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/s/

Maryla Guzewska
4/16/03 07:21:04 AM

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 20-717/S-006

APPROVABLE LETTER



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20-717/S-006

Cephalon, Inc.
Attention: Kenneth L. White, Pharm.D.
Vice President, Regulatory Affairs
145 Brandywine Parkway
West Chester, PA 19380-4245

Dear Dr. White:

Please refer to your supplemental new drug application dated October 18, 2002, received October 21, 2002, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Provigil (modafinil), 100 and 200 mg tablets.

We acknowledge receipt of your submission dated October 18, 2002.

This supplemental new drug application provides for:

1. An additional packaging configuration to be used for physician samples of Provigil Tablets
2. A new site for blister packaging

We completed our review of this application, as amended, and it is approvable. Before this application may be approved, however, it will be necessary for you to address the following:

1. A statement "Manufactured for Cephalon, Inc., West Chester, PA 19380" should be added to the labels for blister units,
2. The strength of the drug (100 mg Tablets) should be made more prominent on both blister units and cartons,
3. The size of the sign indicating the Controlled Drug should be enlarged.

Within 10 days after the date of this letter, you are required to amend this application, notify us of your intent to file an amendment or follow one of your other options under 21 CFR 314.110. If you do not follow one of these options, we will consider your lack of response a request to withdraw the application under 21 CFR 314.65. Any amendment should respond to all the deficiencies listed. We will not process a partial reply as a major amendment nor will the review clock be reactivated until all deficiencies have been addressed.

If you have any questions, call Anna Homonnay, Regulatory Project Manager, at (301) 594-5535.

Sincerely,

{See appended electronic signature page}

Maryla Guzewska, Ph.D.
Chemistry Team Leader, Neurology Drugs for the
Division of Neuropharmacological Drug Products,
(HFD-120)
DNDC I, Office of New Drug Chemistry
Center for Drug Evaluation and Research

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Maryla Guzewska
2/21/03 01:50:25 PM

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:
NDA 20-717/S-006

CHEMISTRY REVIEW(S)

**CHEMIST'S REVIEW
OF SUPPLEMENT**

ORGANIZATION: HFD-120
NDA NUMBER: 20-717
SUPPLEMENT NUMBER: SCP-006

LETTER DATE 18-OCT-02
STAMP DATE 21-OCT-02

AMENDMENTS:
LETTER DATES N/A
STAMP DATES N/A

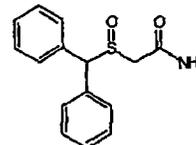
RECEIVED BY CHEMIST: 12-DEC-02

APPLICANT NAME AND ADDRESS: Cephalon, Inc.
145 Brandywine Parkway
West Chester, PA 19380-4245

NAME OF DRUG: Provigil®

NONPROPRIETARY NAME: Modafinil

CHEMICAL NAME / STRUCTURE: 2-[(Diphenylmethyl)sulfinyl]acetamide



DOSAGE FORM(S): Tablets
POTENCY(IES): 100 mg, 200 mg
PHARMACOLOGICAL CATEGORY: Narcolepsy
SPECIAL PRODUCTS: (YES) (NO)
HOW DISPENSED: (Rx) (OTC)
RECORDS / REPORTS CURRENT: (YES) (NO)
RELATED IND / NDA / DMF(s): DMF # DMF # (amendment 92)

SUPPLEMENT PROVIDES FOR: Additional packaging configuration for physician samples. In addition, a new site for blister packaging is added.

COMMENTS: This is a PA supplement for a packaging change. The sponsor describes the new blister sample package, which is a film laminate and a push-through foil backing. Currently approved container closure system is bottles with cap. Accelerated and real-time stability data are provided for similar blister packages, which are currently approved in Europe. The configuration and packaging materials for new blister packages are identical to European but the volume of the blister cavity is different: 8% larger cavity for 100 mg tablets and 25% smaller – for 200 mg tablets. Sponsor is relying on the stability profile of the drug product generated in bottles and European blister packages, and is committing to place on stability first three batches of the drug product in the new blister packs, and one batch per year thereafter. The additional packaging site was inspected and received an Acceptable recommendation from the Office of Compliance (see EER in CMC Review Notes). Two referenced DMFs for the packaging materials were reviewed and found to be adequate. Minor deficiencies have been found in the labeling of the blister unit (see Review Notes).

CONCLUSIONS AND RECOMMENDATIONS: Recommend Approvable.

<u>REVIEWER NAME</u>	<u>SIGNATURE</u>	<u>DATE COMPLETED</u>
Lyudmila N. Soldatova, Ph.D.		February 21, 2003

cc: Orig: NDA 20-717
HFD-120/Div. File
HFD-120/AHomonnay/LSoldatova /MGuzewska
Filename: 20717scp006.doc
INIT: MGuzewska

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Chemistry Review #1

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/s/

Lyudmila Soldatova
2/21/03 01:29:09 PM
CHEMIST

Maryla Guzewska
2/21/03 01:48:41 PM
CHEMIST

**CHEMIST'S REVIEW
OF SUPPLEMENT**

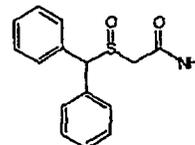
ORGANIZATION: HFD-120
NDA NUMBER: 20-717
SUPPLEMENT NUMBER: SCP-006

LETTER DATE 18-OCT -02
STAMP DATE 21-OCT-02

AMENDMENTS:
LETTER DATE 21-MAR-03
STAMP DATE 24-MAR-03

RECEIVED BY CHEMIST: 25-MAR-03

APPLICANT NAME AND ADDRESS: Cephalon, Inc.
145 Brandywine Parkway
West Chester, PA 19380-4245
NAME OF DRUG: Provigil®
NONPROPRIETARY NAME: Modafinil
CHEMICAL NAME / STRUCTURE: 2-[(Diphenylmethyl)sulfinyl]acetamide



DOSAGE FORM(S): Tablets
POTENCY(IES): 100 mg, 200 mg
PHARMACOLOGICAL CATEGORY: Narcolepsy
SPECIAL PRODUCTS: (YES) XX (NO)
HOW DISPENSED: XX (Rx) (OTC)
RECORDS / REPORTS CURRENT: XX (YES) (NO)
RELATED IND / NDA / DMF(S): IND 42,873, DMF # DMF # DMF

SUPPLEMENT PROVIDES FOR: Revised drafts of the blister unit and carton labeling for physician samples.

COMMENTS: This is an amendment to the Prior Approval Supplement, S-006, dated October 18, 2002 which provides for a packaging change. This amendment address the three requests made in the FDA's Approvable Letter dated February 21, 2003. The sponsor provides a complete response to the minor deficiencies, found in the labeling of the blister units (100 mg and 200 mg tablets) and carton (200 mg).

CONCLUSIONS AND RECOMMENDATIONS: Recommend Approval.

REVIEWER NAME	SIGNATURE	DATE COMPLETED
Lyudmila N. Soldatova, Ph.D.		April 15, 2003

cc: Orig: NDA 20-717
HFD-120/Div. File
HFD-120/AHomonnay/LSoldatova /MGuzewska
Filename: 20717scp006Amend1.doc
INIT: MGuzewska

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Chemistry Review #2

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/s/

Lyudmila Soldatova
4/15/03 02:57:37 PM
CHEMIST

Maryla Guzewska
4/16/03 07:19:37 AM
CHEMIST

ENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 20-717/S-006

ADMINISTRATIVE and
CORRESPONDENCE DOCUMENTS

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Administrative & Correspondence - Memorandum

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/s/

Lyudmila Soldatova
2/20/03 04:37:38 PM
CHEMIST

Maryla Guzewska
2/21/03 01:25:38 PM
CHEMIST



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20-717

PRIOR APPROVAL SUPPLEMENT

Cephalon, Inc.
Attention: Paul M. Kirsch
Senior Director, Regulatory Affairs
145 Brandywine Parkway
West Chester, PA 19380-4245

Dear Mr. Kirsch

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

Name of Drug Product:	PROVIGIL (modafinil) Tablets
NDA Number:	20-717
Supplement number:	S-006
Date of supplement:	October 18, 2002
Date of receipt:	October 21, 2002

Unless we notify you within 60 days of the receipt date that the application is not sufficiently complete to permit a substantive review, this application will be filed under section 505(b) of the Act on December 21, 2002 in accordance with 21 CFR 314.101(a).

All communications concerning this supplement should be addressed 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

NDA 20-717

Page 2

Courier/Overnight Mail:

Food and Drug Administration

Center for Drug Evaluation and Research

Division of Neuropharmacological Drug products, HFD-120

Attention: Division Document Room, 4008

1451 Rockville Pike

Rockville, Maryland 20852

If you have any questions, call Anna Marie Homonnay, R.Ph., Regulatory Health Project Manager, at (301) 594-2850.

Sincerely,

{See appended electronic signature page}

Maryla Guzewska, Ph.D.

Chemistry Team Leader, Neurology Drugs for the

Division of Neuropharmacological Drug Products
(HFD-120)

DNDC I, Office of New Drug Chemistry

Center for Drug Evaluation and Research

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/s/

Maryla Guzewska
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