

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

21-875

PROPRIETARY NAME REVIEW(S)

CONSULTATION RESPONSE

**DIVISION OF MEDICATION ERRORS AND TECHNICAL SUPPORT
OFFICE OF DRUG SAFETY
(DMETS; White Oak 22, Mail Stop 4447)**

DATE RECEIVED: November 30, 2005	DESIRED COMPLETION DATE: March 1, 2006	ODS CONSULT #: 05-0091-1
DATE OF DOCUMENTS: October 28, 2005	PDUFA DATE: April 20, 2006	
TO: Russell G. Katz, M.D. Director, Division of Neurology Products HFD-120		
THROUGH: Linda Kim-Jung, Pharm.D., Team Leader Denise Toyer, Pharm.D., Deputy Director Carol Holquist, R.Ph., Director Division of Medication Errors and Technical Support		
FROM: Laura L. Pincock, Pharm.D., Safety Evaluator Division of Medication Errors and Technical Support		
PRODUCT NAME: Nuvigil (Armodafinil Tablets) 50 mg, 100 mg, 150 mg, 250 mg		
NDA#: 21-875		
NDA SPONSOR: Cephalon, Inc.		
RECOMMENDATIONS: Cephalon, Inc. has not provided persuasive evidence to diminish our concerns with potential confusion between Nuvigil and Norinyl. Therefore, DMETS continues to not recommend the use of the proprietary name Nuvigil. DMETS would appreciate feedback of the final outcome of this consult. We would be willing to meet with the Division for further discussion, if needed. If you have further questions or need clarifications, please contact Diane Smith, project manager, at 301-796-0538.		

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Division of Medication Errors and Technical Support (DMETS)
Office of Drug Safety
HFD-420; White Oak 22, Mail Stop 4447
Center for Drug Evaluation and Research

PROPRIETARY NAME REVIEW

DATE OF REVIEW: January 3, 2006

NDA#: 21-875

NAME OF DRUG: Nuvigil
(Armodafinil Tablets)
50 mg, 100 mg, 150 mg, 250 mg

NDA HOLDER: Cephalon, Inc.

I. INTRODUCTION:

This consult was written in response to a request from the Division of Neurology Products (HFD-120), to reconsider the acceptability of the proprietary name, Nuvigil based on the Sponsor's submission dated October 28, 2005. DMETS reviewed the proposed proprietary name Nuvigil in ODS Consult # 05-0091, dated August 5, 2005. DMETS did not recommend use of the proprietary name, Nuvigil due to its potential look-alike qualities and similar product characteristics to Norinyl 1+50. In addition to the rebuttal submission, the Sponsor has included a market research assessment from the _____, _____ for the proposed proprietary name, Nuvigil, which was conducted in 2004. DMETS did not previously review the _____ Study in the initial consults. b(4)

PRODUCT INFORMATION

Nuvigil is indicated to improve wakefulness in patients with excessive sleepiness associated with obstructive sleep apnea/hypopnea syndrome (OSAHS), narcolepsy, and shift work sleep disorder (SWSD). In OSAHS, Nuvigil is indicated as an adjunct to standard treatment(s) for the underlying obstruction. If continuous positive airway pressure (CPAP) is the treatment of choice for a patient, a maximal effort to treat with CPAP for an adequate period of time should be made prior to initiating Nuvigil. The proposed dose of Nuvigil for OSAHS or narcolepsy is 150 mg or 250 mg once a day. The proposed dose of Nuvigil for SWSD is 150 mg once a day one hour prior to start of the shift period. Dose reductions are recommended for severe hepatic impairment. Nuvigil tablets are proposed to be provided in bottles of 60 count which are stored at room temperature.

II. RISK ASSESSMENT:

The sponsor has requested a re-consideration of the proprietary name, Nuvigil, for Armodafinil Tablets. The sponsor believes the potential for confusion between Nuvigil and Norinyl is low (the sponsor's comments are bolded.) The sponsor has also included a _____ study to support the statements made in their response. We note that the _____ study was not submitted to DMETS during the initial review of the proprietary name. However, we will address the _____ study at the same time we address the sponsor's comments. b(4)

A. Brand Name Look-alike/Sound-alike Similarities

Cephalon tested the name, NUVIGIL through a third party _____, who conducted a research study showing that the name NUVIGIL was not misinterpreted on any verbal or handwritten prescriptions for any existing brand/generic drug name. This report was also provided in the original New Drug Application. b(4)

_____, analyses regarding the potential for look-alike confusion between NUVIGIL and Norinyl indicated no failures for the orthographic measurements. _____ comparison of existing drug product profiles showed little-to-no commonalities for names similar to NUVIGIL, and no medical or prefix/suffix terms were regarded as an issue for prescribing or dispensing of NUVIGIL Tablets. b(4)

In addition, an independent professional review committee evaluated the results from the safety assessments in the present research. Taking into account prescribing, dispensing, and administration of the test agent versus existing products, the committee suggested NUVIGIL be presented to the Agency for consideration.

DMETS Response:

The _____ study was not submitted to DMETS for review and comment in the NDA approval process. We acknowledge _____ overall findings. However, DMETS disagrees with the conclusions that pertain to Norinyl. Furthermore, DMETS notes that the _____ study does not reflect any reasons as to why Nuvigil was acceptable with regards to Norinyl. The charts on pages 11, 21, and 26 list Norinyl, but otherwise Norinyl was not discussed further in the report _____ only cited sound-alike concerns between Norinyl and Nuvigil (see page 11 of _____ report). As we stated previously, prescriptions for either product may look very similar when scripted. Additionally, the potential remains for confusion with the 1+50 strength of Norinyl and the 150 mg strength of Nuvigil, should the “mg” or “+” be omitted from a written prescription. Furthermore, the recommended dosing regimen for each of these products is identical (one tablet once daily). Thus, we believe that the names should not co-exist in the marketplace. b(4)

B. Written Prescriptions

When the prescriptions are written correctly (i.e., “NUVIGIL 150 mg” and “Norinyl 1+50”), the similarity between the two prescriptions decreases. Prescribers most likely will write for 150 “mg” on a prescription for NUVIGIL and not just 150 as postulated by the Agency. This changes the orthographic similarity between “1/50” and “150” and will help the pharmacist distinguish between a Norinyl prescription and a NUVIGIL prescription. In addition, it should be noted that the approved labeling and advertising of Norinyl represents the strength as 1+50 and not 1/50.

Finally, the prescriber will most likely write a specific quantity of NUVIGIL tablets (e.g., #30, #60, or #90) that will be substantially different than a prescription of Norinyl 1+50, which is usually dispensed with a quantity of 3 or 12 months (e.g., #3, #12).

DMETS Response:

DMETS acknowledges that when the prescriptions are written correctly, the modifiers on the prescription (“mg” or “+”) may help to differentiate between the two names. However, not all prescriptions are written correctly or legibly. We maintain that it would be difficult to differentiate between a handwritten prescription written as “Norinyl 1+50, take one tablet daily” or “Nuvigil 150, take one tablet daily” especially if the “mg” designation and/or slash is not clearly scripted or omitted on a written prescription. Additionally, both products share an overlapping dosing frequency of “one tablet orally once daily” which may further compound the confusion between this name pair. Each product is available in multiple strengths (1/35 or 1/50 vs. 50 mg, 100 mg, 150 mg, or 250 mg). However, given the look-alike similarities between Nuvigil and Norinyl when scripted, DMETS is concerned with the likelihood of confusion with the 1/50 strength of Norinyl and the 150 mg strength of Nuvigil. DMETS notes that the study only identified sound-alike concerns between Nuvigil and Norinyl. Moreover, the Nuvigil prescription samples in the studies were written for the 50 mg strength of Nuvigil. Thus, this study did not evaluate the potential for confusion between Norinyl 1/50 and Nuvigil 150 mg. b(4)

DMETS acknowledges that oral contraceptives may be prescribed using a monthly quantity. However, it is also possible for Nuvigil to be prescribed using a monthly quantity, “dispense 1 month supply” or “dispense 3 months supply” in which case the quantity on a prescription may not help to differentiate between the two names. Thus, DMETS has not been convinced that there are sufficient modifiers on prescriptions for Norinyl and Nuvigil to ensure that the two names are not confused.

We also acknowledge the other names identified by as potential sound and/or look-alike names (Provigil, Norinyl, Nuvaring, Nulev, Niacin, Neulasta, Neupogen, and Nuprin). In our initial consult, DMETS also identified Provigil, Norinyl, and Nuvaring as names which could be confused orthographically and/or phonetically with Nuvigil. DMETS concurs with that Provigil and Nuvaring have a low potential for confusion with Nuvigil. After review of the names Nulev, Niacin, Neulasta, Neupogen, and Nuprin, DMETS considers these names to also have low potential for confusion with Nuvigil due to a lack of convincing look-alike/sound-alike similarities with Nuvigil, in addition to numerous differentiating product characteristics such as the product strength, indication for use, frequency of administration, route of administration, or dosage formulation. However, as noted above DMETS disagrees with conclusions regarding Norinyl. b(4)

C. Opportunity for an Error

Out of all the prescriptions dispensed for Norinyl 1+35 and 1+50 from January 2005 to July 2005, there have been prescriptions dispensed for Norinyl 1+35 and prescriptions dispensed for Norinyl 1+50. percent of the total Norinyl 1+50 prescriptions are new prescriptions. b(4)

In addition, a female patient who is expecting a prescription for Norinyl 1+50 would be expecting a blister card-type package by which she could get one tablet a day. If she received NUVIGIL 150 mg in error, the packaging and dosage form would be very different and would likely be questioned by the patient at the time of dispensing.

Likewise, a patient who is expecting a prescription for NUVIGIL 150 mg and received Norinyl 1+50 would receive the Norinyl package, which clearly has the Norinyl 1+50 name on it, and would also receive the patient product information that must accompany every oral contraceptive drug product. It is highly probable that this error would be caught at the time of dispensing to the patient.

DMETS Response:

DMETS acknowledges the prescription drug use data for Norinyl. However, the sponsor's rationale that patients would be able to notice an error and question the medication at the time of dispensing is not applicable to patients who are filling their prescription for the first time. If the patient has a new prescription and has never seen the packaging for the drug before, they are less likely to recognize the error. As the sponsor stated above ~~_____~~ of the Norinyl 1+50 prescriptions are new, therefore the rationale would not hold true for these patients. Furthermore, although the packaging of these two products are different, we cannot assume that the patient is always able to notice they have the wrong medication. Moreover, if the patient is dispensed the wrong medication, the medication error has already occurred. The consequences of a patient taking the wrong medication may be significant (i.e., unintended pregnancy, insomnia, or thrombosis) and could be potentially life-threatening. b(4)

Conclusion:

In summary, the sponsor has not submitted persuasive evidence to diminish our concerns with potential confusion between Nuvigil and Norinyl.

III. COMMENTS TO THE SPONSOR:

The sponsor has requested a re-consideration of the proprietary name, Nuvigil, for Armodafinil Tablets. The sponsor believes the potential for confusion between Nuvigil and Norinyl is low (the sponsor's comments are bolded.) The sponsor has also included a ~~_____~~ study to support the statements made in their response. We note that the ~~_____~~ study was not submitted to DMETS during the initial review of the proprietary name. However, we will address the ~~_____~~ study at the same time we address the sponsor's comments. b(4)

A. Brand Name Look-alike/Sound-alike Similarities

Cephalon tested the name, NUVIGIL through a third party ~~_____~~, who conducted a research study showing that the name NUVIGIL was not misinterpreted on any verbal or handwritten prescriptions for any existing brand/generic drug name. This report was also provided in the original New Drug Application. b(4)

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In addition, an independent professional review committee evaluated the results from the safety assessments in the present research. Taking into account prescribing, dispensing, and administration of the test agent versus existing products, the committee suggested NUVIGIL be presented to the Agency for consideration.

DMETS Response:

The ~~study~~ study was not submitted to DMETS for review and comment in the NDA approval process. We acknowledge ~~the~~ overall findings. However, DMETS disagrees with the conclusions that pertain to Norinyl. Furthermore, DMETS notes that the ~~study~~ study does not reflect any reasons as to why Nuvigil was acceptable with regards to Norinyl. The charts on pages 11, 21, and 26 list Norinyl, but otherwise Norinyl was not discussed further in the report. ~~only~~ only cited sound-alike concerns between Norinyl and Nuvigil (see page 11 of ~~the~~ report). As we stated previously, prescriptions for either product may look very similar when scripted. Additionally, the potential remains for confusion with the 1+50 strength of Norinyl and the 150 mg strength of Nuvigil, should the “mg” or “+” be omitted from a written prescription. Furthermore, the recommended dosing regimen for each of these products is identical (one tablet once daily). Thus, we believe that the names should not co-exist in the marketplace.

b(4)

B. Written Prescriptions

When the prescriptions are written correctly (i.e., “NUVIGIL 150 mg” and “Norinyl 1+50”), the similarity between the two prescriptions decreases. Prescribers most likely will write for 150 “mg” on a prescription for NUVIGIL and not just 150 as postulated by the Agency. This changes the orthographic similarity between “1/50” and “150” and will help the pharmacist distinguish between a Norinyl prescription and a NUVIGIL prescription. In addition, it should be noted that the approved labeling and advertising of Norinyl represents the strength as 1+50 and not 1/50.

Finally, the prescriber will most likely write a specific quantity of NUVIGIL tablets (e.g., #30, #60, or #90) that will be substantially different than a prescription of Norinyl 1+50, which is usually dispensed with a quantity of 3 or 12 months (e.g., #3, #12).

DMETS Response:

DMETS acknowledges that when the prescriptions are written correctly, the modifiers on the prescription (“mg” or “+”) may help to differentiate between the two names. However, not all prescriptions are written correctly or legibly. We maintain that it would be difficult to differentiate between a handwritten prescription written as “Norinyl 1+50, take one tablet daily” or “Nuvigil 150, take one tablet daily” especially if the “mg” designation and/or slash is not clearly scripted or omitted on a written prescription. Additionally, both products share an overlapping dosing frequency of “one tablet orally once daily” which may further compound the confusion between this name pair. Each product is available in multiple strengths (1/35 or 1/50 vs. 50 mg, 100 mg, 150 mg, or 250 mg). However, given the look-alike similarities between Nuvigil and Norinyl when scripted, DMETS is concerned with the likelihood of confusion with the 1/50 strength of Norinyl and the 150 mg strength of Nuvigil. DMETS notes that the ~~study~~ study only identified sound-alike concerns between Nuvigil and Norinyl. Moreover, the Nuvigil prescription samples in the ~~studies~~ studies were written for the 50 mg strength of Nuvigil. Thus, this study did not evaluate the potential for confusion between Norinyl 1/50 and Nuvigil 150 mg.

b(4)

DMETS acknowledges that oral contraceptives may be prescribed using a monthly quantity. However, it is also possible for Nuvigil to be prescribed using a monthly quantity, "dispense 1 month supply" or "dispense 3 months supply" in which case the quantity on a prescription may not help to differentiate between the two names. Thus, DMETS has not been convinced that there are sufficient modifiers on prescriptions for Norinyl and Nuvigil to ensure that the two names are not confused.

We also acknowledge the other names identified by ~~as~~ as potential sound and/or look-alike names (Provigil, Norinyl, Nuvaring, Nulev, Niacin, Neulasta, Neupogen, and Nuprin). In our initial consult, DMETS also identified Provigil, Norinyl, and Nuvaring as names which could be confused orthographically and/or phonetically with Nuvigil. DMETS concurs with ~~that~~ that Provigil and Nuvaring have a low potential for confusion with Nuvigil. After review of the names Nulev, Niacin, Neulasta, Neupogen, and Nuprin, DMETS considers these names to also have low potential for confusion with Nuvigil due to a lack of convincing look-alike/sound-alike similarities with Nuvigil, in addition to numerous differentiating product characteristics such as the product strength, indication for use, frequency of administration, route of administration, or dosage formulation. However, as noted above DMETS disagrees with ~~conclusions~~ conclusions regarding Norinyl. b(4)

C. Opportunity for an Error

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In addition, a female patient who is expecting a prescription for Norinyl 1+50 would be expecting a blister card-type package by which she could get one tablet a day. If she received NUVIGIL 150 mg in error, the packaging and dosage form would be very different and would likely be questioned by the patient at the time of dispensing.

Likewise, a patient who is expecting a prescription for NUVIGIL 150 mg and received Norinyl 1+50 would receive the Norinyl package, which clearly has the Norinyl 1+50 name on it, and would also receive the patient product information that must accompany every oral contraceptive drug product. It is highly probable that this error would be caught at the time of dispensing to the patient.

DMETS Response:

DMETS acknowledges the prescription drug use data for Norinyl. However, the sponsor's rationale that patients would be able to notice an error and question the medication at the time of dispensing is not applicable to patients who are filling their prescription for the first time. If the patient has a new prescription and has never seen the packaging for the drug before, they are less likely to recognize the error. As the sponsor stated above ~~of~~ of the Norinyl 1+50 prescriptions are new, therefore the rationale would not hold true for these patients. Furthermore, although the packaging of these two products are different, we cannot assume that the patient is always able to notice they have the wrong medication. Moreover, if the patient is dispensed the wrong medication, the medication error has already occurred. The consequences of a patient taking the wrong medication may be significant (i.e., unintended pregnancy, insomnia, or thrombosis) and could be potentially life-threatening. b(4)

Conclusion:

In summary, the sponsor has not submitted persuasive evidence to diminish our concerns with potential confusion between Nuvigil and Norinyl.

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3/31/2006 07:55:48 AM
DRUG SAFETY OFFICE REVIEWER

Linda Kim-Jung
3/31/2006 08:12:06 AM
DRUG SAFETY OFFICE REVIEWER

Denise Toyer
3/31/2006 08:21:46 AM
DRUG SAFETY OFFICE REVIEWER

Carol Holquist
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DRUG SAFETY OFFICE REVIEWER

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CONSULTATION RESPONSE
DIVISION OF MEDICATION ERRORS AND TECHNICAL SUPPORT
OFFICE OF DRUG SAFETY
(DMETS; HFD-420)

DATE RECEIVED:

April 5, 2005

DOCUMENT DATE:

April 5, 2005

DESIRED COMPLETION

DATE: November 22, 2005

PDUFA DATE: January 31, 2006

ODS CONSULT #: 05-0091

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

THROUGH: Courtney Calder, Pharm.D.
Project Manager
HFD-120

PRODUCT NAME:

Nuvigil
(Armodafinil Tablets)
50 mg, 100 mg, 150 mg, 250 mg

NDA #: 21-875

SPONSOR:

Cephalon, Inc.

SAFETY EVALUATOR: Laura Pincock, Pharm.D.

RECOMMENDATIONS:

1. DMETS does not recommend the use of the proprietary name, Nuvigil.
2. DMETS recommends implementation of the package insert labeling revisions outlined in Section III of this review in order to minimize user error.
3. DDMAC finds the proprietary name, Nuvigil, acceptable from a promotional perspective.

Denise P. Toyer, Pharm.D.
Deputy Director
Division of Medication Errors and Technical Support
Office of Drug Safety
Phone: (301) 827-3242 Fax: (301) 443-9664

Carol Holquist, R.Ph.
Director
Division of Medication Errors and Technical Support
Office of Drug Safety
Phone: (301) 827-3242 Fax: (301) 443-9664

**Division of Medication Errors and Technical Support
Office of Drug Safety
HFD-420; Parklawn Rm. 6-34
Center for Drug Evaluation and Research**

PROPRIETARY NAME REVIEW

DATE OF REVIEW: May 20, 2005

NDA #: 21-875

NAME OF DRUG: Nuvigil
(Armodafinil Tablets)
50 mg, 100 mg, 150 mg, 250 mg

NDA SPONSOR: Cephalon, Inc.

*****NOTE:** This review contains proprietary and confidential information that should not be released to the public.***

I. INTRODUCTION

This consult was written in response to a request from the Division of Neuropharmacological Drug Products (HFD-120), for assessment of the proprietary name, Nuvigil, regarding potential name confusion with other proprietary or established drug names.

PRODUCT INFORMATION

Nuvigil is indicated to improve wakefulness in patients with excessive sleepiness associated with obstructive sleep apnea/hypopnea syndrome (OSAHS), narcolepsy, and shift work sleep disorder (SWSD). In OSAHS, Nuvigil is indicated as adjunct to standard treatment(s) for the underlying obstruction. If continuous positive airway pressure (CPAP) is the treatment of choice for a patient, a maximal effort to treat with CPAP for an adequate period of time should be made prior to initiating Nuvigil. The proposed dose of Nuvigil for OSAHS or narcolepsy is 150 mg or 250 mg once a day. The proposed dose of Nuvigil for SWSD is 150 mg once a day one hour prior to start of the shift period. Dose reductions are recommended for severe hepatic impairment. Nuvigil tablets are proposed to be provided in bottles of 60 count which are stored at room temperature.

II. RISK ASSESSMENT:

The medication error staff of DMETS conducted a search of several standard published drug product reference texts^{i,ii} as well as several FDA databasesⁱⁱⁱ for existing drug names which sound-alike or look-alike to Nuvigil to a degree where potential confusion between drug names could occur under the usual clinical practice settings. A search of the electronic online version of the U.S. Patent and

ⁱ MICROMEDEX Integrated Index, 2005, MICROMEDEX, Inc., 6200 South Syracuse Way, Suite 300, Englewood, Colorado 80111-4740, which includes all products/databases within ChemKnowledge, DrugKnowledge, and RegsKnowledge Systems.

ⁱⁱ Facts and Comparisons, online version, Facts and Comparisons, St. Louis, MO.

ⁱⁱⁱ AMF Decision Support System [DSS], the Division of Medication Errors and Technical Support proprietary name consultation requests, New Drug Approvals 1998-2005, and the electronic online version of the FDA Orange Book.

Trademark Office's Text and Image Database^{iv} and the data provided by Thomson & Thomson's SAEGISTM Online Service^v were also conducted. An Expert Panel discussion was conducted to review all findings from the searches. In addition, DMETS conducted three prescription analysis studies consisting of two written prescription studies (inpatient and outpatient) and one verbal prescription study, involving health care practitioners within FDA. This exercise was conducted to simulate the prescription ordering process in order to evaluate potential errors in handwriting and verbal communication of the name.

A. EXPERT PANEL DISCUSSION (EPD)

An Expert Panel discussion was held by DMETS to gather professional opinions on the safety of the proprietary name, Nuvigil. Potential concerns regarding drug marketing and promotion related to the proposed name were also discussed. This group is composed of DMETS Medication Errors Prevention Staff and representation from the Division of Drug Marketing, Advertising, and Communications (DDMAC). The group relies on their clinical and other professional experiences and a number of standard references when making a decision on the acceptability of a proprietary name.

1. DDMAC has no objection to the use of the proprietary name, Nuvigil.
2. The Expert Panel identified three proprietary names that were thought to have the potential for confusion with Nuvigil. These products are listed in Table 1 (see below), along with the dosage forms available and usual dosage.

Table 1: Potential Sound-Alike/Look-Alike Names Identified for Nuvigil

Product Name	Established name, Dosage form(s)	Usual adult dose*	Other**
Nuvigil	Armodafinil Tablets: 50 mg, 100 mg, 150 mg, 250 mg	OSAHS or narcolepsy: 150 mg or 250 mg once daily SWSD: 150 mg once daily one hour prior to shift Dose reductions for severe hepatic impairment	N/A
Provigil	Modafinil Tablets: 100 mg, 200 mg	OSAHS or narcolepsy: 200 mg once daily in the morning SWSD: 200 mg once daily one hour prior to shift	SA
Norinyl 1/50 Norinyl 1/35	Norethindrone and Mestranol (1/50) Tablets: 1 mg and 0.05 mg (monophasic) Norethindrone and EE (1/35) Tablets: 1 mg, 0.035 mg (monophasic)	One tablet daily	LA
Nuvaring	Etonogestrel and Ethinyl Estradiol Intravaginal Ring: 0.12 mg/day and 0.015 mg/day	One ring, inserted vaginally and left in place for 3 weeks, then removed for 1 week. A new ring is inserted after the last is removed.	LA
*Frequently used, not all-inclusive. **LA (look-alike), SA (sound-alike)			

^{iv} WWW location <http://www.uspto.gov>.

^v Data provided by Thomson & Thomson's SAEGIS(tm) Online Service, available at www.thomson-thomson.com.

B. PHONETIC ORTHOGRAPHIC COMPUTER ANALYSIS (POCA)

As part of the name similarity assessment, proposed names are evaluated via a phonetic/orthographic algorithm. The proposed proprietary name is converted into its phonemic representation before it runs through the phonetic algorithm. The phonetic search modules return a numeric score to the search engine based on the phonetic similarity to the input text. Likewise, an orthographic algorithm exists which operates in a similar fashion. All names considered having significant phonetic or orthographic similarities to Nuvigil were discussed by the Expert Panel (EPD).

C. PRESCRIPTION ANALYSIS STUDIES

1. Methodology:

Three separate studies were conducted within FDA for the proposed proprietary name to determine the degree of confusion of Nuvigil with other U.S. drug names due to similarity in visual appearance with handwritten prescriptions or verbal pronunciation of the drug name. These studies employed a total of 119 health care professionals (pharmacists, physicians, and nurses). This exercise was conducted in an attempt to simulate the prescription ordering process. An inpatient order and outpatient prescriptions were written, each consisting of a combination of marketed and unapproved drug products and a prescription for Nuvigil. These prescriptions were optically scanned and one prescription was delivered to a random sample of the participating health professionals via e-mail. In addition, the outpatient orders were recorded on voice mail. The voice mail messages were then sent to a random sample of the participating health professionals for their interpretations and review. After receiving either the written or verbal prescription orders, the participants sent their interpretations of the orders via e-mail to the medication error staff.

HANDWRITTEN PRESCRIPTION	VERBAL PRESCRIPTION
<p><u>Outpatient RX:</u></p> <p><i>Nuvigil 150 mg #30 1 po qd</i></p>	<p>“Nuvigil 150 mg, Take one PO qd, dispense 30.”</p>
<p><u>Inpatient RX:</u></p> <p><i>Decrease Nuvigil to 150mg po qd</i></p>	

2. Results:

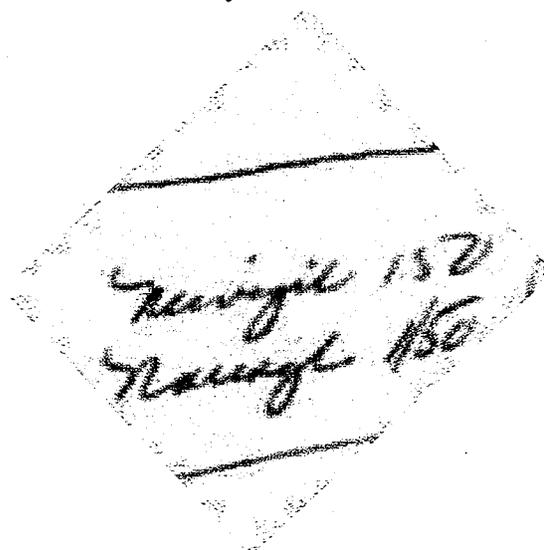
None of the interpretations of the proposed name overlap, sound similar, or look similar to any currently marketed U.S. product. The majority of misinterpretations were misspelled/phonetic variations of the proposed name, Nuvigil. See Appendix A for the complete listing of interpretations from the verbal and written studies.

D. SAFETY EVALUATOR RISK ASSESSMENT

In reviewing the proprietary name, Nuvigil, the primary concerns identified related to look-alike and sound-alike confusion with Provigil, Norinyl 1/50, Norinyl 1/35, and Nuvaring.

Additionally, DMETS conducted prescription studies to simulate the prescription ordering process. In this case, there was no confirmation that the proposed name could be confused with any of the aforementioned names. The majority of misinterpretations were misspelled/phonetic variation of the proposed name, Nuvigil.

1. Nuvigil may look similar to Norinyl. Norinyl 1/35 and Norinyl 1/50 are oral contraceptive tablets indicated for the prevention of pregnancy. The two names have some orthographic similarities. **Each name begins with the letter 'N' and ends with the letter 'l' and the beginnings of each name may "Nuv-" and "Nor-" look similar when scripted. Additionally, the endings of the name may also look similar ('-igil' vs. '-inyl') when scripted. Furthermore, each name has a downstroke in a similar position in each name with the letter 'g' in Nuvigil and the letter 'y' in Norinyl.** Each product is available in multiple strengths (1/35 or 1/50 vs. 50 mg, 100 mg, 150 mg, or 250 mg) so that the strength should be included on a prescription. The product name with strength on the prescription may help to differentiate between the two names. However, given the look-alike similarities between Nuvigil and Norinyl when scripted, DMETS is concerned with the likelihood of confusion with the 1/50 strength of Norinyl and the 150 mg strength of Nuvigil, should the "mg" designation and/or the slash be omitted from a written prescription (see below). Moreover, the recommended dosage regimen for each of these two products is identical: one tablet orally once daily. Finally, if these products are confused, unintended pregnancy or adverse events, such as thromboses, insomnia or headache may result from the patient taking the wrong medication. Due to the look-alike similarities between Nuvigil and Norinyl, in addition to similar product characteristics [i.e., (150 mg vs. 1/50) and (one tablet once daily dosing regimen)], DMETS believes that the names may not co-exist in the market place.



2. Nuvigil may sound similar to Provigil. Provigil is the tradename for modafinil tablets, a prescription drug product to improve wakefulness. The usual dose of Provigil is 200 mg once a day. Nuvigil (Armodafinil) is the r-enantiomer of Provigil (Modafinil); as a result, the drugs share an indication and many of the same characteristics. Each name has three syllables and the **names sound-alike because both names share the same suffix, “-vigil”**. However, the first syllable of each name (Nu- vs. Pro-) sounds different due to the pronunciation of the vowels (-u- vs. -o-) which will help differentiate the two drug names. The two drug products share many of the same product characteristics, such as route of administration (oral), dosage form (tablets), indication (improve wakefulness), and dosage frequency (once daily). However, the strength for each product is usually different (50 mg, 100 mg, 150 mg or 250 mg vs. 100 mg or 200 mg). Since each product is available in multiple strengths, the strength should be indicated on a prescription which may help to differentiate the two names. However, it is possible for the strength to overlap if the patient is ordered the 100 mg dose or a dosage reduction for severe **hepatic impairment, as recommended by each product’s insert labeling**. Despite this overlap, DMETS believes that the phonetic differences will make it unlikely that prescriptions of Nuvigil and Provigil will be confused for one another.
3. Nuvigil may look similar to Nuvaring. Nuvaring is a prescription contraceptive ring containing etonogestrel/ethinyl estradiol (0.12mg/0.015 mg per day). Nuvaring is used as one ring inserted vaginally and left in place for 3 weeks, then removed for 1 week. A new ring is inserted after the four week cycle. The two names have some orthographic similarities because the names share **the same beginning ‘Nuv-’**. However, the ending for Nuvaring (-aring) is noticeably longer and orthographically distinct from the ending for Nuvigil (-igil). Additionally, the letter ‘g’ in Nuvaring is at the end of the name and the letter ‘g’ is near the center of Nuvigil which also helps to orthographically differentiate the two names. Moreover, Nuvigil is available in multiple strengths (50 mg, 100 mg, 150 mg, or 250 mg) so a strength should be included on the prescription which will help to differentiate between the two names. Orthographic differences and different product characteristics such as: strength (50 mg, 100 mg, 150 mg, or 250 mg vs. 0.12 mg/0.015 mg per day), dosing frequency (daily vs. monthly), route of administration (orally vs. intravaginally), dosage form (tablet vs. ring) and context of use will distinguish between these two products and minimize the potential for confusion.

Nuvaring
Nuvigil

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III. COMMENTS TO THE SPONSOR:

DMETS does not recommend the use of the proprietary name Nuvigil. In reviewing the proprietary name, the primary concerns related to look-alike confusion and similar product characteristics with the currently marketed product Norinyl 1/50.

The names Nuvigil and Norinyl have some orthographic similarities. Each name begins with the letter 'N' and ends with the letter 'l' and the beginnings of each name may "Nuv-" and "Nor-" look similar when scripted. Additionally, the endings of the name may also look similar ('-igil' vs. '-inyl') when scripted. Furthermore, each name has a downstroke in a similar position in each name with the letter 'g' in Nuvigil and the letter 'y' in Norinyl. Each product is available in multiple strengths (1/35 or 1/50 vs. 50 mg, 100 mg, 150 mg, or 250 mg) so that the strength should be included on a prescription. The product name with strength on the prescription may help to differentiate between the two names. However, given the look-alike similarities between Nuvigil and Norinyl when scripted, DMETS is concerned with the likelihood of confusion with the 1/50 strength of Norinyl and the 150 mg strength of Nuvigil, should the "mg" designation and/or the slash be omitted from a written prescription (see below). Moreover, the recommended dosage regimen for each of these two products is identical: one tablet orally once daily. Finally, if these products are confused, unintended pregnancy or adverse events, such as thromboses, insomnia or headache may result from the patient taking the wrong medication. Due to the look-alike similarities between Nuvigil and Norinyl, in addition to similar product characteristics [i.e., (150 mg vs. 1/50) and (one tablet once daily dosing regimen)], DMETS believes that the names may not co-exist in the market place.

In the review of the container labels, carton, and insert labeling of Nuvigil, DMETS has attempted to focus on safety issues relating to possible medication errors. The draft container labels and carton labeling were submitted in mostly black and white. Therefore, it is not possible to fully assess the safety of the labels and labeling because the information provided did not reflect the label and labeling presentation that will actually be used on the marketplace. However, DMETS has identified the following areas of possible improvement, which might minimize potential user error.

A. GENERAL COMMENTS

1. **The container labels and carton labeling cite the tradename as "NuVigil". The capitalization of the letter 'V' makes the tradename appear to be two words (i.e., "Nu Vigil"). Because the approved tradename is Nuvigil, the tradename should be communicated without capitalization of the letter 'V' with all letters in the same font size.**
2. Insert a space between the number and milligram unit on the container labels and carton labeling (i.e., 50 mg [not 50mg])
3. Increase the size of the milligram strength (i.e., 50 mg) on the container labels and carton labeling to increase the prominence. We also recommend you relocate the milligram strength directly below the established name to give more prominence.

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4. Ensure that the established name appears at least one-half the size of the proprietary name in accordance with 21 CFR 201.10(g)(2) on the container labels and carton labeling. We also recommend that you center the established name underneath the proprietary name to increase the **prominence of the established name. Additionally, "tablets" should be included in the established name (i.e., armodafinil tablets) and have equal prominence to "armodafinil"**.
5. In a side-by-side comparison of the black and white container labels and carton labeling, we note that these look similar. Ensure to use contrasting color, boxing, or some other means to clearly differentiate between the multiple strengths of this product in order to minimize selection errors. We note that on the draft container labels and carton labeling, the strengths may be differentiated because there is a colored box around each panel. Please submit the full color mock-ups of the labels and labeling when available.
6. **The package insert labeling states that "_____**

_____ **The marketed strengths of Nuvigil are proposed to be 50 mg, 100 mg, 150 mg, and 250 mg. Since the recommended starting dose of Nuvigil according to the PI is either 150 mg or 250 mg, how will patients take a dose of 75 mg or 125 mg? Are the tablets scored so that the tablets may be divided? Please clarify.**
7. The recommended starting dose is 150 mg or 250 mg of Nuvigil. Therefore DMETS questions what indications of use are the 50 mg and 100 mg tablets intended for? Please clarify.

b(4)

B. CONTAINER LABELS [50 mg, 100 mg, 150 mg, and 250 mg (unit-of-use bottles {60 count} _____)]

b(4)

1. See General Comments A1 through A5.
2. **The professional sample blister cards should indicate that "Each Tablet" contains 50 mg, 100 mg, 150 mg, or 250 mg. In our post-marketing review experience, medication errors have occurred because patients thought the entire carton or entire blister carton contained the specified strength (i.e., 50 mg).**
3. **Ensure the "Usual Dosage" statement is on all labels in accordance with 21 CFR 201.55.**
4. **Ensure that all "Unit of Use" bottles (e.g., 60 count bottle) have a Child Resistant Closure to be in accordance with the Poison Prevention Act.**

C. CARTON LABELING [50 mg, 100 mg, 150 mg, and 250 mg (professional sample bulk carton)]

1. See General Comments A1 through A5.
2. Separate the net quantity statement away from the product strength and increase the prominence of the net quantity statement.
3. **We recommend that the professional sample bulk carton read "_____**
_____ instead of' _____

b(4)

b(5)

4. **The professional sample bulk carton should indicate that “Each Tablet” contains 50 mg, 100 mg, 150 mg, or 250 mg.** In our post-marketing review experience, medication errors have occurred because patients thought the entire carton or entire blister carton contained the specified strength (i.e., 50 mg).
5. **Increase the prominence of the “Professional Sample Not For Sale” or “PROFESSIONAL SAMPLE” statements.**

D. INSERT LABELING

1. **In the clinical trial section, there is a typographical error with the term “bradytachycardia” (line 198).** Revise accordingly.
2. **DOSAGE AND ADMINISTRATION section**

- a. Define the abbreviations for OSAHS and SWSD.
- b. We recommend that you separate the indications and doses into two sections. For example,

The recommended dose of Nuvigil for patients with OSAHS or narcolepsy is 150 mg or 250 mg given as a single daily dose in the morning. In patients with OASHS, 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.

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.

V. RECOMMENDATIONS:

- A. DMETS does not recommend the use of the proprietary name, Nuvigil.
- B. DMETS recommends implementation of the package insert labeling revisions outlined in the Section III of this review in order to minimize user error.
- C. DDMAC finds the proprietary name, Nuvigil, acceptable from a promotional perspective.

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DMETS would appreciate feedback of the final outcome of this consult. We are willing to meet with the Division for further discussion as well. If you have any questions concerning this review, please contact Diane Smith at 301-827-1998.

Laura Pincock, Pharm.D.
Safety Evaluator
Division of Medication Errors and Technical Support
Office of Drug Safety

Concur:

Linda Kim-Jung, Pharm.D.
Team Leader
Division of Medication Errors and Technical Support
Office of Drug Safety

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Appendix A.

<u>Voice</u>	<u>Inpatient</u>	<u>Outpatient</u>
Nuvigel	Nuvinzl	Nuvrizil
Neuvagel	Navigil	Nuvigirl
Nevogil	Nuvigil	Nuvrizirl
Mysigil	Novigil	Nuvigil
Nuvagel	Nuvigil	Murzirl
Nuvagil	Nuvigil	Nuirzel
Neuvogil	Nuvigil	Nurrgirl
Misigil	Nuvigil	Nuvizil
Mivigil	Nuvigil	Nuvigil
Mizidil	Nuvigil	Nuvigil
	Navigil	Nuviziel
	Navigil	Nuviziel
	Nuvigil	Nuvigil
	Navigil	
	Nuvigil	
	Nuvigil	

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this page is the manifestation of the electronic signature.**

/s/

Laura Pincock
8/5/05 09:58:34 AM
DRUG SAFETY OFFICE REVIEWER

Denise Toyer
8/5/05 12:07:12 PM
DRUG SAFETY OFFICE REVIEWER

Carol Holquist
8/5/05 12:17:19 PM
DRUG SAFETY OFFICE REVIEWER

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