

CENTER FOR DRUG EVALUATION AND RESEARCH

APPROVAL PACKAGE FOR:

APPLICATION NUMBER

NDA 21-720

Administrative/Correspondence Reviews

EXCLUSIVITY SUMMARY FOR NDA # 21-720 _____ SUPPL # ____ 00 ____

Trade Name Aricept ODT _____ Generic Name donepezil hydrochloride
Applicant Name _____ Eisai Medical Research Inc. _____ HFD #120

Approval Date If Known _____ October 18, 2004 _____

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 question 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.

The application only contained bioequivalence studies comparing the orally disintegrating tablets and the currently approved tablets.

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 /_X/

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 /_X_/

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 /_X /

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 /_X_/ NO /___/

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

NDA# 20-690, Aricept Tablets

NDA#_ 21-719, Aricept Oral Solution

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 NDA'S 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 /_X_/

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

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

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

YES /___/ NO /___/

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

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

YES /___/ NO /___/

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

YES /___/ NO /___/

If yes, explain:

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

YES /___/ NO /___/

If yes, explain:

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

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

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

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

Investigation #1 YES /___/ NO /___/

Investigation #2 YES /___/ NO /___/

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

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

Investigation #1 YES /___/ NO /___/

Investigation #2 YES /___/ NO /___/

If you have answered "yes" for one or more investigation, identify the NDA in which a similar investigation was relied on:

c) If the answers to 3(a) and 3(b) are no, identify each "new" investigation in the application or supplement that is essential to the approval (i.e., the investigations listed in #2(c), less any that are not "new"):

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 !
 IND # _____ YES /___/ ! NO /___/ Explain: _____
 !
 !

Investigation #2 !
 IND # _____ YES /___/ ! 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 !
 YES /___/ Explain _____ ! NO /___/ Explain _____
 !
 !
 _____ !
 _____ !

Investigation #2 !
 YES /___/ Explain _____ ! 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: _____

Signature
Title:

Date

Melina Griffis, RPh, Project Manager

01/11/05

Signature of Office/
Division Director

Date

Russell Katz, MD
Director of Division of Neuropharmacological Drug Products

Form OGD-011347 Revised 05/10/2004

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

/s/

Russell Katz
1/21/05 04:33:51 PM

CONSULTATION RESPONSE

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

DATE RECEIVED:

February 17, 2004

DESIRED COMPLETION DATE:

September 01, 2004

ODS CONSULT #: 04-0049

PDUFA DATE: October 18, 2004

TO: Russell Katz, MD
Director, Division of Neuropharmacological Drug Products
HFD-120

THROUGH: Melina Griffis
Project Manager
HFD-120

PRODUCT NAME:

Aricept® RDT
(Donepezil Hydrochloride Rapidly Disintegrating
Tablets)
5 mg and 10 mg

NDA #: 21-720

NDA SPONSOR:

Eisai Medical Research, Inc.

SAFETY EVALUATOR: Linda M. Wisniewski, RN

RECOMMENDATIONS:

1. DMETS has no objections to the use of the proprietary name Aricept RDT. This is considered a tentative decision and the firm should be notified that this name with its associated labels and labeling must be re-evaluated approximately 90 days prior to the expected approval of the NDA. A re-review of the name prior to NDA approval will rule out any objections based upon approvals of other proprietary or established names from the signature date of this document.
2. DMETS recommends implementation of the label and labeling revisions outlined in section III of this review to minimize potential errors with the use of this product.
3. DDMAC finds the proprietary name Aricept RDT acceptable from a promotional perspective.

Carol Holquist, RPh
Director
Division of Medication Errors and Technical Support
Office of Drug Safety
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**Division of Medication Errors and Technical Support (DMETS)
Office of Drug Safety
HFD-420; PKLN Rm. 6-34
Center for Drug Evaluation and Research**

PROPRIETARY NAME REVIEW

DATE OF REVIEW: March 09, 2004

NDA#: 21-720

NAME OF DRUG: Aricept® RDT
(Donepezil Hydrochloride Rapidly Disintegrating Tablets)
5 mg and 10 mg

NDA HOLDER: Eisai Medical Research, 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, "Aricept® RDT", regarding potential name confusion with other proprietary or established drug names. The sponsor is currently marketing Aricept® in 5 mg and 10 mg tablets. This product was approved November 25, 1996. Draft container labels, carton and insert labeling were provided for review and comment.

PRODUCT INFORMATION:

Aricept® RDT (Donepezil Hydrochloride Rapidly Disintegrating Tablets) is a reversible inhibitor of the enzyme acetylcholinesterase. It is indicated for the treatment of mild to moderate dementia of the Alzheimer's type. It is available for oral administration as rapidly disintegrating tablets (RDT). Each tablet contains 5 mg or 10 mg of donepezil hydrochloride. It is usually dosed at 5 mg and 10 mg per day, taken in the evening, just prior to retiring. Aricept® RDT should be allowed to dissolve on the tongue and followed with a sip of water.

**Appears This Way
On Original**

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

II. RISK ASSESSMENT:

The medication error staff of DMETS conducted a search of several standard published drug product reference texts^{1,2} as well as several FDA databases³ for existing drug names which sound-alike or look-alike to Aricept RDT 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 Trademark Office's Text and Image Database was also conducted⁴. The Saegis⁵ Pharma-In-Use database was searched for drug names with potential for confusion. 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 healthcare 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 Aricept RDT. 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 finds the proposed proprietary name Aricept RDT acceptable from a promotional perspective.
2. The Expert Panel identified two proprietary names that were thought to have the potential for confusion with Aricept RDT. 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 by DMETS Expert Panel

Product Name	Dosage form(s), Established name	Usual adult dose*	Other**
Aricept RDT	Donepezil Hydrochloride Rapidly Disintegrating Tablets: 5 mg and 10 mg	5 mg for 4 to 6 weeks, and individualize the increase to 10 mg.	N/A
Aricept	Donepezil Hydrochloride Tablets 5 mg and 10 mg	5 mg for 4 to 6 weeks, and individualize the increase to 10 mg.	SA/LA
Aricept	Donepezil Hydrochloride Oral Suspension 5 mg/5 mL	5 mg for 4 to 6 weeks, and individualize the increase to 10 mg.	SA/LA
*Frequently used, not all-inclusive. **L/A (look-alike), S/A (sound-alike) *** NOTE: This review contains proprietary and confidential information that should not be released to the public			

¹ MICROMEDEX Integrated Index, 2004, MICROMEDEX, Inc., 6200 South Syracuse Way, Suite 300, Englewood, Colorado 80111-4740, which includes all products/databases within ChemKnowledge, DrugKnowledge, and RegsKnowledge Systems.

² Facts and Comparisons, online version, Facts and Comparisons, St. Louis, MO.

³ The Division of Medication Errors and Technical Support [DMETS] database of Proprietary name consultation requests, New Drug Approvals 98-04, and the electronic online version of the FDA Orange Book.

⁴ WWW location <http://www.uspto.gov/tmdb/index.html>.

⁵ Data provided by Thomson & Thomson's SAEGIS™ Online Service, available at www.thomson-thomson.com

B. PHONETIC and 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 module returns 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. No additional names of concern were identified in POCA that were not discussed in EPD.

C. ADVERSE EVENT REPORTING SYSTEM (AERS)

Aricept has been marketed since November 25, 1996. Therefore DMETS conducted a search of the FDA Adverse Event Reporting System (AERS) for all post-marketing safety reports of medication errors associated with Aricept. The MEDDRA Preferred Terms (PT) "Medication Error", "Accidental Overdose", and "Overdose NOS" and the terms "Aricept", "Donepezil Hydrochloride", "Ari%", and "Done%" were used as search criteria. The search identified a total of thirty-one cases of name confusion with Aricept. There were 28 cases in which the wrong drugs were dispensed or administered: Aciphex (24), Ambien (1), Accupril (1), Aralen (1), and Duricef (1), and three cases reporting a potential similarity between Erycette (2) and Viracept (1). The Aciphex and Aricept errors were primarily the result of similar appearing labels and labeling. DMETS has conducted several post-marketing reviews concerning these errors. The Aciphex sponsor has revised the labels and labeling in response to DMETS' concerns. Except in the case of Erycette, DMETS has received only one case (actual or potential) of name confusion with the remaining names. DMETS received two potential errors involving Erycette and Aricept. One of these errors was reported within the first six months of Aricept's approval while the other was reported in 2000. Despite the sound-alike similarity between Erycette and Aricept no actual errors have been received with regards to this name pair. In summary, the potential for name confusion between Aricept and Ambien, Accupril, Aralen, Duricef, Erycette, or Viracept does not warrant action at this time. However, DMETS will continue to monitor potential confusion between Aricept and Ambien, Accupril, Duricef, Erycette, Viracept, and Aralen.

D. PRESCRIPTION ANALYSIS STUDIES

1. Methodology:

Three separate studies were conducted within the Centers of the FDA for the proposed proprietary name to determine the degree of confusion of Aricept RDT with marketed U.S. drug names (proprietary and established) due to similarity in visual appearance with handwritten prescriptions or verbal pronunciation of the drug name. These studies employed a total of 124 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 Aricept RDT (see page 5). 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>Outpatient RX:</p> <p><i>Aricept RDT 10mg</i> <i>7 po qd</i> <i>#30</i></p>	<p>Aricept RDT 10 mg Sig: 1 po qd # 30</p>
<p>Inpatient RX:</p> <p><i>Aricept RDT 10mg po qd #2</i></p>	

2. Results:

Five of the respondents interpreted the proposed name Aricept RDT as Aricept. Aricept is a currently marketed U.S. product. This occurred in both the verbal and written studies. Four of the respondents interpreted the proposed name as: Erisept RDT (1 response), and Erycept RDT (3 responses). All four of the responses occurred in the verbal study. Erycept and Ericept sound similar to the currently marketed product Erycette.

E. SAFETY EVALUATOR RISK ASSESSMENT

In reviewing the proprietary name Aricept RDT, the primary concerns identified by the EPD to have potential look-alike and sound-alike confusion with Aricept RDT were Aricept Tablets, and Aricept [] Safety concerns related to the “RDT” modifier were also considered.

DMETS conducted prescription studies to simulate the prescription ordering process. In this case, there was confirmation that Aricept RDT could be confused with Aricept. Five respondents (4 inpatient and 1 outpatient) from the written study omitted the modifier and interpreted the name as Aricept. Although there are limitations to the predictive value of these studies, primarily due to sample size, we have acquired safety concerns due to the positive interpretation with this drug product. A positive finding in a study with a small sample size may indicate a high risk and potential for medication errors when extrapolated to the general U.S. population. Additionally, four respondents from the verbal study misinterpreted the name Aricept RDT as names that are similar to the currently marketed drug product, Erycette. The misinterpretations were Erisept RDT (1) and Erycept RDT (3). Thus, this name is also evaluated below.

1. Look-alike and Sound-alike concerns:

- a. Aricept RDT is the latest product extension to Aricept. Aricept is currently approved as an immediate-release tablet. DMETS is concerned that Aricept RDT might be confused with Aricept (tablets) and the pending proprietary name Aricept []*. Since all three products share the root name (Aricept) there was concern that confusion might occur between these products and the root name if the modifier was omitted. The prescription studies confirmed that the modifier RDT could be omitted. Five respondents in the written studies interpreted the name without the modifier. However, the potential harm to the patient is minimal given the products contain the same active ingredient in different dosage forms. If the modifier for Aricept RDT was omitted, the patient would likely receive Aricept tablets or Aricept

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

once it is approved. Although all three products contain the same ingredient, dose and frequency, the formulation may not be optimal for the patient's particular medical situation. Upon approval of Aricept RDT*** and Aricept [redacted], multiple dosage forms of Aricept will be available. Once three different Aricept dosage forms ([redacted] immediate-release tablets and rapidly disintegrating tablets) are marketed, practitioners will need to further clarify which dosage form will be appropriate for the individual patient prior to dispensing the drug. There will need to be an education campaign to alert health care practitioners to the new dosage formulation including product differences.

- b. Four of the respondents in the verbal prescription studies interpreted the proposed name as: Erisept RDT (1 response) and Erycept RDT (3 responses). These responses sound similar to the currently marketed product Erycette. Potential confusion between the root name "Aricept" and "Erycette" has also been reported to the FDA. DMETS has received two cases of potential confusion between these products. One case occurred within six months of Aricept's introduction to the market and the other case in the year 2000. Both cases involving Erycette were potential errors where practitioners indicated that the two names sounded similar. Since DMETS has not received any additional cases since 2000 involving this name pair, no action is warranted at this time. DMETS will continue to monitor potential confusion between the root names Aricept and Erycette. Additionally, the potential for confusion may be minimized by the presence of the modifier "RDT" in association with the proprietary name Aricept. This will help to distinguish the two products as Erycette does not employ the use of a modifier in its proprietary name and exists in only one dosage form, a topical swab.

2. Modifier (RDT) concerns:

Due to the prevalence of numerous drug name modifiers, DMETS is concerned that the modifier "RDT" could cause confusion among healthcare professionals. Currently, there are a number of products that employ a modifier in the proprietary name to identify an orally disintegrating product. They are Maxalt MLT, Zofran ODT, Claritin Reditabs, Pepcid RPD, Remeron Soltab, Zomig-ZMT, and Zyprexa Zydis. Additionally, there is a pending application, [redacted] that proposes to use the modifier [redacted]. Thus, there is the potential that nine different modifiers (MLT, ODT, Reditabs, RDT, [redacted] RPD, Soltab, ZMT and Zydis) could be used to identify orally disintegrating tablets. Postmarketing research has shown that there can be confusion with modifiers within and across product lines. The most likely modifiers to be confused with RDT are ODT, [redacted] and RPD. Additionally, Pepcid RPD is listed in the Orange Book as being discontinued. Although Pepcid RPD is no longer marketed, the proprietary name still appears in electronic references, thus the potential for confusion still exists. Even if the modifier RDT is confused with ODT or RPD, DMETS believes that it is unlikely that the root names of the aforementioned drugs would be confused with the root name Aricept due to the different orthographic and phonologic presentation. Despite the decreased possibility that the patient would receive the wrong medication, the medication error would have already occurred. Thus, practitioners will need to be educated upon approval of the product Aricept RDT with regards to the use of the appropriate modifier to decrease the potential for confusion with other currently used modifiers and within the Aricept product line. Additionally, DMETS is not aware of any common medical interpretations for the letters [redacted]' except for [redacted].

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and it is unlikely that this interpretation would be associated with a medication order.

Modifiers for Orally Disintegrating Tablets	
Product Name	Modifier
Maxalt MLT	MLT (Melt)
Zofran ODT	ODT (Orally Disintegrating Tablets)
Claritin Reditabs	Reditabs
Pepcid RPD	(RPD) No discernable meaning **
Remeron Soltab	Soltab
Zomig ZMT	(ZMT) No discernable meaning ***
Zyprexa Zydis	Zydis
Aricept RDT*	RDT (Rapidly Disintegrating Tablets)
* Proposed not FOI releasable.	
** Per United States Patent and Trademark Office	
*** Per DMETS consult # 99-0109.	

III. LABELING, PACKAGING, AND SAFETY RELATED ISSUES:

In the review of the container labels, carton and insert labeling of Aricept RDT, DMETS has attempted to focus on safety issues relating to possible medication errors. DMETS has identified the following areas of possible improvement, which might minimize potential user error.

A. GENERAL COMMENT

1. In order to minimize confusion between dosage forms, please ensure that the unit-dose packaging of Aricept RDT is different from the unit-dose packaging of Aricept.
2. The color for both the 5 mg and 10 mg blister is the same. Consider implementing a method to distinguish between two strengths, i.e. contrasting color, boxing or other method to provide differentiation. Revise accordingly.

B. BLISTER LABEL (5 mg and 10 mg)

1. See General Comments.
2. Revise the label to read "tablet" rather than "tablets", since only one tablet is contained in each blister.

C. POUCH LABEL (5 mg and 10 mg)

1. See General Comments.
2. We note that the Aricept RDT blisters are packaged in a pouch. If this is for stability, it is unlikely that the blisters will remain in the pouch, particularly in an in-patient setting where medications are delivered to the nursing units in unit-dose packaging. Additionally, there are no directions to the patient/health care practitioner that indicate that the product must remain in the pouch. Please elaborate.
3. Decrease the prominence of the manufacturing and marketing information.

C. CARTON LABELING (5 mg and 10 mg)

1. See General Comments.
2. We note that this carton containing 30 tablets appears to be "Unit-of-Use" packaging. Please indicate whether the carton is child-resistant.

D. INSERT LABELING

No comments.

IV. RECOMMENDATIONS:

- A. DMETS has no objections to the use of the proprietary name. This is considered a tentative decision and the firm should be notified that this name with its associated labels and labeling must be re-evaluated approximately 90 days prior to the expected approval of the NDA. A re-review of the name prior to NDA approval will rule out any objections based upon approvals of other proprietary and established names from the signature date of this document.
- B. DMETS recommends implementation of the label and labeling revisions outlined in section III of this review that might lead to safer use of the product. We would be willing to revisit these issues if the Division receives another draft of the labeling from the manufacturer.
- C. DDMAC finds the proprietary name Aricept RDT acceptable from a promotional perspective.

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 Sammie Beam, project manager, at 301-827-3242.

Linda M. Wisniewski, RN
Safety Evaluator
Division of Medication Errors and Technical Support
Office of Drug Safety

Concur:

Denise P. Toyer, PharmD.
Team Leader
Division of Medication Errors and Technical Support
Office of Drug Safety

Appendix A:

Aricept RDT

NDA: 21-720

ODS Consult: 04-0049

Voice	Inpatient	Outpatient
Aerocept RDT	Aricept	Aricept
Airasept RDT	Aricept	Aricept - RDT
Aracept RDT	Aricept	Aricept RDS
Aricept DBT	Aricept	Aricept RDT
Aricept RDT	Aricept RDT	Aricept RDT
Aricept RDT	Aricept RDT	Aricept RDT
Aricept RDT	Aricept RDT	Aricept RDT
Aricept RDT	Aricept RDT	Aricept RDT
Aricept RDT	Aricept RDT	Aricept RDT
Aricept RDT	Aricept RDT	Aricept RDT
Aricept RDT	Aricept RDT	Aricept RDT
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		Aricept-RDT
		Aricept-RDT
		Aricept-ROT
		Aucipt ROT



7/2/04

NDA 21-720

Eisai Medical Research Inc
Attention: Charles Callaghan
Glenpointe Centre West
500 Frank W. Bur Blvd
Teaneck, NJ 07666

Dear Mr. Callaghan:

Please refer to your December 17, 2003 new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Aricept® RDT.

Our reviews of the Nomenclature proposal by this Division and the Division of Medication Errors and Technical Support (DMETS) are complete. We have identified the following deficiencies.

1. The proposed name Aricept RDT (donepezil hydrochloride rapidly disintegrating tablets) is not acceptable. As an alternative, it would be acceptable to change the name to Aricept ODT (donepezil hydrochloride orally disintegrating tablets).
2. DMETS has recommended the implementation of the following label revisions in order to minimize potential errors with the use of the product.

GENERAL COMMENT

1. In order to minimize confusion between dosage forms, please ensure that the unit-dose packaging of Aricept RDT is different from the unit-dose packaging of Aricept.
2. The color for both the 5 mg and 10 mg blister is the same. Consider implementing a method to distinguish between two strengths, i.e. contrasting color, boxing or other method to provide differentiation. Revise accordingly.

BLISTER LABEL (5 mg and 10 mg)

1. See General Comments.
2. Revise the label to read "tablet" rather than "tablets", since only one tablet is contained in each blister.

POUCH LABEL (5 mg and 10 mg)

1. See General Comments.
2. We note that the Aricept RDT blisters are packaged in a pouch. If this is for stability, it is unlikely that the blisters will remain in the pouch, particularly in an in-patient setting where medications are delivered to the nursing units in unit-dose packaging. Additionally, there are no directions to the patient/health care practitioner that indicate that the product must remain in the pouch. Please elaborate.
3. Decrease the prominence of the manufacturing and marketing information.

CARTON LABELING (5 mg and 10 mg)

1. See General Comments.
2. We note that this carton containing 30 tablets appears to be "Unit-of-Use" packaging. Please indicate whether the carton is child-resistant.

Based on the above recommendations please submit revised carton and container labels (black & white are acceptable).

If you have any questions, call Melina Griffis, R. Ph, Senior Regulatory Project Manager, at (301) 594-5526.

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
7/2/04 08:16:28 AM



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

FILING COMMUNICATION

2/13/04

NDA 21-720

Eisai Medical Research Inc
Attention: Charles Callaghan
Glenpointe Centre West
500 Frank W. Bur Blvd
Teaneck, NJ 07666

Dear Mr. Callaghan:

Please refer to your December 17, 2003 new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Aricept® RDT 5 mg and 10 mg.

We have completed our filing review and have determined that your application is sufficiently complete to permit a substantive review. Therefore, this application has been filed under section 505(b) of the Act on February 15, 2004 in accordance with 21 CFR 314.101(a).

Additionally, we request that you submit the following information:

1. An additional set of review volumes for the CMC section.
2. The dissolution method development report for Aricept rapidly disintegrating tablets. This report should include dissolution in three dissolution media (different pH). If this data has already been submitted, please indicate the location and provide a desk copy of the volume.
3. To facilitate the review process, please provide the following dissolution data in an electronic format:
 - a) data from the bioequivalence batches
 - b) data from the full scale batches

Please respond only 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.

NDA 21-720

Page 2

If you have any questions, call Melina Griffis, R.Ph., Sr. Regulatory Project Manager, at (301) 301-594-5526.

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
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