CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-853

21654s016

PROPRIETARY NAME REVIEW(S)

CONSULTATION RESPONSE

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

DATE RECEIVED: 02/18/04	**DESIRED COMPLETION DATE:** 04/09/04 **PDUFA DATE:** 11/12/04	**ODS CONSULT #:** 04-0042

TO: David G. Orloff, M.D.
Director, Division of Metabolic and Endocrine Drug Products
HFD-510

THROUGH: Valerie Jimenez
Project Manager
HFD-510

PRODUCT NAME: **Omacor** (Omega-3-Acid Ethyl Ester Capsules) 1 gram **NDA #:** 21-654	**NDA SPONSOR:** Ross Products Division, Abbott Laboratories

SAFETY EVALUATOR: Jinhee L. Jahng, Pharm.D.

RECOMMENDATIONS:

1. DMETS does not recommend the use of the proprietary name, Omacor.

2. DMETS recommends implementation of the label and labeling revisions outlined in section III of this review in order to minimize potential errors with the use of this product.

3. DDMAC finds the proprietary name, Omacor, acceptable from a promotional perspective.

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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: April 2, 2004

NDA #: 21-254

NAME OF DRUG: Omacor (Omega-3-Acid Ethyl Ester Capsules)
1 gram

NDA HOLDER: Ross Products Division, Abbott Laboratories

I. INTRODUCTION:

This consult was written in response to a request from the Division of Metabolic and Endocrine Drug Products (HFD-510), for assessment of the proprietary name, "Omacor", regarding potential name confusion with other proprietary or established drug names. Container labels and insert labeling were provided for review and comment.

PRODUCT INFORMATION

Omacor (Omega-3-acid ethyl ester capsules), a lipid-regulating agent, may reduce the synthesis of TG's in the liver because eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) are poor substrates for the enzymes responsible for TG synthesis, and EPA and DHA inhibit esterification of other fatty acids. The mechanism of action of Omacor is not completely understood. Omacor is indicated in adjunct to diet to reduce the triglyceride (TG) levels in adult patients with Fredrickson and Lees' type [redacted] V hyperlipidemia. Omacor reduces TG levels when used as monotherapy or when used in conjunction with HMG-CoA reductase inhibitors. The daily dose of Omacor is 4 grams per day. The daily dose may be taken as a single 4 gram dose or as two 2 gram doses. Omacor capsules will be supplied as 1 gram transparent soft-gelatin capsules in bottles of 120 count. b(4)

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 databases[3] for existing drug names which sound-alike or look-alike to Omacor to a degree where potential confusion between

[1] MICROMEDEX Integrated Index, 2003, 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] AMF Decision Support System [DSS], the Division of Medication Errors and Technical Support [DMETS] database of Proprietary name consultation requests, New Drug Approvals 98-03, and the electronic online version of the FDA Orange Book.

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 conducted[4]. The Saegis[5] 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 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, Omacor. 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 proprietary name, Omacor, acceptable from a promotional perspective.

2. The Expert Panel identified two proprietary names that were thought to have the potential for confusion with Omacor. These products are listed in Table 1 (see page 4), along with the dosage forms available and usual dosage.

[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

Table 1: Potential Sound-Alike/Look-Alike Names Identified by DMETS Expert Panel

Product Name	Dosage form(s), Established name	Usual adult dose*	Other**
Omacor	Omega-3-Acid Ethyl Ester Capsules 1 gram	4 grams per day.	
Inocor (not marketed)	Inamrinone Lactate Injection 5 mg/mL	For congestive heart failure: 0.75 milligram/kilogram intravenous bolus dose over 2 to 3 minutes, followed by a maintenance infusion of 5 to 10 micrograms/kilogram/minute. Doses up to 40 mcg/kg/min have been used for acute management of severe refractory congestive heart failure.	LA
Amicar	Aminocaproic Acid Injection 250 mg/mL Aminocaproic Acid Syrup 1.25 gram/5 mL Aminocaproic Acid Tablets 500 mg	16 to 20 mL (4 to 5 g) in 250 mL of diluent administered by infusion during the first hour of treatment, followed by a continuing infusion at a rate of 4 mL (1 g) per hour in 50 mL of diluent. 10 tablets (5 g) or 4 teaspoonfuls of syrup (5 g) administered during the first hour of treatment, followed by a continuing rate of 2 tablets (1 g) or 1 teaspoonful of syrup (1.25 g) per hour. Treatment would ordinarily be continued for about 8 hours or until the bleeding situation has been controlled.	SA/LA

*Frequently used, not all-inclusive.
**L/A (look-alike), S/A (sound-alike)

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. All names considered to have significant phonetic or orthographic similarities to Omacor were discussed by the Expert Panel (EPD).

C. 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 Omacor 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 Omacor (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
Outpatient RX: Omacor 2 caps BID #120	Omacor Take 2 capsules bid #120
Inpatient RX: Omacor 2 pb BID	

2. Results:

   Most of the interpretations of the proposed name did not overlap, sound similar, or look similar to any currently marketed U.S. product. However, one of the misinterpreted names from the inpatient prescription study, Amacor, resembles the currently marketed U.S. product, Amicar. Many of the incorrect name interpretations were misspelled/phonetic variations of "Omacor". See Appendix A for the complete listing of interpretations from the verbal and written studies.

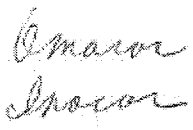
D. SAFETY EVALUATOR RISK ASSESSMENT

In reviewing the proprietary name, Omacor, the primary concerns related to look-alike and sound-alike confusion with Inocor and Amicar.

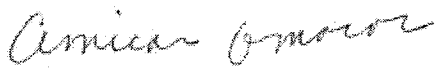
Additionally, DMETS conducted prescription studies to simulate the prescription ordering process. In this case, there was no confirmation that the proposed name could be confused with any of the aforementioned names. The majority of misinterpretations were misspelled/phonetic variations of the proposed name, Omacor. However, negative findings are not predicative as to what may occur once the drug is widely prescribed, as these studies have limitations primarily due to a small sample size.

1. Inocor has the potential to look like Omacor. Inocor is a prescription product which was discontinued in March 2000 and is no longer marketed in the United States. Inocor contains inamrinone, a phosphodiesterase inhibitor with positive inotropic and vasodilator activity. Inamrinone is used for the treatment of severe acute congestive heart failure refractory to other treatment modalities, including digitalis glycosides and vasodilators. Inocor and Omacor begin with letters which resemble each other when scripted ("Ino-" vs. "Oma-"), and they share the same suffix, "-cor" (see page 6). The products differ in strength (5 mg/mL vs. 1 gram), dosage form (injectable vs. capsule), route of administration (intravenous vs. oral), and dosing schedule. Although it was determined that the name Inocor is still available in the online version of MICROMEDEX, the name is not listed in the online Physicians Desk Reference, Drugstore.com, Destinationrx.com, 2003 Red Book, and Drug Facts and Comparisons. The generic product, inamrinone (a.k.a. amrinone) is available in the United States. Had the discontinuation date been more recent, the potential for generic substitution of Inocor might have raised some concerns. However, DMETS believes the potential for generic substitution is remote given its discontinuation

date. DMETS believes that the differences between the two drugs, coupled with the information that Inocor is no longer marketed in the United States, minimize the potential for confusion and error between Inocor and Omacor.



2. Amicar and Omacor were found to have look-alike and sound-alike similarities to one another. Amicar (aminocaproic acid) is a hemostatic agent that prevents the conversion of plasminogen to plasmin. Amicar is useful in enhancing hemostasis when fibrinolysis contributes to bleeding. Both Amicar and Omacor have three syllables and share similar sounds ("Am-" vs. "Om-" and "-car" vs. "-cor"). Additionally, they each have six letters and the prefixes, "Ami-" vs. "Oma-", as well as the suffixes, "-car" vs. "-cor", which resemble each other when scripted (see below). A loading dose of 4 to 5 grams of Amicar is administered followed by 1 gram doses every hour as needed for about 8 hours or until the bleeding situation is controlled. Amicar is available for oral or intravenous use. Similarly, Omacor has a daily dose of 4 grams which is administered orally. Confusion and error may occur if a verbal or written prescription order for "Amicar 4 grams" is misinterpreted for "Omacor 4 grams" or vice versa. Routes of administration are often omitted and the overlapping characteristics of Amicar and Omacar are significant. The opportunities for errors are likely in any situation where the prescriber communication is unclear or incomplete to the practitioners interpreting the medication order. Especially of concern is the fact that both products are available in only one strength, in which case a prescriber would not necessarily have to specify the product strength. A patient inadvertently receiving Amicar instead of Omacor may be subject to hypotension, heart failure, rhabdomyolysis, seizures, myopathy, renal failure, thrombosis formation, bleeding, and hepatic failure. On the contrary, inadvertent administration of Omacor instead of Amicar may subject the patient to an unresolved bleeding event and taste perversion. Any interruption in therapy is undesirable and should be prevented if possible. DMETS believes a likelihood for a dispensing error with Amicar and Omacor is likely.



Amicar Omacor

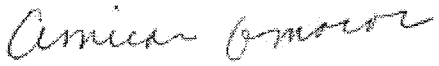
III. COMMENTS TO THE SPONSOR:

DMETS does not recommend the use of the proprietary name, Omacor.

A. In reviewing the proprietary name, the primary concerns related to look-alike and sound-alike confusion with Amicar.

Amicar and Omacor were found to have look-alike and sound-alike similarities to one another. Amicar (aminocaproic acid) is a hemostatic agent that prevents the conversion of plasminogen to plasmin. Amicar is useful in enhancing hemostasis when fibrinolysis contributes to bleeding. Both Amicar and Omacor have three syllables and share similar sounds ("Am-" vs. "Om-" and "-car" vs. "-cor"). Additionally, they each have six

letters and the prefixes, "Ami-" vs. "Oma-", as well as the suffixes, "-car" vs. "-cor", which resemble each other when scripted (see below). A loading dose of 4 to 5 grams of Amicar is administered followed by 1 gram doses every hour as needed for about 8 hours or until the bleeding situation is controlled. Amicar is available for oral or intravenous use. Similarly, Omacor has a daily dose of 4 grams which is administered orally. Confusion and error may occur if a verbal or written prescription order for "Amicar 4 grams" is misinterpreted for "Omacor 4 grams" or vice versa. Routes of administration are often omitted and the overlapping characteristics of Amicar and Omacar are significant. The opportunities for errors are likely in any situation where the prescriber communication is unclear or incomplete to the practitioners interpreting the medication order. Especially of concern is the fact that both products are available in only one strength, in which case a prescriber would not necessarily have to specify the product strength. A patient inadvertently receiving Amicar instead of Omacor may be subject to hypotension, heart failure, rhabdomyolysis, seizures, myopathy, renal failure, thrombosis formation, bleeding, and hepatic failure. On the contrary, inadvertent administration of Omacor instead of Amicar may subject the patient to an unresolved bleeding event and taste perversion. Any interruption in therapy is undesirable and should be prevented if possible. DMETS believes a likelihood for a dispensing error with Amicar and Omacor is likely.



Amicar Omacor

B. In the review of the container labels and insert labeling of Omacor, 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.

1. CONTAINER LABEL

   a. We recommend that the established name be printed in letters that are at least half as large as the proprietary name to be in accordance with 21 CFR 201.10 (g)(2).

   b. The product strength should appear immediately following or below the established name and be more prominent on the label.

   c. Relocate the net quantity (ex. "120 Capsules") away from the product strength.

   d. We are unable to identify from the submitted materials that the container closure is child resistant. However, the packages should include Child Resistant Closures (CRC).

2. INSERT LABELING

   No comments.

IV. RECOMMENDATIONS:

A. DMETS does not recommend the use of the proprietary name, Omacor.

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, Omacor, 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.

Jinhee L. Jahng, Pharm.D.
Safety Evaluator
Division of Medication Errors and Technical Support
Office of Drug Safety

Concur:

Alina R. Mahmud, R.Ph.
Team Leader
Division of Medication Errors and Technical Support
Office of Drug Safety

Appendix A – DMETS Prescription Study Results

Inpatient	Voice	Outpatient
Omacor	Onacor	Omacor
Omacor	Onacor	Omaquar
Omacor	Onacor	Omaquar
Omacor	Omacor	Avocor
Omacor	Onacor	Omacor
Omacor	Onacor	Omacor
Omacor	Onacor	Omacor
Omacir	Oracor	Omocore
Omacar	Onacor	Emacor
Omacor	Onacor	Omacor
Omacor	Onacor	Omacor
Amacor	Onacor	Omicor
Omacir	Omacor	Omicor
Omacor	Onacor	Omaquar
omacor	Omacor	Omacor
Omacor	Onacor	Omaquar
Omacor	Onacor	Omacor
Omacor	Onacor	Omacor
Omacer	Onacor	Omacor
Omacor	Onacor	Omacore
Omacor	Onacor	Omacor
Omacor	Onacor	Omacor
Omacor	Omacor	Omacor
	Onacor	
	Oracor	

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/s/

Jinhee Jahng
4/21/04 11:29:04 AM
DRUG SAFETY OFFICE REVIEWER

Alina Mahmud
4/21/04 11:36:45 AM
DRUG SAFETY OFFICE REVIEWER

Carol Holquist
4/23/04 07:52:18 AM
DRUG SAFETY OFFICE REVIEWER

Jerry Phillips
4/27/04 07:52:21 AM
MEDICAL OFFICER

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

REQUEST FOR CONSULTATION

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

FROM: Valerie Jimenez, HFD-510
(301) 827-9090

DATE	IND NO.	NDA NO.	TYPE OF DOCUMENT	DATE OF DOCUMENT
February 6, 2004		21-654	New NDA	January 9, 2004

NAME OF DRUG	PRIORITY CONSIDERATION	CLASSIFICATION OF DRUG	DESIRED COMPLETION DATE
Omacor (omega-3-acid ethyl ester)	Standard	Lipid Altering (5)	June 1, 2004

NAME OF FIRM: Ross Products Division, Abbott Laboratories

REASON FOR REQUEST

I. GENERAL

- ☐ NEW PROTOCOL
- ☐ PROGRESS REPORT
- ☐ NEW CORRESPONDENCE
- ☐ DRUG ADVERTISING
- ☐ ADVERSE REACTION REPORT
- ☐ MANUFACTURING CHANGE/ADDITION
- ☐ MEETING PLANNED BY
- ☐ PRE–NDA MEETING
- ☐ END OF PHASE II MEETING
- ☐ RESUBMISSION
- ☐ SAFETY/EFFICACY
- ☐ PAPER NDA
- ☐ CONTROL SUPPLEMENT
- ☐ RESPONSE TO DEFICIENCY LETTER
- ☐ FINAL PRINTED LABELING
- ☐ LABELING REVISION
- ☐ ORIGINAL NEW CORRESPONDENCE
- ☐ FORMULATIVE REVIEW
- ☒ OTHER *(SPECIFY BELOW)*: Trade name review

II. BIOMETRICS

STATISTICAL EVALUATION BRANCH	STATISTICAL APPLICATION BRANCH
☐ TYPE A OR B NDA REVIEW ☐ END OF PHASE II MEETING ☐ CONTROLLED STUDIES ☐ PROTOCOL REVIEW ☐ OTHER (SPECIFY BELOW):	☐ CHEMISTRY REVIEW ☐ PHARMACOLOGY ☐ BIOPHARMACEUTICS ☐ OTHER (SPECIFY BELOW):

III. BIOPHARMACEUTICS

- ☐ DISSOLUTION
- ☐ BIOAVAILABILTY STUDIES
- ☐ PHASE IV STUDIES
- ☐ DEFICIENCY LETTER RESPONSE
- ☐ PROTOCOL-BIOPHARMACEUTICS
- ☐ IN-VIVO WAIVER REQUEST

IV. DRUG EXPERIENCE

- ☐ PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL
- ☐ DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES
- ☐ CASE REPORTS OF SPECIFIC REACTIONS (List below)
- ☐ COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP
- ☐ REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY
- ☐ SUMMARY OF ADVERSE EXPERIENCE
- ☐ POISON RISK ANALYSIS

V. SCIENTIFIC INVESTIGATIONS

- ☐ CLINICAL
- ☐ PRECLINICAL

COMMENTS, CONCERNS, and/or SPECIAL INSTRUCTIONS:
We are requesting your comments for a new molecular entity, "OMACOR".
Please call if additional information is needed, Valerie Jimenez, Regulatory Project Manager, (301) 827-9090.

PDUFA DATE: November 12, 2004
ATTACHMENTS: Draft Package Insert
Container Labels

SIGNATURE OF REQUESTER	METHOD OF DELIVERY (Check one) ☐ MAIL X HAND
SIGNATURE OF RECEIVER	SIGNATURE OF DELIVERER

9 Page(s) Withheld

_____ Trade Secret / Confidential (b4)

✓ Draft Labeling (b4)

_____ Draft Labeling (b5)

_____ Deliberative Process (b5)

Withheld Track Number: Proprietary Name Review- 1

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/s/

Valerie Jimenez
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