

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

BLA 125164

PROPRIETARY NAME REVIEW(S)

CONSULTATION RESPONSE

**DIVISION OF MEDICATION ERRORS AND TECHNICAL SUPPORT
OFFICE OF SURVEILLANCE AND EPIDEMIOLOGY
(DMETS; WO22, M/S 4447)**

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TO: George Q. Mills, M.D.
Director, Division of Medical Imaging and Hematology Products

THROUGH: Alina Mahmud, R.Ph., M.S., Team Leader *Alina Mahmud 10/5/06*
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Division of Medication Errors and Technical Support

FROM: Laura Pincock, Pharm.D., Safety Evaluator *Laura Pincock 10/5/06*
Division of Medication Errors and Technical Support

PRODUCT NAME: **Mircera**
(Pegserepoetin Alfa)
Vials: 50, 100, 200, 300, 400, 600, or 1000 mcg in 1 mL solution
Syringes: 50, 75, 100, 150, 200, 250, or 400 mcg in 0.3 mL solution
and 600 or 800 mcg in 0.6 mL solution

BLA#: **125164/0 (IND# 10,158)**

BLA SPONSOR: Hoffman La-Roche Inc.

RECOMMENDATIONS:

1. DMETS has no objections to the use of the proprietary name, Mircera. 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 BLA. A re-review of the name 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 container labels, carton, package insert and patient information 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, Mircera, 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 Diane Smith, Project Manager, at 301-796-0538.

Division of Medication Errors and Technical Support (DMETS)
Office of Surveillance and Epidemiology
HFD-420; WO22, Mailstop, 4447
Center for Drug Evaluation and Research

PROPRIETARY NAME, LABEL, AND LABELING REVIEW

DATE OF REVIEW: June 2, 2006

BLA#: 125164/0 (IND# 10,158)

NAME OF DRUG: Mircera (Pegserepoetin Alfa)
Vials: 50, 100, 200, 300, 400, 600, or 1000 mcg/mL
Syringes: 50, 75, 100, 150, 200, 250, or 400 mcg/0.3 mL and
600 or 800 mcg/0.6 mL

BLA HOLDER: Hoffman La-Roche, Inc.

I. INTRODUCTION:

This consult was written in response to a request from the Division of Medical Imaging and Hematology Products for a review of the proprietary name, "Mircera", regarding potential name confusion with other proprietary and/or established drug names. The Sponsor has submitted the labels and labeling for review and comment.

PRODUCT INFORMATION

Mircera (Pegserepoetin Alfa) is a polymer-based erythropoietic compound that activates the erythropoietin receptors. Mircera is proposed for the treatment of anemia associated with chronic kidney disease including patients on dialysis and patients not on dialysis. Mircera will be administered intravenously or subcutaneously, once every 2 weeks or once every month. The proposed dose and dosage interval is as follows:

For patients not currently treated with an erythropoiesis stimulating agent:

0.6 mcg/kg body weight administered as a single IV or SC injection once every two weeks.

For patients currently treated with an erythropoiesis stimulating agent:

When converting from epoetin alfa or darbepoetin alfa, Mircera can be administered once monthly, or if desired, once every two weeks. The dose of Mircera, given as a single IV or SC injection, should be based on the total weekly epoetin or darbepoetin alfa dose at the time of conversion.

Conversion from Epoetin Alfa

Previous Weekly Epoetin Alfa Dose (units/week)	Mircera Dose	
	Once Monthly (mcg/month)	Once every Two Weeks (mcg/every 2 weeks)
<8000	120	60
8000-16000	200	100
>16000	360	180

Conversion from Darbepoetin Alfa

Previous Weekly Darbepoetin Alfa Dose (units/week)	Mircera Dose	
	Once Monthly (mcg/month)	Once every Two Weeks (mcg/every 2 weeks)
<40	120	60
40-80	200	100
>80	360	180

Mircera will be available in single-use vials and single-use prefilled syringes. The vial caps and plungers of prefilled syringes are color coded for identification. The prefilled syringes will be supplied with a 27 gauge, ½ inch needle. Each prefilled syringe is equipped with a needle guard that covers the needle during disposal.

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^{3,4} for existing drug names which sound-alike or look-alike to Mircera 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 conducted⁵. The SAEGIS™ Online service⁶ 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.

¹ MICROMEDEX Integrated Index, 2006, 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, Missouri.

³ AMF Decision Support System [DSS], the Division of Medication Errors and Technical Support [DMETS] database of Proprietary name consultation requests, New Drug Approvals 98-06, and the electronic online version of the FDA Orange Book.

⁴ Phonetic and Orthographic Computer Analysis

⁵ www location <http://www.uspto.gov/tmdb/index.html>.

⁶ Data provided by Thomson & Thomson's SAEGIS™ Online service, available at www.thomson-thomson.com

A. EXPERT PANEL DISCUSSION (EPD)

An Expert Panel discussion was held by DMETS to gather professional opinions on the safety of the proprietary name Mircera. 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 did not have concerns with the name, Mircera, in regard to promotional claims.
2. The Expert Panel identified eight proprietary names that were thought to have the potential for confusion with Mircera. These products are listed in Table 1 (pages 4-5), along with the dosage forms available and usual dosage.

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

Product Name	Dosage forms	Established name	Usual adult dose	Other
Mircera	<p>Precedent in Alfa Vials: 50, 100, 200, 400, 500, or 1000 mcg/mL</p> <p>Syringes: 50, 75, 100, 150, 200, 250, or 400 mcg/0.5 mL and 500 or 800 mcg/0.5 mL</p> <p>Stored in refrigerator at 2 to 8 degrees C</p>		<p>For patients not currently treated with an erythropoiesis stimulating agent: 600 mcg/kg body weight administered as a single IV or SC injection once every two weeks.</p> <p>For patients currently treated with an erythropoiesis stimulating agent: When converting from epoetin alfa or darbepoetin alfa, Mircera can be administered once monthly or if cleared, once every two weeks. The dose of Mircera, given as a single IV or SC injection, should be based on the total weekly epoetin or darbepoetin alfa dose at the time of conversion. (See conversion chart on page 4)</p>	N/A
Mirena	<p>Levonorgestrel Intrauterine Device: 52 mg/device (releases 20 mcg/day)</p>		To be inserted into uterine cavity; should be inserted within 7 days of onset of menstruation or immediately after 1st trimester abortion; releases 20 mcg levonorgestrel/day over 5 years. May be removed and replaced with a new unit at anytime during menstrual cycle.	LA
Minirin	<p>Desmopressin Acetate Nasal Spray, Metered: 0.1 mg/mL (5 mL spray pump bottle contains 50 doses of 10 mcg)</p> <p>Stored in refrigerator at 2 to 8 degrees C</p>		The recommended starting dose for those > 6 years of age: 20 mcg (2 sprays=1 spray per nostril) intranasally at bedtime. Adjust dose upward to 40 mcg if patient does not respond. Some patients will respond to 10 mcg and dose reduction may be done if patient responds.	LA

Product Name	Dosage form(s) / Established name	Usual adult dose	ONH
Micelle	Vitamin E product Capsules: 100, 200, 300, 400, 600, 800 IU Syringes: 50, 75, 100, 200, 250, 400 mg Oral emulsion: 100, 200, 400 mg	1000 IU daily 100 mg of active ingredient as a single dose or in divided doses every two weeks	
Micelle E	Vitamin E product Foreign product marketed in New Zealand, Australia	Additional information not available	SA
Micetal	Flutrimazole 1% cream, gel, powder, or solution Topical foreign product marketed in Mexico, Spain, Chile, Hungary, Czech Republic, Europe	Additional information not available	LA
Maxair	Pirbuterol Acetate Autohaler Inhaler: 0.2 mg/actuation	<u>Adults and adolescents:</u> the recommended dosage is 2 inhalations (0.4 mg) from a metered-dose inhaler every 4–6 hours. A lower dosage of 1 inhalation (0.2 mg) every 4–6 hours may be sufficient for some patients.	SA
Mircette	Ethinyl Estradiol (EE) Desogestrel White tablets: 0.15 mg Desogestrel/ 20 mcg EE Green tablets: inert Yellow tablets: 10 mcg EE	<u>Adult and adolescent females:</u> 1 tablet orally once daily for 28 days; first as white tablets for 21 days, then 2 green tablets, and then followed by 5 yellow tablets.	SA
Mucinex Mucinex D Mucinex DM OTC	Guaifenesin Extended-release Tablets (Mucinex): 600 mg Extended-release Tablets (Mucinex D): 600 mg with 60 mg pseudoephedrine Extended-release Tablets (Mucinex DM): 600 mg with 30 mg dextromethorphan	<u>Adults and children 12 years of age and over:</u> One or two tablets every 12 hours. (Mucinex D is two tablets every 12 hours) Do not exceed 4 tablets in 24 hours.	LA
Minocin	Minocycline Hydrochloride Capsules: 50 mg and 100 mg	Dose varies due to indication and severity of infection: 50 mg, 100 mg, or 200 mg by mouth every 12 hours	

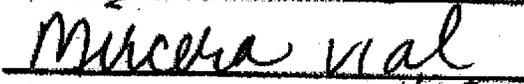
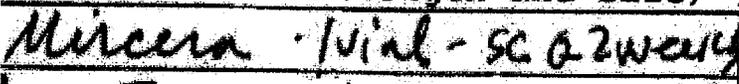
*Frequently used, not all-inclusive.

**LA (look-alike); SA (sound-alike)

B. 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 Mircera 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. Two requisition orders were written, each consisting of a combination of marketed and unapproved drug products and a prescription for Mircera (see below). These prescriptions were optically scanned and one prescription was delivered to a random sample of the participating health professionals via e-mail. In addition, one order was 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 requisition orders, the participants sent their interpretations of the orders via e-mail to the medication error staff.

HANDWRITTEN REQUISITION ORDERS	VERBAL ORDER
<p>Requisition Sample 1:</p> 	<p>"Mircera, 1 vial, give subcutaneously every 2 weeks"</p>
<p>Requisition Sample 2:</p> 	

2. Results:

One respondent from the verbal study interpreted the proposed name, Mircera, as the word "laser". However, DMETS does not consider this to be a safety issue. None of the interpretations of the proposed name overlap, sound similar, or look similar to any currently marketed U.S. product. See Appendix A for the complete listing of interpretations from the verbal and written studies.

C. SAFETY EVALUATOR RISK ASSESSMENT

In reviewing the proprietary name Mircera, the primary concerns were related to the look-alike and/or sound-alike properties with the names Mirena, Minirin, Micelle E, Micetal, Maxair, Mircette, Mucinex, and Minocin .

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, Mircera. We also note that one respondent from the verbal study interpreted the proposed name, Mircera, as the word "laser". However, DMETS does not consider this to be a safety issue.

DMETS would like to acknowledge that a search found two look and sound-alike medication marketed in other countries, Micetal – Mexico, Spain, Chile, Hungary, Czech Republic, Europe and, Micelle E – New Zealand and Australia. Although these two names share some look and sound-alike similarities with Mircera, DMETS believes the actual possibility for confusion with these product names to be minimal due to the area of marketing. Furthermore, it is difficult to ascertain how or when an error would occur with these foreign products given the variance in drug distribution laws outside of the United States.

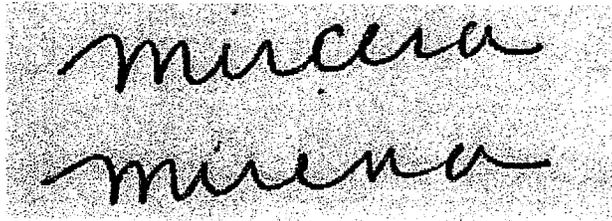
Upon initial review of Maxair, Mircette, Mucinex, and Minocin, it was determined that these names lack convincing look-alike/sound-alike similarities with Mircera, in addition to numerous different product characteristics such as the product strength, route of administration, indication for use, frequency of administration, and/or dosage formulation and thus will not be discussed further in this review.

Upon review of the remaining names of concern we have the following comments.

1. Mirena was identified as a name that may look similar to Mircera. Mirena is the proprietary name for an intrauterine device which releases levonorgestrel and is intended to prevent pregnancy. Mirena is inserted by a healthcare professional and may be left in place for up to 5 years.

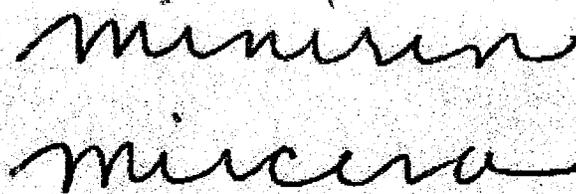
The names Mirena and Mircera share the same beginning 'Mir-' and both end with the letter 'a' which contributes to the look alike properties. However, the scope of use and patient population for these two products are different and are not expected to overlap. Mirena is used for birth control in healthy women of child-bearing age, whereas Mircera will be used to treat anemia in patients with chronic kidney disease who may or may not be on dialysis. Additionally, Mirena is inserted by a healthcare professional who is familiar with its use and is not stocked by pharmacies for dispensing directly to patients, whereas Mircera is administered intravenously or subcutaneously, under the supervision of a healthcare provider. Thus, it is not likely for both products to be stored in the same location and dispensed to patients which decreases the potential for confusion between the two names. Furthermore, prescriptions written for Mircera will require a package strength and size due to the multiple strengths, sizes, and packaging available. Additional information on the prescription such as directions for use, route of administration, and frequency for use (i.e., inject 200

microgram subcutaneously every month) would help to differentiate a prescription for Mircera from a prescription for Mirena. Therefore, the unique administration product characteristics for both Mirena and Mircera make it unlikely the products would be confused.



2. Minirin was identified as a name that may look similar to Mircera. Minirin is the tradename for a prescription Desmopression Acetate metered nasal spray used for the treatment of primary nocturnal enuresis and central cranial diabetes insipidus.

The names share the same beginning letters 'Mi-' and the middle part of each name (-cer- vs. nir-) can look similar when scripted. Minirin is available in the one package size of nasal spray, thus it is possible for prescriptions for Minirin to be ordered without a strength or package size and without additional directions for use (i.e. Minirin, dispense one, use as directed). However, Mircera has several strengths, sizes and packaging configurations available (vials and syringes) so prescriptions for Mircera will require additional information before dispensing the product. Furthermore, Mircera is to be administered under the supervision of a healthcare provider. It is possible for a patient to self-administer Mircera, however the patient will need to be instructed how to prepare and inject the dose themselves. The unique product characteristics and method of administration for Mircera make it unlikely to be confused with Minirin.



5 Page(s) Withheld

 Trade Secret / Confidential

X Draft Labeling

 Deliberative Process

Withheld Track Number: Administrative-10

X A – DMETS Prescription Study Results for Mircera

Inpatient

Mirce
Mircera
Mircera
Mircera
Mircera
Mircera
Mircera
Mirce
Mircera
Mircera
Mircera
Mircera
Mircera
Mircera
Mercera

Outpatient

Mircera
Mircera
Mircera
Mircera
Mircera
Mircera
Mircera
Mirce
Mircera
Mirceva

Voice

Mersera
Mersera
Mersera
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