CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-990

PROPRIETARY NAME REVIEW(S)

CONSULTATION RESPONSE

DIVISION OF MEDICATION ERRORS AND TECHNICAL SUPPORT
OFFICE OF SURVEILLANCE AND EPIDEMIOLOGY
(DMETS; WO22, Mail Stop Room 4447)

DATE RECEIVED:	**DESIRED COMPLETION DATE:**	**OSE CONSULT #:** 05-0313
November 18, 2005	May 16, 2006	
DATE OF DOCUMENT:		
November 2, 2005		

TO: Norman Stockbridge, MD
Director, Division of Cardiovascular and Renal Products
HFD-110

THROUGH: Linda Kim-Jung, PharmD, Team Leader
Denise Toyer, PharmD, Deputy Director
Carol Holquist, RPh, Director
Division of Medication Errors and Technical Support

FROM: Kristina C. Arnwine, PharmD, Safety Evaluator
Division of Medication Errors and Technical Support

PRODUCT NAME:
Exforge
(Valsartan/Amlodipine Besylate Tablets)
5 mg/160 mg, 5 mg/320 mg, 10 mg/160 mg, and 10 mg/320 mg

IND #: 65,174

IND SPONSOR: Novartis Pharmaceuticals Corporation

RECOMMENDATIONS:

1. DMETS has no objections to the use of the proprietary name, Exforge. 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 upon submission of the NDA and 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. Submit container labels, carton and insert labeling when available for review and comment.

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

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

PROPRIETARY NAME REVIEW

DATE OF REVIEW: January 11, 2006

IND # 65,174

NAME OF DRUG: Exforge (Valsartan/Amlodipine Besylate Tablets)
——— 5 mg/160 mg, 5 mg/320 mg, 10 mg/160 mg, and 10 mg/320 mg

IND HOLDER: Novartis Pharmaceuticals Corporation

I. INTRODUCTION:

This consult was written in response to a request from the Division of Cardiovascular and Renal Products (HFD-110), for assessment of the proprietary name, Exforge, regarding potential name confusion with other proprietary or established drug names. Container labels, carton and insert labeling were not provided for review and comment.

PRODUCT INFORMATION

Exforge is a combination product consisting of amlodipine, a calcium channel blocker, and valsartan, an angiotensin receptor blocker. Exforge is indicated for the treatment of hypertension. The usual dose is one tablet by mouth once daily. Exforge will be available in five fixed-dose combinations of amlodipine and valsartan: ——— 5 mg/160 mg, 5 mg/320 mg, 10 mg/160 mg, and 10 mg/320 mg.

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 Ferinject 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 conducted[5]. The Saegis[6] 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

[1] 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.
[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 98-05, and the electronic online version of the FDA Orange Book.
[4] Phonetic and Orthographic Computer Analysis (POCA)
[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

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 Exforge. 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 objections to the proprietary name, Exforge, from a promotional perspective.

2. The Expert Panel identified one proprietary name that was thought to have the potential for confusion with Exforge. 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

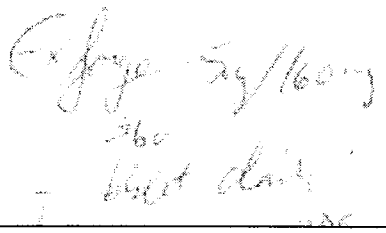
Product Name	Dosage form(s), Established name	Usual adult dose*	Other**
Exforge	Valsartan/Amlodipine Tablets [redacted]5 mg/160 mg, 5 mg/320 mg, 10 mg/160 mg, and 10 mg/320 mg	1 tablet by mouth daily	
Exjade	Desferasirox Tablet for Oral Suspension 125 mg, 250 mg, and 500 mg	20mg/kg/day; doses should be calculated to the nearest whole tablet	LA

*Frequently used, not all-inclusive.
**L/A (look-alike), S/A (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 Exforge 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 125 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 Exforge (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, 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: 	"Next is Exorge is 5mg/ 160 mg. Dispense #60, with the directions one tablet po qd."
Inpatient RX: 	

2. Results:

None of the interpretations of the proposed name overlap, sound similar, or look similar to any currently marketed U.S. product. However, one respondent from the outpatient written study misinterpreted the name as ExLorge, which looks similar to the term extra large or Ex Large. Additionally, one respondent from the verbal study misinterpreted the name as the word export. 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 Exforge, the primary concerns related to look-alike and sound-alike confusion with Exjade.

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. However, negative findings with regard to currently marketed tradenames 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. The majority of misinterpretations were misspelled/phonetic variations of the proposed name, Exforge. However, one respondent from the outpatient written study misinterpreted the name as ExLorge, which look similar to the term extra large or Ex Large. DMETS does not believe the terms extra large or Ex Large can be misconstrued as a drug. Therefore this issue will not be discussed further in this review.

Exforge can look similar to Exjade when scripted. Exjade is an oral iron-chelating agent indicated for use in the treatment of chronic iron overload in patients with transfusion-dependent anemias. The principal contribution to the look-alike characteristics of each name is that both names begin with the same two letters ('Ex'). Additionally, if scripted, Exforge and Exjade both have a downstroke presented at the third letter of each name resulting from the letters 'f' and 'j' respectively (see page 5). However, the endings of each name differ ('orge' vs. 'ade'), which helps to distinguish the two names orthographically. Exforge and Exjade overlap with regard to route of administration (oral), dosage form (**tablet** vs. **tablet** for oral suspension), and dosing frequency (once daily). However, since Exjade is a tablet for oral suspension, it is likely that there will be additional instructions included in the prescription order, such as, "dissolve tablet in water or juice," which may help to distinguish the two products from each other. Since both products are available in multiple strengths, the product strength may help to distinguish the two products as well (———— 5 mg/160 mg, 5 mg/320 mg, 10 mg/160 mg, and 10 mg/320 mg

vs. 125 mg, 250 mg, and 500 mg). Overall, differences between the endings of each name along with the differing conditions of use and product strengths decrease the potential for name confusion between Exforge and Exjade.

Exforge

Exjade

E. INDEPENDENT NAME ANALYSIS

Novartis solicited ———————————————————————, a ———————————————————————, to assess the tradename Exforge. The assessment findings indicate that overall the proposed tradename, Exforge, has low vulnerability for look-alike and sound-alike confusion. The analysis conducted by ———————— did not identify any drug products as potential sound or look-alike products with Exforge. However, a respondent in the ———————— assessment mentioned the medical term 'engorge' as having the potential for look-alike and/or sound-alike confusion with Exforge. ———————— concluded that the aforementioned medical term had a low potential for confusion with Exforge. Following review of the proprietary name analysis submitted by ———————— DMETS concurs that the aforementioned medical term does not pose a significant safety risk. We concur with the overall findings of the study.

Attachment A

Outpatient Written	Inpatient Written	Verbal
Ex forge	Exforge	Exforce
Exfonge	Exforge	Exforge
Exforge	Exforge	Exforge
Exforge	Exforge	Exforge
Exforge	Exforge	Exforge
Exforge	Exforge	Exforge
Exforge	Exforge	Exforge
Exforge	Exforge	Exfort
Exforge	Exforge	ExForte
Exforge	Exforge	Export
Exforge	Exforge	Xforage
ExForge	Exforge	Xforge
Exforge	Exforge	Xforge
Exforge	Exforge	X-forge
Exforge	Exforge	X-Forte
Exforge	Exforge	
Exforge	exforge	
Exforge	Exforge	
ExJorge	Xforage	
ExLorge		
Ex-Sorge		

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/s/

Kristina Arnwine
6/9/2006 04:09:57 PM
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Also signing for Carol Holquist, Director DMETS, in her absence