

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

22-023

PROPRIETARY NAME REVIEW(S)

MEMORANDUM

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

To: Daniel Shames, MD
Director, Division of Gastroenterology Products
HFD-180

Through: Linda Y. Kim-Jung, PharmD, Team Leader
Denise P. Toyer, PharmD, Deputy Director
Carol A. Holquist, RPh, Director
Division of Medication Errors and Technical Support, HFD-420

From: Kristina C. Arnwine, PharmD, Safety Evaluator
Division of Medication Errors and Technical Support, HFD-420

Date: January 3, 2008

Subject: **DMETS Proprietary Name Review**
Drug: Emend (Fosaprepitant Dimeglumine for injection)
NDA#: 22-023
Sponsor: Merck and Company, Inc

Review #: 2007-2383

This review was written in response to a request from the Division of Gastroenterology Products (HFD-180), for a re-review of the proposed proprietary name, Emend, regarding potential name confusion with other proprietary or established drug names. Revised package insert labeling was provided for review and comment. DMETS reviewed the proposed proprietary name, Emend IV for this product under IND # 48,924, in OSE Consults 05-0242 (dated December 1, 2005) and 05-0242-1 (dated December 13, 2005) and found the name Emend IV unacceptable at that time. DMETS' primary concern was the use of the same root name (Emend) for two different drug products with different active ingredients (i.e. Aprepitant and Fosaprepitant Dimeglumine). After discussion between DMETS, ONDQ, and the Division, the Division decided that the name Emend (Fosaprepitant Dimeglumine for Injection), would be acceptable.

A. Look-Alike and Sound-Alike Concerns

Since our previous review of the name, the following additional names have been identified as having a similar appearance and/or sound to Emend: Emadine, Vfend, M-End, and Amen.

Upon initial review of the four names identified as having similar appearance and/or sound to Emend, it was determined that they would not be considered further for the following reasons:

- In addition to lacking orthographic and/or phonetic similarities with Emend; Emadine and Vfend do not share product commonalities such as dosage form, route of administration, product strength, usual dose, dosing frequency, and/or indication of use.

- Amen was identified as drug name with similar appearance and/or sound to Emend. DMETS also notes that in our previous review, OSE review 00-0298-4, DMETS identified one case of name confusion between Emend capsules and Amen. Although there are some similar product characteristics between the Emend capsules and Amen [dosage form (solid oral dosage form), route of administration (oral), and the usual dose of Emend (80 mg) could be achieved with eight Amen 10 mg tablets], the proposed injectable Emend provides for more distinguishing characteristics which should help to minimize the confusion between the Emend product line and Amen. For example, the proposed product differs from Amen with regard to product characteristics such as dosage form (for injection vs. tablet), route of administration (intravenous vs. oral), product strength (115 mg vs. 10 mg), usual dose (115 mg vs. 5 mg to 10 mg), and indication (prevention of chemotherapy induced nausea and vomiting vs. secondary amenorrhea and dysfunctional uterine bleeding). Thus, the differing product characteristics introduced by the proposed product should help to reduce the potential for medication errors.
- M-End was identified as a drug name with similar appearance and/or sound to Emend. DMETS notes that in our previous review, OSE review 00-0298-4, DMETS identified three cases where healthcare practitioners voiced concern regarding the similarity between Emend and M-End, a regional cough and cold product. Emend capsules overlapped with M-End with regard to route of administration (oral). However, conversely, the proposed product differs from M-End with regard to product characteristics such as dosage form (for injection vs. oral solution), route of administration (intravenous vs. oral), product strength (115 mg vs. 2.5 mg/15 mg/2mg/5 mL), usual dose (115 mg vs. 1 teaspoonful to 2 teaspoonful), and indication (prevention of chemotherapy induced nausea and vomiting vs. cough and congestion). Thus, the differing product characteristics introduced by the proposed product should help to reduce the potential for medication errors.

B. Adverse Events Reporting System (AERS)

DMETS initially conducted an AERS search for medication errors associated with Emend capsules in OSE review 00-0298-4, dated June 15, 2006. The search was conducted using the high group level term “medication errors,” and the preferred terms “medication error”, “pharmaceutical product complaint”, “accidental overdose”, and “overdose,” and “circumstance or information capable of leading to medication error,” as well as the active ingredient “aprepitant,” the tradename “Emend,” and the verbatim terms “aprepitant%” and “Emend%.” For this review, an updated AERS search was conducted to determine if there were any additional cases of name confusion between Emend and other marketed drug products since the last AERS search was conducted on December 7, 2006.. We did not identify any additional cases of confusion between Emend and other marketed drug products.

C. Labeling, Packaging, and Safety Related Issues

In the review of the package insert labeling of Emend, DMETS has applied principles of human factors and evaluated the labels and labeling using a Failure Modes and Effects Analysis (FMEA) and identified the following areas of needed improvement.

1. General Comment

We note that the sponsor presents the proprietary and established names in various formats throughout the insert labeling [EMEND (fosaprepitant dimeglumine) For Injection], [EMEND For Injection (fosaprepitant)], and [EMEND For Injection]. We recommend that one format be used consistently throughout the labels and labeling.

2. Dosage and Administration Section

- a. Under the "Preparation of Emend for Injection" after step #3, include a statement that indicates 'after reconstitution and dilution, each mL contains XX mg of drug.
- b. The preparation instructions refer to 'saline'. The word 'saline' is defined by Dorland's Medical Dictionary¹ as 'salty; of the nature of a salt' containing a salt or salts'. Clearly identify which 'saline' solution is compatible with this product (for example: 0.9% Sodium Chloride for Injection, USP).

In summary, DMETS did not identify any proprietary or established names that would preclude the approval of the proprietary name, Emend, for this product. However, if approval of the NDA is delayed beyond 90 days from the signature date of this review, the name must be re-evaluated. A re-review of the name before NDA approval will rule out any objections based upon approvals of other proprietary/established names from the signature date of this document. DMETS recommends implementation of the labeling recommendations as outlined above. Additionally, the Division of Drug Marketing, Advertising, and Communications (DDMAC) finds the proprietary name, Emnd, 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. Please copy DMETS on any correspondence to the sponsor pertaining to this issue. If you have further questions or need clarification, please contact Cheryle Milburn, OSE Project Manager, at 301-796-2084.

APPEARS THIS WAY ON ORIGINAL

¹ www.dorlands.com

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

/s/

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1/3/2008 04:52:49 PM
DRUG SAFETY OFFICE REVIEWER
Also signing for Kristina Arnwine 1/3/08.

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CONSULTATION RESPONSE
DIVISION OF MEDICATION ERRORS AND TECHNICAL SUPPORT
OFFICE OF SURVEILLANCE AND EPIDEMIOLOGY
(DMETS; WO 22, STOP: 4447)

DATE RECEIVED: July 31, 2006	DESIRED COMPLETION DATE: November 1, 2006	OSE REVIEW #: 05-0242-2
DATE OF DOCUMENT: March 31, 2006 & July 6, 2006	PDUFA DATE: February 3, 2007	

TO: Brian Harvey, MD, PhD.
Director, Division of Gastroenterology Products, HFD-180

THROUGH: Nora Roselle, PharmD., Team Leader
Denise Toyer, PharmD., Deputy Director
Carol Holquist, RPh., Director
Division of Medication Errors and Technical Support, HFD-420

FROM: Linda M. Wisniewski, RN, Safety Evaluator
Division of Medication Errors and Technical Support, HFD-420

PRODUCT NAME: Emend
(Fosaprepitant Dimeglumine) For Injection
115 mg

NDA#: 22-023

NDA SPONSOR: Merck & Co., Inc.

RECOMMENDATIONS:

- DMETS has no objections to the use of the proprietary name, Emend. This is considered a final decision. However, if the approval of this application is delayed beyond 90 days from the signature date of this document, the name must be re-evaluated. A re-review of the name will rule out any objections based upon approval of other proprietary or established names from the signature date of this document.
- 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.
- DDMAC finds the proprietary name, Emend, 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
WO 22, STOP: 4447
Center for Drug Evaluation and Research**

PROPRIETARY NAME, LABEL, AND LABELING REVIEW

DATE OF REVIEW: August 25, 2006

NDA#: 22-023

NAME OF DRUG: Emend
(Fosaprepitant Dimeglumine) For Injection
115 mg

NDA HOLDER: Merck & Co., Inc.

I. INTRODUCTION:

This consult was written in response to a request from the Division of Gastroenterology Products (HFD-180), for a re-assessment of the proprietary name, "Emend", regarding potential name confusion with other proprietary or established drug names. DMETS reviewed the proposed proprietary name, Emend IV for this product under IND # 48,924, in OSE Consults 05-0242 (December 1, 2005) and 05-0242-1 (December 13, 2005) and found the name Emend IV unacceptable at that time. DMETS' primary concern was the use of the same root name (Emend) for two different drug products with different active ingredients (i.e. Aprepitant and Fosaprepitant Dimeglumine). After discussion between DMETS, ONDQ, and the Division, the Division decided that the name Emend (Fosaprepitant Dimeglumine for Injection), would be acceptable. The sponsor now proposes the following: Emend (Fosaprepitant Dimeglumine) for Injection. Draft container labels, carton and insert labeling for Emend were provided for review and comment at this time.

PRODUCT INFORMATION

Emend (fosaprepitant dimeglumine) for Injection is an addition to the current Emend product line. It is a prodrug of aprepitant and in combination with other antiemetic agents, is indicated for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy including high-dose cisplatin and in the prevention of nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy. Emend is administered at a dose of 115 mg given 30 minutes prior to chemotherapy on Day 1 only of the CINV regimen as an intravenous infusion over 15 minutes. It is supplied in 115 mg single dose vials that are to be reconstituted with 5 mL of saline and further diluted into an infusion bag containing 110 mL of saline, yielding a final drug volume of 115 mL. Emend is stable for 24 hours after reconstitution.

II. SEARCH OF THE ADVERSE EVENT REPORTING SYSTEM (AERS)

An AERS search was conducted in OSE Consult # 00-0298-4, dated June 15, 2006. Since that review no additional cases were identified since that review.

III. SAFETY EVALUATOR RISK ASSESSMENT

DMETS did not identify any proprietary or established names that would preclude the approval of the proprietary name, Emend, for this product.

IV. LABELING, PACKAGING, AND SAFETY RELATED ISSUES

In the review of the container labels, carton and insert labeling of Emend, DMETS has focused on safety issues relating to possible medication errors. DMETS has identified the following areas of improvement, which may minimize potential user error.

A. CONTAINER LABEL

1. Delete the 'swoosh' graphic emanating from the 'n' of Emend as it distorts the presentation of the proprietary name.
2. Relocate the strength so that it immediately follows the established name and revise it to read '115 mg/vial'.
3. Relocate the statement 'FOR INTRAVENOUS USE AFTER RECONSTITUTION AND DILUTION' to the principal display panel.
4. The statement '*Single-Dose 115 mg Vial*' is repetitive since the product strength is presented adjacent to it. Revise this statement to read '~~_____~~' and delete the phrase '~~_____~~' b(4)
b(5)
5. Relocate the '*Rx only*' statement to the bottom 1/3 of the principal display panel so that it does not interfere with the readability of the proprietary name.
6. Include a statement that indicates 'after reconstitution and dilution, each mL contains XX mg', if space permits.
7. To avoid substitution of the oral for the intravenous use product and vice versa, DMETS suggests that the sponsor include the statement '*Emend for Injection (115 mg) may be substituted for Emend (125 mg) 30 minutes prior to chemotherapy, on day 1 only of the CINV regimen as an infusion administered over 15 minutes*'.
8. If space permits, include information regarding the incompatible solutions for reconstitution.
9. Decrease the size of the company logo and relocate it so that is not in close proximity to the proprietary name.

B. CARTON LABELING (1 vial)

1. See comments A1, A2, A5, A6, A7, A8, and A9.
2. Increase the size of the established name so that it is at least ½ the size of the proprietary name.
3. On the main display panel, delete the statement _____, as it is duplicative since the preparation directions are on the side panel. b(4)
b(5)
4. Revise the wording in the blue square background to read _____ and delete _____ from the statement as the strength is listed outside of the blue square. b(4)
5. The preparation instructions refer to 'saline'. The word 'saline' is defined by Dorland's Medical Dictionary¹ as 'salty; of the nature of a salt' containing a salt or salts'. Clearly identify which 'saline' solution is compatible with this product (for example: 0.9% Sodium Chloride for Injection, USP).

C. CARTON LABELING (10 vials)

See comments A1, A2, A5, A6, A7, A8, A9, B2, B3, B4, and B5.

D. INSERT LABELING

1. We also note that the sponsor presents the proprietary and established names in various formats throughout the insert labeling [EMEND (fosaprepitant dimeglumine) For Injection], [EMEND For Injection (fosaprepitant)], and [EMEND For Injection]. We recommend that one format be used consistently throughout the labels and labeling.
2. See comments A6 and B5.

E. PATIENT PACKAGE INSERT

No comment.

¹ www.dorlands.com

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/s/

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