

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**22-127**

**PROPRIETARY NAME REVIEW(S)**

**CONSULTATION RESPONSE**

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

<b>DATE RECEIVED:</b> June 20, 2007	<b>DESIRED COMPLETION DATE:</b> August 1, 2007	<b>OSE REVIEW #:</b> 2007-1402
<b>DATE OF DOCUMENT:</b> June 13, 2007	<b>PUDFA DATE:</b> October 20, 2007	

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

**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

**FROM:** Loretta Holmes, BSN, PharmD, Safety Evaluator  
Division of Medication Errors and Technical Support

**PRODUCT NAME:** **Renvela**  
(Sevelemer Carbonate) Tablets  
800 mg

**NDA #:** 22-127

**SPONSOR:** Genzyme Corporation

**RECOMMENDATIONS:**

1. DMETS has no objections to the use of the proprietary name, Renvela. 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.
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, Renvela, 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 clarifications, please contact Darrell Jenkins, OSE Project Manager, at 301-796-0558.

**Division of Medication Errors and Technical Support (DMETS)  
Office of Surveillance and Epidemiology  
White Oak Bldg #22, Mailstop 4447  
Center for Drug Evaluation and Research**

**PROPRIETARY NAME AND LABEL REVIEW**

**DATE OF REVIEW:** August 9, 2007

**NDA #:** 22-127

**NAME OF DRUG:** Renvela  
(Sevelamer Carbonate) Tablets  
800 mg

**NDA HOLDER:** Genzyme Corporation

**I. INTRODUCTION:**

This review was written in response to a request from the Division of Cardiovascular and Renal Products (HFD-110), for a final review of the proposed proprietary name "Renvela", regarding potential name confusion with other proprietary or established drug names. Container labels and carton labeling were provided for review and comment.

**PRODUCT INFORMATION**

Renvela is a non-absorbed phosphate binding crosslinked polymer indicated for the control of serum phosphorus in patients with Chronic Kidney Disease (CKD) on dialysis. The recommended starting dose is 2.4 grams to 4.8 grams orally per day which can be administered as one or two 800 mg tablets, three times per day with meals based on serum phosphorus level. The dose should be increased or decreased by one tablet per meal at two week intervals, as necessary, with the goal of controlling serum phosphorus within the target range of 3.5 mg/dL to 5.5 mg/dL. Renvela will be available in 800 mg tablets and supplied in 270-count bottles.

**II. RISK ASSESSMENT:**

The medication error staff of DMETS conducted a search of the internet, several standard published drug product reference texts<sup>1,2</sup> as well as several FDA databases<sup>3,4</sup> for existing drug names which sound-alike or look-alike to Renvela 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<sup>5</sup>. The Saegis<sup>6</sup>

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<sup>1</sup> MICROMEDEX Integrated Index, 2007, MICROMEDEX, Inc., 6200 South Syracuse Way, Suite 300, Englewood, Colorado 80111-4740, which includes all products/databases within ChemKnowledge, DrugKnowledge, and RegsKnowledge Systems.

<sup>2</sup> Facts and Comparisons, online version, Facts and Comparisons, St. Louis, MO.

<sup>3</sup> AMF Decision Support System [DSS], the Division of Medication Errors and Technical Support [DMETS] database of Proprietary name consultation requests, and the electronic online version of the FDA Orange Book.

<sup>4</sup> Phonetic and Orthographic Computer Analysis (POCA)

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

<sup>6</sup> Data provided by Thomson & Thomson's SAEGIS™ Online Service, available at [www.thomson-thomson.com](http://www.thomson-thomson.com)

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. Prescription studies were not repeated for this third review. Following completion of these initial steps, an overall risk assessment is conducted that does not evaluate the name alone. The assessment considers the findings from above and more importantly integrates post-marketing experience in assessing the risk of name confusion, product label/labeling, and product packaging. Because it is the drug product that is inserted into the complex and unpredictable U.S. healthcare environment, all product characteristics of a drug must be considered in the overall safety evaluator risk assessment.

A. EXPERT PANEL DISCUSSION (EPD)

An Expert Panel discussion was held by DMETS to gather professional opinions on the safety of the proposed proprietary name, Renvela. 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, Renvela, acceptable from a promotional perspective.
2. The Expert Panel identified eight proprietary names that were thought to have the potential for confusion with Renvela. They are: Rena-Vite/Rena-Vite RX, Renagel, Renedil, Pen-Vee K, PenFill, Ponstel, Prinivil, and Kenonel.

B. SAFETY EVALUATOR RISK ASSESSMENT

In evaluating Renvela, we considered the risk of co-marketing this product with Renagel. We also evaluated eight additional names since our last review as having a similar appearance or sound to Renvela. These names are: Rena-Vite/Rena-Vite RX, Renagel, Renedil, Pen-Vee K, PenFill, Ponstel, Prinivil, and Kenonel.

1. Safety Concerns with the Co-Marketing of Renagel and Renvela

DMETS does not believe that there are significant orthographic similarities between the names Renagel and Renvela. However, based on similar product characteristics between the two products, such as indication of use, strength, dose, frequency of administration, dosage form, and same sponsor, DMETS anticipates that there will be opportunities for confusion and medication errors when these two products are co-marketed.

These errors may occur during any step of the medication use process such as errors in the preparation, dispensing, administering, and monitoring phases of the the medication use system. However, the greatest risk appears to be in the preparation, dispensing, and monitoring phases of the medication use system. For example, computer order entry errors in the preparation and dispensing phases may occur because the tradenames begin with the letters "Ren" and the established names begin with the letters "sel" and may therefore appear in close proximity to one another on a computer screen as prescriptions are electronically processed. Furthermore, the products have an overlapping strength and

similar indications of use which may further increase the potential for possibility for the wrong product to be selected during the order entry process.

Product selection errors may also occur during these phases because these products may be placed in close proximity to one another on a pharmacy shelf due to the similarity of the established names, overlapping strength, and same manufacturer. If errors in the preparation and dispensing phases go undetected and the wrong product is selected, it will have an impact on the monitoring phase of the medication use system. However, the administration of an incorrect salt will not have a significant effect on the patient.

According to the medical officer, although Renagel requires more frequent monitoring of the serum chloride and serum bicarbonate levels, the clinical consequences of receiving the wrong product are not significant. Additionally, through email correspondence with the OND project manager on October 3, 2007, we learned that the sponsor plans \_\_\_\_\_ . Although the consequences of receiving the wrong drug are not significant, DMETS believes that the expected \_\_\_\_\_ occur between the two products.

Therefore, in the interest of minimizing selection errors that will likely occur \_\_\_\_\_ and to minimize confusion among healthcare practitioners as to what the differences are between these two products, we recommend recommend the sponsor launch an educational campaign aimed at healthcare professionals informing them of the differences between the products with regard to the salt, indication of use and different monitoring parameters, etc.

## 2. Look-alike/Sound-Alike Name Concerns

Since our last name review, eight additional names (Rena-Vite/Rena-Vite RX, Renagel, Renedil, Pen-Vee K, PenFill, Ponstel, Prinivil, and Kenonel) were identified as having a similar appearance and/or sound to Renvela. Upon review of these names it was determined that the following six names lacked convincing look-alike and/or sound-alike similarities with Renvela in addition to having numerous differentiating product characteristics such as the product strength, indication of use, frequency of administration, route of administration and/or dosage form. These names include Renedil, Pen-Vee K, PenFill, Ponstel, Prinivil, and Kenonel. Additionally, Renedil (felodipine) is a foreign product (Canada, Netherlands, and Belgium) and Pen-Vee K has been discontinued (similar generic products are available, however, differences in product characteristics between these products and Renvela will help distinguish between them). Furthermore, "Penfill" is the name for the Novo Nordisk line of insulin pen refill cartridges, however, "Penfill" is preceded by the name of the insulin product (e.g., Novolin R Penfill, Novolin N Penfill, Novolin 70/30 Penfill, etc.) which further minimizes the potential to confuse Penfill with Renvela. Thus the following names will not be reviewed further: Renedil, Pen-Vee K, Penfill, Ponstel, Prinivil, and Kenonel.

The remaining two names: Rena-Vite/Rena-Vite RX, and Renagel are listed in Table 1, page 5.

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

Product Name	Dosage form(s), Established name	Usual adult dose*	Other**
Renvela	Sevelamer carbonate Tablets 800 mg	Control of serum phosphorus in patients with Chronic Kidney Disease on dialysis: Starting dose: One or two 800 mg tablets three times per day with meals. Adjust by 1 tablet per meal in 2 week intervals as needed to obtain serum phosphorus target.	NA
Renagel	Sevelamer hydrochloride Tablets 400 mg and 800 mg	Control of serum phosphorus in patients with Chronic Kidney Disease on dialysis: Starting dose: 800 mg to 1600 mg orally three times per day with meals. Adjust by 1 tablet per meal in 2 week intervals as needed to obtain serum phosphorus target.	LA
Rena-Vite (OTC product)  Rena-Vite RX (Rx product)	Multiple vitamin (B complex with Vitamin C) Tablets	Nutritional/vitamin supplement: 1 tablet orally daily.	LA
*Frequently used, not all-inclusive. **LA (look-alike), SA (sound-alike)			

The two names, Renagel and Rena-Vite were evaluated and determined to not pose significant safety concerns for the reasons discussed in detail below.

- a. Renagel was identified as a name with similar appearance to Renvela. Renagel (sevelamer hydrochloride) is indicated for the control of serum phosphorus in patients with Chronic Kidney Disease (CKD) on dialysis. The recommended starting dose is 800 mg to 1600 mg orally three times per day with meals. The dosage should be adjusted based on the serum phosphorus concentration with a goal of lowering serum phosphorus to 5.5 mg/dL or less. The dose may be increased or decreased by one tablet per meal in two week intervals as needed. Renagel is available in 400 mg and 800 mg tablets.

Renagel and Renvela may look similar because both names begin with the letters “Ren” and contain the letters “el” (R-E-N-A-G-E-L vs. R-E-N-V-E-L-A). However, the downstroke character of the letter “g” in Renagel, when scripted, and the ending letter “a” in Renvela may help to differentiate the names.

Renagel and Renvela share multiple overlapping characteristics such as indication of use (control of serum phosphorus in patients with CKD on dialysis), dose (initial dose of 800 mg to 1600 mg), dosage form (tablets), strength (800 mg), frequency of administration (three times per day with meals) and route of administration (oral). The orthographic differences between the names will minimize the potential to confuse the products from a look-alike perspective.

However, DMETS has safety concerns with the concurrent marketing of both products. See Section IIB(1) for further discussion.

- b. Rena-Vite was identified as a name with similar appearance to Renvela. There are two Rena-Vite products available: Rena-Vite and Rena-Vite RX. Rena-Vite is an over-the-counter product whereas Rena-Vite RX is a prescription product. Both products contain B complex vitamins with Vitamin C. Some of the vitamin strengths contained in Rena-Vite RX are higher than in Rena-Vite. The recommended dosage for both products is one tablet orally once daily.

Rena-Vite may look similar to Renvela because both names begin with the letters "Ren". Additionally, the letters "vite" may look similar to "vela" when the letter "r" is not crossed. Furthermore, the dash in the name Rena-Vite may be omitted and the letter "v" written in lower case when the name is scripted which may contribute to the look-alike similarities between the names. However, the "RX" in Rena-Vite RX helps to further differentiate that name from Renvela .

*Renavite Renvela*

Rena-Vite/Rena-Vite RX and Renvela have overlapping product characteristics such as dosage form (tablet), route of administration (oral), and number of strengths available (one). However, the products differ in indication of use (nutritional/vitamin supplement vs. control of serum phosphorus in patients with CKD on dialysis) and frequency of administration (once daily vs. three times per day with meals) which may help to differentiate the names. For example, a prescription for Renvela would likely state the frequency of administration (three times per day with meals) which would help to differentiate it from Rena-Vite/Rena-Vite RX which is administered once daily. Additionally, a prescription is not needed in order to obtain Rena-Vite since it is an OTC product. Therefore, a prescription for Rena-Vite may be questioned as to which product is intended since it does not require a prescription whereas Rena-Vite RX does. Despite some orthographic similarities between the names, the different product characteristics will minimize the potential to confuse Rena-Vite/Rena-Vite RX with Renvela.

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### III. LABELING, PACKAGING, AND SAFETY RELATED ISSUES:

In the review of the container label and carton labeling, DMETS has focused on human factors and safety issues relating to possible medication errors. DMETS has identified the following areas of improvement in order to minimize potential user error.

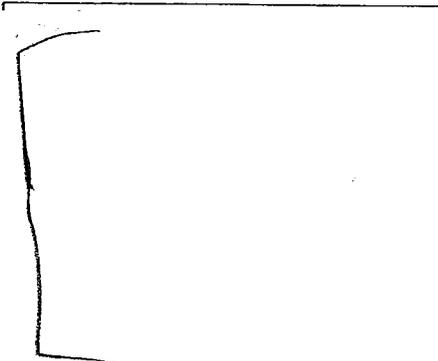
#### A. GENERAL COMMENTS FOR ALL LABELS/LABELING

1. In order to minimize the potential for medication errors between Renagel and Renvela, DMETS recommends that the sponsor launch an educational campaign aimed at healthcare professionals informing them of the differences between the products with respect to the differences in the salts, indications of use, and different monitoring parameters, etc.
2. Ensure that the established name is at least ½ the size of the proprietary name in accordance with 21 CFR 201.10(g)(2).
3. The dosage form statement (“tablets”) is placed next to the statement of strength (“800 mg”). Please relocate the dosage form statement so that it immediately follows the established name so as to maximize the visibility and prominence of the statement of strength. Additionally, increase the size of the statement of strength so that it is commensurate in size with the proprietary name in order to increase its prominence on the label. See the example below.

Example of placement:

Renvela  
(sevelamer carbonate) tablets  
800 mg

4. The letter “v” in Renvela is detracts from the readability of the name. Please print the letter “v” in the same type, font and size as the other letters in the proprietary name.
5. If the container is a unit-of-use bottle to be dispensed on an outpatient basis, ensure that the container has a Child Resistant Closure in accordance with the Poison Prevention Act.



B. CONTAINER LABEL (270-count)

1. See General Comments A-2 through A-5.
2. Relocate the net quantity statement to the principal display panel. However, ensure that it is not in close proximity to the statement of strength.

C. CONTAINER LABEL (PROFESSIONAL SAMPLE, 30-count)

1. See General Comments A-2 through A-5.
2. Decrease the size and prominence of the net quantity statement (as currently presented, it is more prominent than the strength) and relocate it so that it is not in close proximity to the statement of strength. This will help to minimize the potential to confuse the strength and net quantity with each another.
3. Relocate the "Sample: Not To Be Sold" wording to the principal display panel for better prominence.

D. CARTON LABELING (PROFESSIONAL SAMPLE, 30 count)

See General Comments A-2, A-3, and A-4 and Comment C-2.

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/s/

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Loretta Holmes  
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DRUG SAFETY OFFICE REVIEWER

Linda Kim-Jung  
10/18/2007 10:54:25 AM  
DRUG SAFETY OFFICE REVIEWER

Denise Toyer  
10/18/2007 01:27:58 PM  
DRUG SAFETY OFFICE REVIEWER  
Also signing for Carol Holquist, DMETS Director, in her  
absence

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## REQUEST FOR CONSULTATION

TO (Division/Office):

**Director, Division of Medication Errors and  
Technical Support (DMETS), HFD-420  
WO22, RM 4447**

FROM: Alisea Crowley, RPM

Division of Cardiovascular and Renal Products  
301-796-1144

DATE  
August 9, 2007

IND NO.  
66,710

NDA NO.  
22-127

TYPE OF DOCUMENT  
NDA

DATE OF DOCUMENT  
December 20, 2006

NAME OF DRUG  
Renvela (sevelamer  
carbonate)

PRIORITY CONSIDERATION  
Standard

CLASSIFICATION OF DRUG

DESIRED COMPLETION DATE  
October 1, 2007

NAME OF FIRM: Genzyme Corporation

### REASON FOR REQUEST

#### I. GENERAL

- |  |  |  |
|--|--|--|
| <input type="checkbox"/> NEW PROTOCOL                  | <input type="checkbox"/> PRE--NDA MEETING        | <input type="checkbox"/> RESPONSE TO DEFICIENCY LETTER                       |
| <input type="checkbox"/> PROGRESS REPORT               | <input type="checkbox"/> END OF PHASE II MEETING | <input type="checkbox"/> FINAL PRINTED LABELING                              |
| <input type="checkbox"/> NEW CORRESPONDENCE            | <input type="checkbox"/> RESUBMISSION            | <input type="checkbox"/> LABELING REVISION                                   |
| <input type="checkbox"/> DRUG ADVERTISING              | <input type="checkbox"/> SAFETY/EFFICACY         | <input type="checkbox"/> ORIGINAL NEW CORRESPONDENCE                         |
| <input type="checkbox"/> ADVERSE REACTION REPORT       | <input type="checkbox"/> PAPER NDA               | <input type="checkbox"/> FORMULATIVE REVIEW                                  |
| <input type="checkbox"/> MANUFACTURING CHANGE/ADDITION | <input type="checkbox"/> CONTROL SUPPLEMENT      | <input checked="" type="checkbox"/> OTHER (SPECIFY BELOW): Trade name review |
| <input type="checkbox"/> MEETING PLANNED BY            |  |  |

#### 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  
 BIOAVAILABILITY 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/SPECIAL INSTRUCTIONS: A tradename was originally completed by DMETS in August 2006 under the IND. On January 25, 2007, DMETS completed another tradename review dated April 12, 2007. We are requesting a final tradename review for the above application.

**PDUFA DATE: October 20, 2007**

**ATTACHMENTS:** Draft Package Insert, Container and Carton Labels

CC: Archival IND/NDA 22-127

HFD-110/Division File

HFD-Alisea Crowley/RPM

HFD-110/Reviewers and Team Leaders

NAME AND PHONE NUMBER OF REQUESTER  
Alisea Crowley 301-796-1144

METHOD OF DELIVERY (Check one)

DFS ONLY

MAIL

HAND

SIGNATURE OF RECEIVER

SIGNATURE OF DELIVERER

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/s/

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Alisea R. Crowley  
8/9/2007 04:08:56 PM

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