

Review of Proposed Proprietary Name - RECOTHROM

- **MEMORANDUM**

Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Biologics Evaluation and Research

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From:

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Through: Ele Ibarra-Pratt, Branch Chief, APLB (HFM-602)
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To: Nisha Jain, MD, OBRR/DH/CRB, (HFM-392)
Mark Shields, RPM, DBA/OBRR, (HFM-380)

Subject:

Review of Proposed Proprietary Name -----/RECOTHROMT
Recombinant Human Thrombin
BLA 125248/0.4

Recommendation: -- ----- - **UNACCEPTABLE**
RECOTHROMT - ACCEPTABLE

Executive Summary:

APLB recommends that the proposed proprietary names -----recombinant human thrombin is found **Unacceptable** and **RECOTHROMT** recombinant human thrombin is found **Acceptable**.

Executive Summary:

APLB recommends that the proposed proprietary names ----- is found **Unacceptable**. There appears to be a high risk for medication error with proprietary names for other marketed products, taking into account spelling, handwriting, pronunciation, indication, dosage form, usual dose, route of administration, and storage. **RECOTHROM** is found Acceptable.

Background:

On July 11, 2006, APLB reviewed the proposed proprietary names ----- which were submitted to the Investigational New Drug Application (IND) BB-IND ----- for Thrombin (Human, Recombinant) (rhThrombin) and found the names to be acceptable. On July 21, 2006 APLB re-evaluated the proposed proprietary names because of concerns raised by OBRR and still found it acceptable. In August 2006, OBRR informed Zymogenetics that the proposed proprietary names ----- were unacceptable because they were found to be misleading and fanciful. OBRR requested

Zymogenetics to submit another proprietary name for consideration along with the chemical and established name and marketing research to verify that the proposed proprietary name does not have the potential to be confused with or cause medication errors due to similarity in spelling and pronunciation with the proprietary name or the established name of different marketed products and also that is not false, misleading, or fanciful.

On April 27, 2007, Zymogenetics, Inc. submitted a request to the FDA Center for Biologics Evaluation and Research (CBER) Advertising and Promotional Labeling Branch (APLB) to review two proposed proprietary names. These proposed proprietary names in order of preference are -----/RECOTHROMT. This request was submitted as an amendment to Recombinant Human Thrombin BLA and also included the established name and the marketing research as requested.

-----/RECOTHROM Thrombin Recombinant is a coagulation factor produced from a genetically engineered Chinese hamster ovary (CHO) cell line shown to be free of known infectious agents. The protein is purified with a chromatographic purification process that yields a high-purity active product. Thrombin recombinant is not sourced from human or animal blood or plasma. And contains no added human or animal components.

Rationale for use of the proprietary names:

The sponsor's rationale for choosing -----:

- -----
 - -----
- The sponsor's rationale for choosing RECOTHROM:
- "Reco" is derived from *recombinant* "thrombin"
 - "throm" is derived from thrombin

Overview of the Proposed Indication, Dose, Dosage Form, Administration, and Storage Information:

-----/ **RECOTHROM** is indicated as a general adjunct to hemostasis when control of bleeding by conventional surgical techniques, including suture, ligature, and cautery, is ineffective, insufficient, or impractical. -----/ **RECOTHROM** may be applied directly to the bleeding site or used in conjunction with an absorbable gelatin sponge for hemostasis during surgery. -----/ **RECOTHROM** is a sterile, lyophilized powder in vials containing 5,000 IU/vial with a 5-mL prefilled diluent syringe and accessories for transfer. The proposed dose is 1,000 IU/mL of Thrombin (recombinant) in single or multiple applications for topical use only. The sterile powder vials should be stored at 2° C to 25° C (36 F to 77 F), the reconstituted solution may be stored for up to 24 hours at 2° C to 25° C (36 F to 77 F.).

Proposed Proprietary Name Evaluation

1. False or Misleading [21 CFR 201.6 (a)]:

The proposed proprietary names ----- and **RECOTHROM** are not regarded to be false or misleading.

2. Fanciful [21CFR 201.10 (c)(3)]:

A proprietary name would be found unacceptable if it were fanciful and implied that the product had some unique effectiveness. The proposed proprietary names ----- and **RECOTHROM** are not regarded to be fanciful and do not imply a unique composition, advanced formulation, or superiority over existing products beyond that supported by the data.

3. Similarity in Spelling or Pronunciation [21 CFR 201.10 (c) (5)]:

APLB identified some proprietary names with similarity in spelling and pronunciation with the proposed proprietary name ----- and **RECOTHROM**.

- a.
- b. -----

| Name | Dosage Form | Rx or OTC | Dose & Admin. | Indication | Storage | Potential |
|----------------------|----------------|-----------|---|--|----------|-----------|
| ----- | Sterile powder | Rx | 1,000 IU/mL, topical | An adjunct to hemostasis when control of bleeding by conventional surgical techniques, including suture, ligature, and cautery, is ineffective, insufficient, or impractical. May be applied directly to the bleeding site or used in conjunction with an absorbable gelatin sponge for hemostasis during surgery. | 2°-25° C | |
| Thrombin-JMI | Sterile powder | Rx | 5,000 IU/mL, 20,000IU/ 20 mL topical | Aid to hemostasis whenever oozing blood and minor bleeding from capillaries and small venules is accessible. May be used in conjunction with an absorbable gelatin sponge for hemostasis. | “ | High |
| Thrombate III | Sterile powder | Rx | 500 mL IU and 1000 IU for intravenous injection | For the treatment of patients with hereditary antithrombin III deficiency in connection with surgical or obstetrical procedures, or | “ | low |

| Name | Dosage Form | Rx or OTC | Dose & Admin. | Indication | Storage | Potential |
|------|-------------|-----------|---------------|--|---------|-----------|
| | | | | when they suffer from thromboembolism... | | |

c. RECOTHROM

| Proprietary Name | Dosage Form | Rx or OTC | Dose & Admin. | Indication | Storage | Potential |
|----------------------|------------------------|-----------|--|--|--|-----------|
| RECOTHROM | Sterile powder | Rx | 1,000 IU/mL, topical | Same as for ---- ----- | 2°-25° C | |
| Thrombin-JMI | Sterile powder | RX | 5,000 IU/mL, 20,000IU/ 20 mL topical | Same as the above chart | | High |
| Recombinate | Sterile powder | Rx | 250 IU, 500IU, 1000IU Powder for injection | indicated in hemophilia A for the prevention and control of hemorrhagic episodes. Also indicated in the perioperative management of patients with hemophilia A | 2-8° C or at room temp. not to exceed 30° C. | “ |
| Recombivax HB | Injection for solution | Rx | 0.5-1 mL at birth, 1 and 6 months. | Vaccination against hepatitis B virus | | “ |

-----:

The following risk factors were considered when evaluating the degree to which ----- may be of concern for medication errors:

Strength/ Dose/Dosage Form/Route of Administration:

Two different products with similar or identical strengths and with proprietary names that sound or look alike could be more easily confused than two products with very different strengths. The risk of confusion increases substantially if two products with similar proprietary names have identical strengths and dosing intervals.

The risk of a medication error is increased when products with similar proprietary names are dosed or prescribed in an identical manner (i.e., once a day). In addition, there is evidence that medication errors can occur even between different dosage forms and routes of administration (capsule vs. injection) and between products with similar routes of administration when similar proprietary names exist.

----- is a sterile, lyophilized powder in vials containing 5,000 IU/vial with a 5-mL prefilled diluent syringe yields a solution containing 1000 IU/mL. ----- may be applied directly to the bleeding site or used in conjunction with an absorbable gelatin sponge. surgery. Thrombin-JMI is also a sterile, lyophilized powder in vials containing 5,000 IU/mL, 20,000 IU/20 mL administered topically. Thrombate III is a sterile, lyophilized powder in vials containing 500 IU and 1000 IU for intravenous injection. Therefore, there is low potential for confusion with ----- and Thrombate III and a high potential for confusion with ----- and Thrombin-JMI. We recommend that the sponsor ensure that the products have container and package labeling that is distinctive from one another to avoid medication error.

Indications and/or Pharmacological-Therapeutic Categories:

The proposed indication for ----- is as a general adjunct to hemostasis when control of bleeding by conventional surgical techniques, including suture, ligature, and cautery, is ineffective, insufficient, or impractical. Thrombin-JMI has the same indication. Thrombate III is indicated for the treatment of patients with hereditary antithrombin III deficiency in connection with surgical or obstetrical procedures, or when they suffer from thromboembolism. There is low potential for confusion with ----- and Thrombate III, however, a high potential for confusion with ----- and Thrombin-JMI because of similar indications. Since Thrombin-JMI is a bovine product repeated applications may increase the formation of antibodies against thrombin and patients with antibodies to bovine thrombin preparations should not be re-exposed to these products. In addition, patients who are known to be sensitive to products of bovine origin should not be administered Thrombin-JMI. Thus, the consequences of inadvertently receiving Thrombin-JMI instead of ----- --- raise significant safety concerns.

Storage Location:

The use of a different storage location (i.e., refrigerator vs. room temperature, oral dosage form location vs. intravenous dosage form location) for two different products with similar names does not significantly decrease the risk of wrong product selection by the health care professional. Therefore, the use of different storage locations for drugs with names that look or sound alike may not mitigate the potential risk of medication errors.

----- powder will be stored in the refrigerator, the reconstituted solution may be stored for up to 24 hours. Thrombin-JMI powder is also stored in the refrigerator and after reconstitution may be stored for up to three hours in the refrigerator. Thrombate III will be stored in a refrigerator. All three products have a high potential for confusion.

Marketing Status:

Two products with similar proprietary names that are in the same marketing arena (e.g., prescription drug products) could more easily be confused than two products with similar names in different markets (one Rx and the other OTC).

The name review search revealed a number of products (Thrombin-JMI and Thrombate III) with similarity with the "Thrombin" portion of ----- that were for prescription use.

Packaging and Labeling:

When the container labels, carton labeling, and/ or packaging is similar for two different drug products with similar proprietary names, the risk for confusion with similar proprietary names is increased. The packaging/labeling of ----- is similar to Thrombin-JMI, this would increase the risk for confusion between the products.

RECOTHROM is the second choice for proprietary names:

RECOTHROM has a look-alike potential with Thrombin-JMI because they share the root "Throm", however the "reco" prefix also supports the fact that **RECOTHROM** is a recombinant product, therefore minimizing the confusion with Thrombin-JMI. **RECOTHROM** also has a look-alike potential with Recombinate and Recombivax HB because they share the first four letters, "reco". Recombinate is a sterile powder for injection indicated in hemophilia A for the prevention and control of hemorrhagic episodes and also for the perioperative management of patients with hemophilia A. Recombivax HB is a solution for injection and indicated for vaccination against hepatitis B virus. Therefore, these factors will minimize the potential for confusion and error with **RECOTHROM**.

Recommendations for proposed names:

APLB recommends that the proposed proprietary names ----- be found unacceptable and **RECOTHROM** be found acceptable. There appears to be a high risk for medication errors between ----- and Thrombin-JMI taking into account similarity in spelling, pronunciation, handwriting, indication, dosage form, route of administration, storage and marketing status.

If OBRR accepts our recommendation that the proposed proprietary name ----- be found unacceptable and **RECOTHROM** be found acceptable please include the following text in your letter to the manufacturer:

We have considered your proposed proprietary names ----- and **RECOTHROM** in consultation with CBER's Advertising and Promotional Labeling Branch (APLB) and conclude that under 21 CFR Part 201 the proposed proprietary name **RECOTHROM** is found acceptable and ----- is found unacceptable. Specifically, the proposed name ----- is found unacceptable because the name has a high potential for confusion with Thrombin-JMI given the similarity with the spelling, pronunciation, handwriting, dosage form, route of administration, storage and marketing status.

If you have any questions regarding this review, please contact Maryann Gallagher at 301-827-6330.

The following references were used:

1. <http://www.thomsonhc.com/pdrel/librarian> (Electronic Physicians' Desk Reference 2007)
2. <http://www.fda.gov/cder/ob> (Electronic Orange Book) through January 2007.
3. <http://www.rxlist.com> (RxList)
4. <http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm> (CDER approved drug products through February 5, 2007)
5. <http://www.factsandcomparisons.com/efacts.asp> (Drug Facts and Comparisons)
6. <http://www.ama-assn.org/ama/pub> American Medical Association Website-Newly Approved USAN stems through January 25, 2007.
7. <http://www.fda.gov/cber/products/htm> (CBER New BLA, 510(k) Devices, NDA and PMA approvals lists through February 5, 2007).
8. APhA Handbook of Nonprescription Drugs, 13th Edition, ©2002
9. 2002 American Drug Index.