HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use RECOTHROM safely and effectively. See full prescribing information for RECOTHROM.
RECOTHROM
Thrombin, topical (Recombinant)
Powder for solution - For Topical Use Only
Initial U.S. Approval: 2008

INDICATIONS AND USAGE

RECOTHROM is indicated as an aid to hemostasis whenever oozing blood and minor bleeding from capillaries and small venules is accessible and control of bleeding by standard surgical techniques (such as suture, ligature, or cautery) is ineffective or impractical (1).
RECOTHROM may be used in conjunction with an absorbable gelatin sponge, USP (1).

DOSAGE AND ADMINISTRATION

- **For topical use only. DO NOT INJECT (2).**
- Reconstitute RECOTHROM powder with sterile 0.9% sodium chloride, USP, yielding a solution containing 1000 units[1]/mL (2.1).
- Apply RECOTHROM solution directly to bleeding site surface or in conjunction with absorbable gelatin sponge. The amount required depends upon the area of tissue to be treated (2.2).

DOSAGE FORMS AND STRENGTHS

RECOTHROM is available as 5000-unit and 20,000-unit vials of sterile recombinant topical thrombin powder for solution. When reconstituted as directed with the provided sterile 0.9% sodium chloride, USP, the final solution contains 1000 units/mL of RECOTHROM (3).

CONTRAINDICATIONS

- **Do not inject directly into the circulatory system (4).**
- **Do not use for the treatment of massive or brisk arterial bleeding (4).**
- Do not administer to patients with known hypersensitivity to RECOTHROM, any components of RECOTHROM or hamster proteins (4).

WARNINGS AND PRECAUTIONS

- **Potential risk of thrombosis if absorbed systemically** (5).
- In patients with known hypersensitivity to snake proteins, there may be a potential for allergic reaction (5).

ADVERSE REACTIONS

- The serious adverse event that occurred in ≥ 1% (n=6/583) of patients exposed to RECOTHROM in completed clinical trials was atrial fibrillation. The most common adverse events reported in clinical trials of RECOTHROM were incision site pain, procedural pain, and nausea (6.1).
- The incidence of antibody formation to RECOTHROM in completed clinical trials is 0.9%, (n=5/552). None of the antibodies detected in RECOTHROM treated patients neutralized native human thrombin (6.1).

To report SUSPECTED ADVERSE REACTIONS, contact ZymoGenetics, Inc. at 1-888-784-7662, or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

To report SUSPECTED ADVERSE REACTIONS, contact at or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch

USE IN SPECIFIC POPULATIONS

Pregnancy: No human or animal data. Use only if clearly needed (8.1).

[1] Units used herein represent international units of potency determined using a reference standard that has been calibrated against the World Health Organization Second International Standard for Thrombin.

Revised: 09/2012

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

RECOTHROM® Thrombin, topical (Recombinant), is indicated as an aid to hemostasis whenever oozing blood and minor bleeding from capillaries and small venules is accessible and control of bleeding by standard surgical techniques (such as suture, ligature, or cautery) is ineffective or impractical.
RECOTHROM may be used in conjunction with an absorbable gelatin sponge, USP.

2 DOSAGE AND ADMINISTRATION

For topical use only. **DO NOT INJECT.**
Apply on the surface of bleeding tissue only.
The volume of reconstituted RECOTHROM required will vary, depending on the size and number of bleeding sites to be treated and the method of application. The healthcare professional should determine the number of vials required to produce a sufficient volume of reconstituted product.
Inspect the integrity of the RECOTHROM package and contents. Do not use if the packaging or contents have been damaged or opened.

2.1 Reconstitution of RECOTHROM

The lyophilized powder is reconstituted, using the supplied diluent, in less than 1 minute at room temperature.
NOTE: Use aseptic technique when handling vials and syringes.

5,000-unit[1] RECOTHROM Reconstitution

[1] *Units used herein represent international units of potency determined using a reference standard that has been calibrated against the World Health Organization Second International Standard for Thrombin.*

1. Remove flip-off cap from the top of the RECOTHROM vial.
2. Attach the needle-free transfer device and snap it into place on the vial by placing the vial flat on a surface and attaching the transfer device straight into the center of the vial stopper.
3. Attach the prefilled diluent syringe to the needle-free transfer device.
4. Inject the 5 mL of diluent from the syringe into the product vial. Keep the syringe plunger depressed.
5. DO NOT re-use the diluent syringe for transfer of the reconstituted product. Remove and discard the diluent syringe.
6. Gently swirl and invert the product vial until the powder is completely dissolved (avoid excessive agitation).
7. Apply the pre-printed “DO NOT INJECT” label to the sterile, empty transfer syringe provided, then draw up the RECOTHROM solution.

20,000-unit RECOTHROM Reconstitution

1. Remove the flip-off cap from the top of the RECOTHROM vial and the diluent vial.
2. Attach a needle-free transfer device (one each) to the RECOTHROM and diluent vials and snap them into place by placing the vial flat on a surface and attaching the transfer device straight into the center of the vial stopper.
3. Open the sterile, empty 20-mL syringe package and apply the pre-printed “DO NOT INJECT” label to the syringe.
4. Attach the labeled 20-mL syringe to the needle-free transfer device on the diluent vial (injection of air into the diluent vial may facilitate withdrawal of the diluent).
5. Draw up 20 mL of diluent from the vial into the syringe.
6. Remove the diluent-filled syringe from the diluent vial and attach it to the transfer device on the RECOTHROM vial.
7. Transfer the 20 mL of diluent from the syringe into the RECOTHROM vial; the vacuum in the vial facilitates transfer.
8. Leave the syringe attached and gently swirl and invert the RECOTHROM vial until the powder is completely dissolved (avoid excessive agitation).
9. With the same syringe, draw up the RECOTHROM solution.

2.2 Application Techniques

DO NOT INJECT

Topically apply RECOTHROM solution directly to bleeding site or in conjunction with absorbable gelatin sponge.

Use with Absorbable Gelatin Sponge

1. Refer to the absorbable gelatin sponge labeling for instructions on appropriate use.
2. Transfer solution from syringe to a sterile bowl or basin.
3. Place the desired size pieces of the absorbable gelatin sponge into the bowl containing reconstituted RECOTHROM to completely saturate the sponge(s).
4. Remove the saturated sponge(s) and squeeze gently to remove excess RECOTHROM.
5. Apply the sponge to the bleeding site in a single layer.

Use with ZymoGenetics Spray Applicator Kit

1. Hold the outer sealed tray, peel back the lid, and aseptically transfer the inner sealed sterile tray to the sterile field.
2. Open the inner tray seal and use the sterile bowl as the receptacle for reconstituted RECOTHROM solution.
3. Refer to Spray Applicator Kit instructions for spray pump and syringe spray assembly and use.

The amount of RECOTHROM required depends upon the area of tissue to be treated and the method of application.

Vials are for single use only. Discard unused contents.

3 DOSAGE FORMS AND STRENGTHS

The 5000- and 20,000-unit vials of RECOTHROM powder, when reconstituted as directed with the provided sterile 0.9% sodium chloride, USP, yield a solution containing 1000 units/mL of Thrombin, topical (Recombinant).

4 CONTRAINDICATIONS

Do not inject directly into the circulatory system.

Do not use for the treatment of massive or brisk arterial bleeding.

Do not administer to patients with known hypersensitivity to RECOTHROM or any components of RECOTHROM.

Do not use in patients with known hypersensitivity to hamster proteins.

5 WARNINGS AND PRECAUTIONS

Potential risk of thrombosis if absorbed systemically.

In patients with known hypersensitivity to snake proteins, there may be a potential for allergic reaction.

6 ADVERSE REACTIONS

The serious adverse event that occurred in ≥ 1% (n=6/583) of patients exposed to RECOTHROM in completed clinical trials was atrial fibrillation. The most common adverse events in patients exposed to RECOTHROM in clinical trials (N=583) were incision site pain (51%), procedural pain (30%), and nausea (28%).

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug product cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice.

Clinical trials have been performed with RECOTHROM applied with absorbable gelatin sponge (Phase 2, Phase 3, and Phase 3b studies) and applied with a spray applicator (Phase 2 study). Adverse events reported in clinical trials were consistent with those commonly observed in surgical patients.

Clinical Trials of RECOTHROM Used in Conjunction with Gelatin Sponge

Among the 411 patients treated with study drug in the randomized, double-blind, Phase 3 study that compared RECOTHROM to bovine thrombin, both applied with gelatin sponge, in patients undergoing spinal surgery, hepatic resection, peripheral arterial bypass surgery, or arteriovenous graft formation for hemodialysis access, all but 2 patients (1 patient/treatment group) reported adverse events [1]. Most events were moderate in severity and had a similar incidence in the RECOTHROM and bovine thrombin treatment groups. The most common adverse events were incision site pain (63% for both treatment groups), procedural pain (RECOTHROM 29%; bovine thrombin 34%), and nausea (RECOTHROM 28%; bovine thrombin 35%). Serious adverse events were reported by 18% of patients treated with RECOTHROM and 22% with bovine thrombin.

Adverse events of interest were pre-specified, based on the thrombin mechanism of action, use of absorbable gelatin sponge, USP, historical reporting in association with cross-reacting antibodies to bovine thrombin product, and results from Phase 2 clinical trials of RECOTHROM applied with absorbable gelatin sponge. The incidences of these pre-specified adverse events were similar between treatment groups (see Table 1).

Table 1. Events of Interest in the RECOTHROM Phase 3 Study

AE Category*	RECOTHROM (N=205) n (%)	Thrombin-JMI† (N=206) n (%)
Patients with any event category	124 (60%)	136 (66%)
Bleeding	27 (13%)	24 (12%)
Cardiac	41 (20%)	38 (18%)
Hypersensitivity	30 (15%)	37 (18%)
Nausea + vomiting	68 (33%)	83 (40%)
Other infection	26 (13%)	31 (15%)
Post-operative wound infection	19 (9%)	22 (11%)
Thromboembolic	12 (6%)	10 (5%)

*Adverse events were included in event categories based on a blinded review of the investigator verbatim and coded terms.

†Thrombin-JMI® Thrombin, Topical (Bovine)

In an open-label, single-group Phase 3b study, 209 patients with documented or highly likely prior exposure to bovine thrombin within the previous 3 years were treated with RECOTHROM when undergoing surgeries (spinal or peripheral arterial bypass or arteriovenous graft formation for hemodialysis access). The most common adverse events were incision site pain (45%), procedural pain (39%), and nausea (27%) [2]. Similar to the Phase 3 study, serious adverse events were reported by 22% of patients treated with RECOTHROM.

Clinical Trials of RECOTHROM Applied with Spray Applicator

In an open-label, single-group, Phase 2 study in burn patients, 72 patients were treated with RECOTHROM applied with a spray applicator at the burn wound excision site prior to autologous skin grafting [3]. This study included both adults (≥ 17 years of age, n=68) and pediatric patients ≤ 16 years of age (n=4). The most common adverse events in the adult and pediatric age groups included procedural pain (35%), pruritis (25%), and constipation (19%).

Immunogenicity

The potential development of antibodies to RECOTHROM has been evaluated in multiple clinical trials. These pre-specified evaluations were performed in order to characterize the immunogenicity of RECOTHROM and the neutralizing potential of any detected antibodies. In completed clinical studies 5 of 552 (0.9%) patients exposed to RECOTHROM with both baseline and post-treatment antibody specimens available developed specific anti-RECOTHROM product antibodies. None of these antibodies were found to neutralize native human thrombin.

In the randomized, double-blind, Phase 3 study that compared RECOTHROM to bovine thrombin, both applied with gelatin sponge, in patients undergoing spinal surgery, hepatic resection, peripheral arterial bypass surgery, or arteriovenous graft formation for hemodialysis access, the development of specific anti-product antibodies was evaluated in both treatment groups [1]. Blood samples were collected at baseline and at day 29 for 97% of the patients in both treatment groups. For patients randomized to RECOTHROM, the samples were analyzed by ELISA for antibodies to RECOTHROM, Chinese hamster ovary (CHO) host cell protein, and pro-thrombin activator (used in the conversion of single chain precursor to active RECOTHROM). For patients randomized to bovine thrombin, the samples were analyzed by ELISA for antibodies to bovine thrombin product.

At baseline 1.5% of patients (n=3/198) in the RECOTHROM group had positive anti-product antibody titers compared with 5% of patients in the bovine thrombin group (n=10/200). Of the patients who had detectable anti-product antibodies at baseline, 0 of 3 in the RECOTHROM group and 8 of 10 in the bovine thrombin group exhibited ≥ 1.0 titer unit (≥ 10-fold) increases in antibody levels after study treatment.

Treatment with RECOTHROM applied with absorbable gelatin sponge resulted in a statistically significantly lower incidence of specific anti-product antibody development. Three of 198 (1.5%; 95% CI, 0 to 4%) of the patients in the RECOTHROM arm developed specific anti-thrombin product antibodies (1 patient also developed anti-CHO host cell protein antibodies). No patients developed antibodies to pro-thrombin activator. Forty-three of 200 patients (22%; 95% CI, 16 to 28%) in the bovine thrombin arm developed specific antibodies to bovine thrombin product. None of the antibodies in the RECOTHROM group neutralized native human thrombin. Antibodies against bovine thrombin product were not tested for neutralization of native human thrombin. Because the study was not powered to detect a difference in clinical outcomes attributable to antibody formation, no conclusions can be drawn regarding the clinical significance of the difference in antibody formation based on the results of this study.

In the open-label, single group, Phase 3b study in patients with a high likelihood of prior bovine thrombin exposure undergoing spinal, peripheral arterial bypass surgery, or arteriovenous graft formation for hemodialysis access, 15.6% of patients (n=32/205) had anti-bovine thrombin product antibodies at baseline prior to treatment with RECOTHROM. Following treatment, none of the 200

evaluable patients (patients for whom specimens were available for antibody testing at baseline and post-RECOTHROM treatment) developed antibodies to RECOTHROM.
In the randomized, double-blind, controlled Phase 2 studies of RECOTHROM compared to placebo (RECOTHROM excipients reconstituted with 0.9% sodium chloride, USP) applied in conjunction with absorbable gelatin sponge, which were performed across a range of surgical settings (spinal surgery, hepatic resection, peripheral arterial bypass surgery, or arteriovenous graft formation for hemodialysis access), the incidence of antibody development to RECOTHROM was 1.2% in the RECOTHROM group (n=1/83) compared to 2.4% (n=1/41) in the placebo group. In the open-label, single group Phase 2 study of RECOTHROM applied with the spray applicator to excised burn wounds, 1 patient developed antibodies following treatment (1.6%, n=1/62).
The detection of antibody formation is highly dependent upon the sensitivity and specificity of the assay. The absolute immunogenicity rates reported here are difficult to compare with results from studies of other products due to differences in assay methodology, patient populations, and other underlying factors.

7 DRUG INTERACTIONS
Drug interactions have not been formally studied.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy
Pregnancy Category C. Animal reproduction studies have not been conducted with RECOTHROM. It is also not known whether RECOTHROM can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. RECOTHROM should be given to a pregnant woman only if clearly needed.

8.4 Pediatric Use
Of the 72 patients undergoing burn wound excision and grafting treated with RECOTHROM applied with the spray applicator in the open-label, single group, Phase 2 study, 4 were pediatric patients. All were age 12 to 16 years. The safety and effectiveness of RECOTHROM in all pediatric age groups have not been fully established.

8.5 Geriatric Use
Of the total number of patients in Phase 2 and Phase 3 clinical studies of RECOTHROM with absorbable gelatin sponge, 38% were 65 years old and over, while 16% were 75 years old and over.
No substantive differences in safety or effectiveness were observed between these patients and younger patients, and other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

11 DESCRIPTION
RECOTHROM Thrombin, topical (Recombinant), is a human coagulation protein produced via recombinant DNA technology from a genetically modified CHO cell line. RECOTHROM is identical in amino acid sequence and structurally similar to naturally occurring human thrombin. RECOTHROM precursor is secreted to culture medium as single chain form that is proteolytically converted to a two-chain active form and is purified by a chromatographic process that yields a product having hemostatic activities similar to native human thrombin. The cell line used to manufacture RECOTHROM has been tested and shown to be free of known infectious agents. The cell culture process used in the manufacture of RECOTHROM employs no additives of human or animal origin. The purification process includes solvent-detergent treatment and nano-filtration steps dedicated to viral clearance.
RECOTHROM is provided as a sterile, white to off-white, preservative-free, lyophilized powder in vials for reconstitution with diluent (sterile 0.9% sodium chloride, USP). RECOTHROM is available in a 5-mL vial containing 5000 units and a 20-mL vial containing 20,000 units of recombinant thrombin. Reconstitution with the provided diluent, as described [see *DOSAGE AND ADMINISTRATION (2.1)*], yields a solution with a pH of 6.0 containing 1000 units/mL of recombinant thrombin for topical use. The formulated product is a clear, colorless solution upon reconstitution and contains the following excipients: histidine, mannitol, sucrose, polyethylene glycol 3350, sodium chloride, and calcium chloride dihydrate, USP.

12 CLINICAL PHARMACOLOGY
RECOTHROM Thrombin, topical (Recombinant), is a highly specific human serine protease that promotes hemostasis and acts locally when applied topically to a site of bleeding [*see NONCLINICAL TOXICOLOGY (13.3)*]. RECOTHROM activates platelets and catalyzes the conversion of fibrinogen to fibrin, which are steps that are essential for blood clot formation.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
Long-term animal studies to evaluate the carcinogenic potential of RECOTHROM have not been performed. The in vitro mutagenic potential of RECOTHROM has not been evaluated. In vitro cytotoxicity studies have been performed in mouse L929 fibroblast cell cultures and demonstrate a concentration dependent effect on cell morphology. The thrombin induced morphological changes were similar to those seen with bovine thrombin. The effect of RECOTHROM on fertility has not been characterized.

13.2 Animal Toxicology and/or Pharmacology

RECOTHROM was found to be well tolerated with minimal immunogenicity in nonhuman primates when applied directly to a liver wound with an absorbable gelatin sponge, USP. RECOTHROM was also well tolerated and minimally immunogenic when administered subcutaneously once weekly for 4 weeks to nonhuman primates following repeat doses of 5405 units/m^2. RECOTHROM was found to be non-irritating when instilled in the eyes (200 units) or applied to normal or abraded skin of rabbits (up to 1000 units/site).

13.3 Pharmacology

To evaluate RECOTHROM inhibition and clearance from the bloodstream, radiolabeled RECOTHROM was administered intravenously or subcutaneously to non-human primates and applied with an absorbable gelatin sponge, USP, in a rabbit hepatic wound model. RECOTHROM did not circulate in the blood as free, active molecule, but was rapidly inactivated (<5 minutes) after formation of complexes with endogenous inhibitors (e.g., antithrombin III); these complexes were cleared by the liver.
RECOTHROM applied with an absorbable gelatin sponge, USP, was shown to significantly decrease time to hemostasis (TTH) when compared to saline in a rabbit hepatic wound model and rat heminephrectomy model. RECOTHROM significantly reduced TTH when directly applied in a porcine partial-thickness excisional skin-wound model as compared to saline control (or no treatment).
RECOTHROM applied with a gauze sponge decreased TTH in a concentration-dependent manner in both the rabbit and rat models. Concentrations of RECOTHROM > 1000 units/mL were no different than 1000 units/mL while the effect of RECOTHROM diluted to a concentration of 100 units/mL on TTH was indistinguishable from placebo.

14 CLINICAL STUDIES

14.1 Study Design and Objectives

RECOTHROM was evaluated in a Phase 3 study conducted in 411 patients undergoing surgery in 1 of 4 surgical settings: spinal surgery, hepatic resection, peripheral arterial bypass surgery, and arteriovenous graft formation for hemodialysis access. The study was a multiple-site, randomized, double-blind, controlled evaluation of RECOTHROM compared to bovine thrombin, each at a nominal concentration of 1000 U/mL topically applied to bleeding sites with an absorbable gelatin sponge [1].
A heterogeneous surgical population was enrolled in the Phase 3 study with no comorbidity exclusions except for prior heparin-induced thrombocytopenia. Patient ages ranged from 21 to 89 years, gender was 53% male and 47% female, and the distribution by race was 68% white,18% black or African American, and 14% other. The distribution of these characteristics was similar in both the RECOTHROM and bovine thrombin treatment groups.
The objectives of the study were to evaluate the comparative efficacy, safety, and immunogenicity of RECOTHROM and bovine thrombin in combination with an absorbable gelatin sponge as adjuncts to hemostasis in surgery. Efficacy was evaluated by the incidence of hemostasis within 10 minutes. Bleeding appropriate for evaluation was defined as mild to moderate bleeding, either on its own or remaining after brisk bleeding was controlled by standard surgical modalities. Although multiple bleeding sites could be treated, only 1 bleeding site per patient was used to determine primary effectiveness (the proximal anastomosis for peripheral arterial bypass surgery and the arterial anastomosis for arteriovenous graft formation).

14.2 Clinical Study Results

The Phase 3 study included 411 patients undergoing spinal surgery (n=122, 30%), hepatic surgery (n=125, 30%), peripheral arterial bypass surgery (n=88, 21%), and arteriovenous graft formation (n=76, 18%). Table 2 summarizes the incidence of hemostasis within 10 minutes for each treatment for the 401 efficacy evaluable patients. Ten patients were not included in the primary efficacy evaluation because they were not treated at 1 of 4 primary bleeding site types. Overall, the incidence of hemostasis within 10 minutes was 95.4% for patients in the RECOTHROM group and 95.1% for patients in the comparator group. This represents a 0.3% (95% CI, -3.7 to 4.4%) difference in patients receiving RECOTHROM compared to those receiving bovine thrombin, demonstrating that the 2 treatments have comparable efficacy.

Table 2. Hemostasis Within 10 Minutes*

		RECOTHROM (N=198) (%)	**Thrombin-JMI† (N=203) (%)**
Overall		95.4%	95.1%
	Spinal surgery	98.4%	98.4%
	Hepatic resection	98.4%	96.8%
	Peripheral arterial bypass	85.0%	85.7%
	Arteriovenous graft formation	97.1%	97.3%

*****The primary efficacy analysis evaluated incidence of hemostasis at ≤10 minutes for patients treated at 1 of 4 primary TTH bleeding site types: epidural venous plexus, hepatic resection site, peripheral arterial bypass proximal anastomosis, and arteriovenous graft arterial anastomosis (401 efficacy evaluable patients).

†THROMBIN-JMI® Thrombin, Topical (Bovine)

The percentage of patients achieving hemostasis at 1.5, 3, 6, and 10 minutes is listed in Table 3.

Table 3. Cumulative Incidence of Hemostasis Over Time*,†

Time (Minutes)	RECOTHROM (N=198) n (%)	Thrombin-JMI‡ (N=203) n (%)
1.5	95 (48%)	93 (46%)
3	160 (81%)	146 (72%)
6	183 (92%)	178 (88%)
10	189 (95%)	193 (95%)

*Includes 401 efficacy evaluable patients.
†Percentages are rounded to whole numbers.
‡THROMBIN-JMI® Thrombin, Topical (Bovine)

15 REFERENCES

1. Chapman WC, Singla N, Genyk Y, McNeil JW, Renkens Jr KL, Reynolds TC, Murphy A, Weaver FA. A Phase 3, Randomized, Double-Blind Comparative Study of the Efficacy and Safety of Topical Recombinant Human Thrombin and Bovine Thrombin in Surgical Hemostasis. J Am Coll Surg 2007;205:256–265.
2. Singla NK, Ballard JL, Moneta G, et al. A Phase 3b Open-Label, Single-Group Immunology and Safety Study of Topical Recombinant Thrombin (rThrombin) in Surgical Hemostasis. J Am Coll Surg 2009;209:68-74.
3. Greenhalgh DG, Gamelli RL, Collins J, et al. Recombinant Thrombin: Safety and Immunogenicity in Burn Wound Excision and Grafting. J Burn Care Res 2009;30:371-379.

16 HOW SUPPLIED/STORAGE AND HANDLING

RECOTHROM Thrombin, topical (Recombinant), is supplied in single-use, preservative-free vials in the following packages:

NDC 28400-105-41	A 5000-unit vial of RECOTHROM with a 5-mL prefilled diluent syringe (containing sterile 0.9% sodium chloride, USP), a sterile needle-free transfer device, a 5-mL sterile empty syringe, and a pre-printed label.
NDC 28400-120-41	A 20,000-unit vial of RECOTHROM with a 20-mL vial of diluent (containing sterile 0.9% sodium chloride, USP), 2 sterile needle-free transfer devices, a 20-mL sterile empty syringe, and a pre-printed label.
NDC 28400-120-50	The 20,000-unit RECOTHROM kit co-packaged with the ZymoGenetics Spray Applicator Kit containing a spray pump, a spray bottle, a syringe spray tip, a syringe, a bowl, and 2 blank labels.

No RECOTHROM kit components contain latex.
Store RECOTHROM sterile powder vials at 2 °C to 25 °C (36 °F to 77 °F). Do not freeze.
Reconstituted solutions of RECOTHROM prepared with sterile 0.9% sodium chloride, USP, may be stored for up to 24 hours at 2 °C to 25 °C (36 °F to 77 °F). Discard reconstituted solution after 24 hours.
Manufactured for ZymoGenetics Inc., 1201 Eastlake Avenue East, Seattle, WA 98102
U.S. License No. 1758
RECOTHROM is a registered trademark of ZymoGenetics, Inc. All other trademarks are the property of their respective owners.
Version: 1010-07

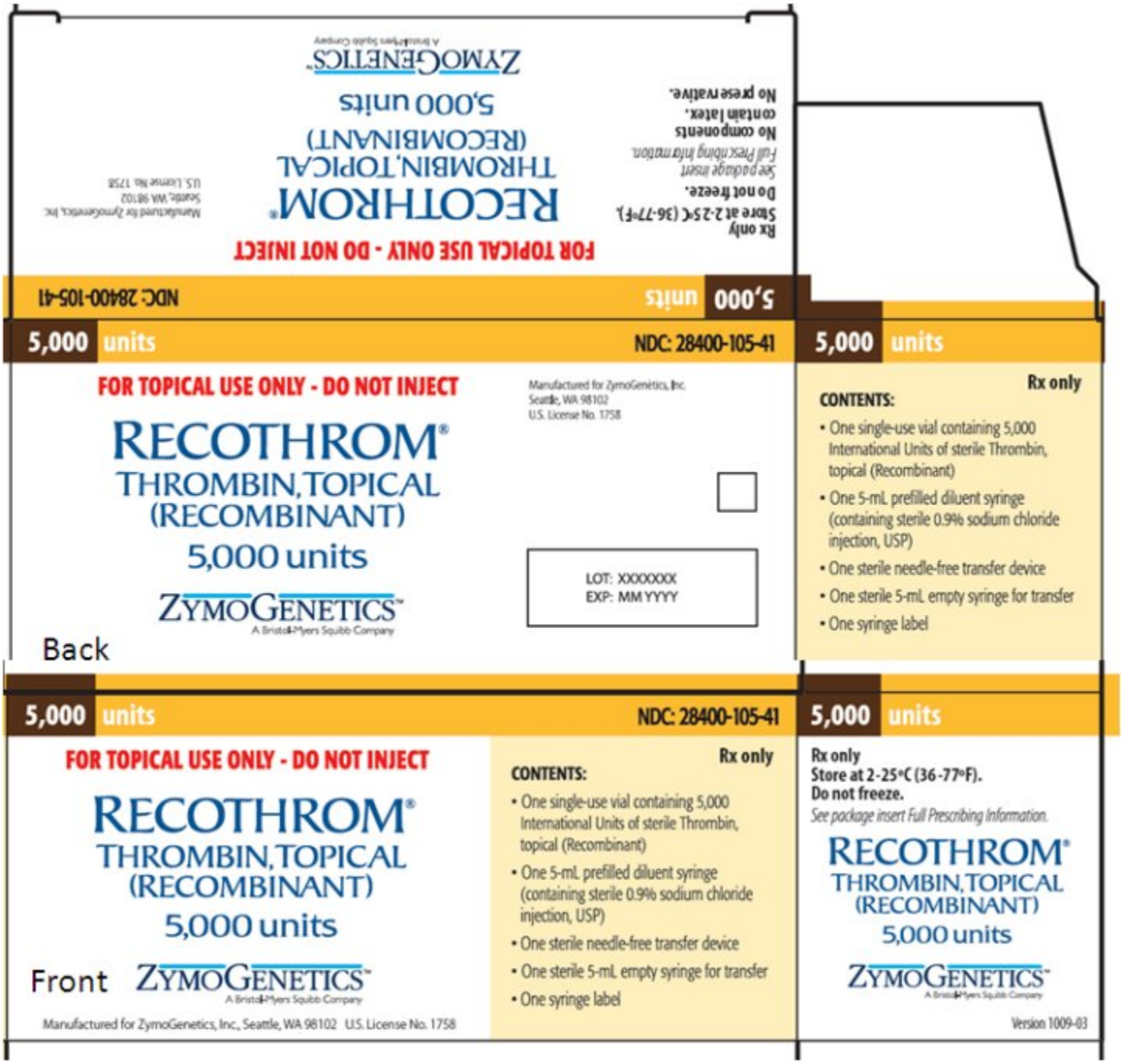
REPRESENTATIVE PACKAGING

See **How Supplied** section for a complete list of available packages of RECOTHROM.

5,000 units
NDC: 28400-105-41
FOR TOPICAL USE ONLY - DO NOT INJECT
RECOTHROM®
THROMBIN, TOPICAL (RECOMBINANT)
5,000 units
ZymoGenetics™

A Bristol-Myers Squibb Company
Manufactured for ZymoGenetics, Inc., Seattle, WA 98102
U.S. License No. 1758
Rx only
CONTENTS:

- One single-use vial containing 5,000 International Units of sterile Thrombin, topical (Recombinant)
- One 5-mL prefilled diluent syringe (containing sterile 0.9% sodium chloride injection, USP)
- One sterile needle-free transfer device
- One sterile 5-mL empty syringe for transfer
- One syringe label



20,000 units
NDC: 28400-120-41

FOR TOPICAL USE ONLY - DO NOT INJECT

RECOTHROM®
THROMBIN, TOPICAL (RECOMBINANT)
20,000 units
Rx only
Store at 2-25°C (36-77°F)
Do not freeze.
See package insert Full Prescribing Information.
Manufactured for ZymoGenetics, Inc. Seattle, WA 98102
U.S. License No. 1758
Copyright 2012 ZymoGenetics, Inc.

CONTENTS:

- One single-use vial containing 20,000 International Units of sterile Thrombin, topical (Recombinant)
- One vial diluent syringe (containing 20-mL sterile 0.9% sodium chloride injection, USP)
- Two sterile needle-free transfer devices
- One sterile 20-mL empty syringe for transfer
- One syringe label