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) Lysophospholipid Powder for Solution - For Topical Use Only Initial U.S. Approval: 2008

INDICATIONS AND USAGE
RECOTHROM® Thrombin topical (Recombinant), in a topical thrombin matrix, is intended for the treatment of bleeding from cancellous bone and cancellous bone surfaces and its sequelae and control of bleeding on sawed standard surgical techniques (such as suction, ligature, or cautery) is ineffective or impractical in adults and pediatric populations greater than or equal to one month of age. RECOTHROM® may be used in conjunction with an absorbable gelatin sponge, USP (1.1, 2.1). Do not administer to patients with a history of hypersensitivity to bovine thrombin or bovine products. (4, 5.1)

DOSE AND ADMINISTRATION
For topical use only: DO NOT INJECT.

1. Transfer solution from syringe to a sterile bowl or basin.
2. Apply the sponge to the bleeding site in a single layer.
3. Open the sterile, empty 20-mL syringe package and apply the pre-printed “DO NOT INJECT” label to the syringe.
4. Attach the needle-free transfer device and snap into place on the vial. Push the plunger to dissolve the powder. Avoid excessive agitation. The powder should dissolve in less than one minute at room temperature.
5. Remove the diluent-filled syringe from the diluent vial and attach it to the transfer device with the powder. Use with RECOTHROM® solution. (3)

DOSE FORMS AND STRENGTHS

RECOTHROM® is available as 2000-unit and 20,000-unit vials of sterile recombinant topical thrombin lyophilized powder for solution. The amount required depends upon the area of tissue to be treated and the method of application. (3, 5.1, 6.2, 9.1, 11.1)

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6.2 Immunogenicity

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Table 1: Incidence of Adverse Reactions with RECOTHROM and Bovine Thrombin

Adverse Reaction

Category

RECOTHROM®

(Bovine Thrombin)*

(N=205)

(N=371)

Thromboembolic events

13 (5.0)

26 (6.9)

* THROMBIN-JMI® Thrombin, Topical (Bovine)

An open-label, single-blind study (n=205), patients with documented or highly likely exposure to bovine thrombin within the previous three years were treated with RECOTHROM when undergoing surgeries (single, peripheral arterial bypass, arteriovenous graft formation, percutaneous balloon dilation transvenous catheter ablation for hemodialysis access). The incidence of thromboembolic adverse reactions in this study was 5.0%.

In an open-label, single-group trial of re-exposure to bovine thrombin (n=15), patients with documented prior exposure to bovine thrombin were treated with RECOTHROM during surgery (spinal, peripheral arterial bypass, arteriovenous graft formation, percutaneous balloon dilation transvenous catheter ablation for hemodialysis access). The incidence of thromboembolic adverse reactions in this study was 1.0%.

In another randomized, double-blind trial across a range of surgical settings (n=335), spinal surgery, hepatic resection, peripheral arterial bypass surgery, and arteriovenous graft formation for hemodialysis access), the safety of RECOTHROM (n=88 patients) was compared to placebo: RECOTHROM recipients re-exposed with sterile 0.9% sodium chloride (USP) (n=40 patients). The incidence of thromboembolic adverse reactions in this study was 5% for RECOTHROM and 12% for placebo.
patients (one month to 17 years of age) undergoing synchronous burn wound excision and autologous skin grafting (N=30; ≤16 years of age, (n=26); ≥17 years of age, (n=4)). In the first study, the incidence of thrombocytopenia adverse reactions was 1%. In the second study, there were no thrombocytopenia adverse reactions (see Common Adverse Reactions (4.8)).

6.2 Immunogenicity

The detection of antibody formation is highly dependent upon the sensitive method used for testing for antibodies.

Populations (8.4)

No differences in safety or effectiveness were observed between these groups. 2

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In a study in nonhuman primates, RECOTHROM was applied directly to a tissue wound with an absorbable gelatin sponge. RECOTHROM was administered subcutaneously once weekly for four to six months. No animals developed anti-RECOTHROM product antibodies in either study. RECOTHROM was found to be non-immunogenic when instilled in the eye (when applied to ocular tissue) or applied to normal or abraded skin of rabbits up to 100 units/site.

To evaluate RECOTHROM’s ability to enhance coagulation, a whole blood clotting assay was used to examine whether RECOTHROM reduced the time to reach a clot (TTH). The TTH was measured using citrated whole blood from healthy adult volunteers. The effect of RECOTHROM on TTH was evaluated in a dose-dependent manner in both the rabbit and rat models.

RECOTHROM is provided as a sterile, white to off-white, preservative-free vials in the following packages: 100 units/mL, 250 units/mL, 500 units/mL, 1000 units/mL, and 20,000 units/mL. 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. 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.

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.

Clinical studies have been performed in rabbits (up to 1000 units/site) and nonhuman primates following repeat doses of 5405 units/m². In both studies, RECOTHROM had no effect on clinical signs, serum chemistry, coagulation parameters, or histopathology; only normal postsurgical findings were observed. No animals developed anti-RECOTHROM product antibodies in either study.

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Table 2: Hemostasis Within 10 Minutes*

At Day 29, three of 198 (1.5%; 95% CI, 0%-4%) patients in the bovine thrombin group exhibited ≥1.0 titer unit (≥10-fold) increase in anti-product antibody level after study treatment. None of the evaluable patients (n=30) had anti-RECOTHROM product antibodies at baseline and none developed antibodies at Day 29.

1.5 48% 46%

3 81% 72%

9 92% 88%

18 95% 93%

6.3 Geriatric Use

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