



In patients at risk for
thrombotic complications

FRAGMIN TO REDUCE RISK

Dosing and Administration Information

Please see indications on page 4.

Please see the complete Important Safety Information, including **Boxed WARNING** for spinal/epidural hematomas, on pages 2 to 3 and also shown throughout this brochure.

Please see enclosed Full Prescribing Information in pocket.

Fragmin[®]
(dalteparin sodium injection)
POWER OF RISK REDUCTION

FRAGMIN: Important Safety Information

WARNING: SPINAL/EPIDURAL HEMATOMA

Epidural or spinal hematomas may occur in patients who are anticoagulated with low molecular weight heparins (LMWH) or heparinoids and are receiving neuraxial anesthesia or undergoing spinal puncture. These hematomas may result in long-term or permanent paralysis. Consider these risks when scheduling patients for spinal procedures. Factors that can increase the risk of developing epidural or spinal hematomas in these patients include:

- Use of indwelling epidural catheters
- Concomitant use of other drugs that affect hemostasis, such as non-steroidal anti-inflammatory drugs (NSAIDs), platelet inhibitors, other anticoagulants
- A history of traumatic or repeated epidural or spinal punctures
- A history of spinal deformity or spinal surgery

Monitor patients frequently for signs and symptoms of neurological impairment. If neurological compromise is noted, urgent treatment is necessary.

Consider the benefits and risks before neuraxial intervention in patients anticoagulated or to be anticoagulated for thromboprophylaxis [see **Warnings and Precautions** and **Drug Interactions**].

- FRAGMIN is contraindicated in patients with active major bleeding, history of heparin induced thrombocytopenia, hypersensitivity to dalteparin sodium, heparin, or pork products.
- FRAGMIN is contraindicated in patients undergoing epidural/neuraxial anesthesia as a treatment for unstable angina and non-Q-wave MI and for prolonged VTE prophylaxis due to an increased risk of bleeding associated with the dosage of FRAGMIN recommended for these indications.
- FRAGMIN, like other anticoagulants, should be used with extreme caution in patients who have an increased risk of hemorrhage; bleeding can occur at any site during therapy. An unexpected drop in hematocrit or blood pressure should lead to a search for a bleeding site.
- FRAGMIN should be used with caution in patients with bleeding diathesis, thrombocytopenia or platelet defects, severe liver or kidney insufficiency, hypertensive or diabetic retinopathy, and recent gastrointestinal bleeding.
- Thrombocytopenia of any degree should be monitored closely. Heparin-induced thrombocytopenia can occur with administration of FRAGMIN. The incidence of this complication is unknown at present. In clinical practice, rare cases of thrombocytopenia with thrombosis have also been observed.

- **FRAGMIN should be used with extreme caution in patients with history of heparin-induced thrombocytopenia.**
 - In FRAGMIN clinical trials supporting non-cancer indications, platelet count of $<50,000/\text{mm}^3$ occurred in $<1\%$ of patients.
 - In FRAGMIN clinical trials supporting the extended treatment of symptomatic VTE in patients with cancer, platelet counts of $<100,000/\text{mm}^3$ occurred in 13.6% of patients, including 6.5% who also had platelet counts less than $50,000/\text{mm}^3$. In the same clinical trial, thrombocytopenia was reported as an adverse event in 10.9% of patients in the FRAGMIN arm and 8.1% of patients in the oral anticoagulant arm. FRAGMIN dose was decreased or interrupted in patients whose platelet counts fell below $100,000/\text{mm}^3$.
- Each multiple-dose vial of FRAGMIN contains benzyl alcohol as a preservative. Benzyl alcohol has been reported to be associated with a fatal "Gasping Syndrome" in premature infants. Because benzyl alcohol may cross the placenta, use caution when administering FRAGMIN preserved with benzyl alcohol to pregnant women. If anticoagulation with FRAGMIN is needed during pregnancy, use preservative-free formulations, where possible.
- Periodic routine complete blood counts, including platelet count, blood chemistry, and stool occult blood tests are recommended during the course of treatment with FRAGMIN.
- The most commonly reported side effect is hematoma at the injection site.
- Allergic reactions (i.e., pruritus, rash, fever, injection site reaction, bulleous eruption) have occurred. A few cases of anaphylactoid reactions have been reported.
- Use FRAGMIN with care in patients receiving oral anticoagulants, platelet inhibitors, and thrombolytic agents because of increased risk of bleeding.
- FRAGMIN cannot be used interchangeably (unit for unit) with unfractionated heparin or other low molecular weight heparins.
- FRAGMIN® Injection is not intended for intramuscular administration.

Dosing in the Hospital

When patients are at thrombotic risk

Prophylaxis of DVT*

- ◆ Medical
 - For patients who are at risk for thromboembolic complications due to severely restricted mobility during acute illness
- ◆ Orthopedics
 - In patients undergoing hip replacement surgery
- ◆ Surgery
 - In patients undergoing abdominal surgery who are at risk for thromboembolic complications

Treatment of symptomatic VTE†

- ◆ Oncology
 - Extended treatment of symptomatic VTE to reduce the recurrence of VTE in patients with cancer. In these patients, the FRAGMIN therapy begins with the initial VTE treatment and continues for 6 months
 - FRAGMIN is not indicated for the acute treatment of VTE

Prophylaxis of ischemic complications

- ◆ Cardiology
 - Prophylaxis of ischemic complications in unstable angina (UA) and non-Q-wave myocardial infarction (NQWMI) when concurrently administered with aspirin therapy

*DVT=deep venous thrombosis.

†VTE=venous thromboembolism.

Please see the complete Important Safety Information, including **Boxed WARNING for spinal/epidural hematomas**, on pages 2 to 3.

REDUCE RISK

In abdominal surgery

FRAGMIN is indicated for the prophylaxis of DVT, which may lead to PE, in patients undergoing abdominal surgery who are at risk for thromboembolic complications.

	Evening before surgery	Day of surgery	12 hours post surgery	Once-daily dosing postoperatively, from 24 hours after surgery
Postoperative		2500 IU SC 1 to 2 hr preoperatively	2500 IU SC	5000 IU SC QD for 5 to 10 days
Preoperative		2500 IU SC 1 to 2 hr preoperatively		2500 IU SC QD for 5 to 10 days
Preoperative High Risk	5000 IU SC			5000 IU SC QD for 5 to 10 days

Dosage adjustment and routine monitoring of coagulation parameters are not required if the dosage and administration recommendations specified above are followed.

Important Safety Information

FRAGMIN should be used with caution in patients with bleeding diathesis, thrombocytopenia or platelet defects, severe liver or kidney insufficiency, hypertensive or diabetic retinopathy, and recent gastrointestinal bleeding.

Fragmin[®]
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For the Extended Treatment of Symptomatic VTE to Reduce the Recurrence of VTE, Specifically in Patients With Cancer for up to 6 Months*

Recommended dosing for extended treatment of VTE in patients with cancer

Body weight (lb)	Body weight (kg)	First 30 days (prefilled syringe) SC once daily	Months 2 to 6 (prefilled syringe) SC once daily
≤124	≤56	10,000 IU	7500 IU
125–150	57–68	12,500 IU	10,000 IU
151–181	69–82	15,000 IU	12,500 IU
182–216	83–98	18,000 IU	15,000 IU
≥217	≥99	18,000 IU	18,000 IU

The total daily dose of FRAGMIN should not exceed 18,000 IU.

- ◆ **First 30 days:** 200 IU/kg total body weight, SC once daily
- ◆ **Months 2 to 6:** 150 IU/kg total body weight, SC once daily
- ◆ **No need for routine coagulation monitoring**
 - Periodic routine lab tests are recommended
- ◆ **Safety and efficacy beyond 6 months have not been evaluated in patients with cancer and acute symptomatic VTE**

*In these patients, the FRAGMIN therapy begins with the initial VTE treatment and continues for 6 months. FRAGMIN is not indicated for the acute treatment of VTE.

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In patients with cancer and renal insufficiency

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- ◆ In patients with severely impaired renal function ($\text{CrCl} < 30 \text{ mL/min}$):
 - Monitoring for anti-Xa levels is recommended to determine the appropriate FRAGMIN dose
 - Target anti-Xa range is 0.5 to 1.5 IU/mL
- ◆ When monitoring anti-Xa in these patients:
 - Sampling should be performed 4 to 6 hours after FRAGMIN dosing
 - Sample only after the patient has received 3 to 4 doses

In patients with cancer and thrombocytopenia

Platelet counts
between 50,000
and 100,000/ mm^3

Reduce the daily dose of FRAGMIN by 2500 IU until the platelet count recovers to $\geq 100,000/\text{mm}^3$

Platelet counts
<50,000/ mm^3

Discontinue FRAGMIN until the platelet count recovers above 50,000/ mm^3

Important Safety Information

FRAGMIN should be used with extreme caution in patients with history of heparin-induced thrombocytopenia.

In FRAGMIN clinical trials supporting the extended treatment of symptomatic VTE in patients with cancer, platelet counts of $< 100,000/\text{mm}^3$ occurred in 13.6% of patients, including 6.5% who also had platelet counts less than $50,000/\text{mm}^3$. In the same clinical trial, thrombocytopenia was reported as an adverse event in 10.9% of patients in the FRAGMIN arm and 8.1% of patients in the oral anticoagulant arm. FRAGMIN dose was decreased or interrupted in patients whose platelet counts fell below $100,000/\text{mm}^3$.

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In UA* and NQWMI

FRAGMIN is indicated for the prophylaxis of ischemic complications in UA and NQWMI, when concurrently administered with aspirin therapy.

Recommended dosing for UA and NQWMI†

Body weight (lb)	Body weight (kg)	FRAGMIN dose (IU)	3.8 mL vial (25,000 IU/1 mL)	Graduated syringe (10,000 IU/1 mL)
			Volume of FRAGMIN (mL)	
<110	<50	5500	0.22	0.55
110–131	50–59	6500	0.26	0.65
132–153	60–69	7500	0.30	0.75
154–175	70–79	9000	0.36	0.90
176–197	80–89	10,000	0.40	1.0
≥198	≥90	10,000	0.40	1.0

*With EKG changes.

†The multiple-dose vial contains 25,000 anti-Factor Xa IU per 1 mL and the graduated syringe contains 10,000 anti-Factor Xa IU per 1 mL for a total of 95,000 anti-Factor Xa IU in each.

Please see the complete Important Safety Information, including **Boxed WARNING for spinal/epidural hematomas**, on pages 2 to 3.

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REDUCE RISK

- ◆ In patients with UA or NQWMI, the recommended dose is 120 IU/kg, but not more than 10,000 IU SC every 12 hours:
 - Concurrent with oral aspirin (75–165 mg once daily)
 - Treatment should be continued until the patient is clinically stabilized
- ◆ The usual duration of therapy is 5 to 8 days



Syringe shown is not actual size.

Important Safety Information

FRAGMIN is contraindicated in patients undergoing epidural/neuraxial anesthesia as a treatment for unstable angina and non-Q-wave MI and for prolonged VTE prophylaxis due to an increased risk of bleeding associated with the dosage of FRAGMIN recommended for these indications.

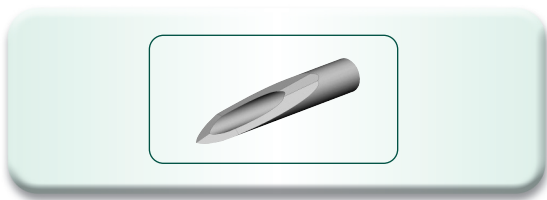
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Simplified Management

- ◆ Convenient color-coded syringes

Single-dose prefilled syringes			
2500 IU/0.2 mL	5000 IU/0.2 mL	7500 IU/0.3 mL	10,000 IU/1 mL
			(Graduated syringe)

- ◆ 5-bevel needle for ease of administration



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REDUCE RISK

12,500 IU/0.5 mL	15,000 IU/0.6 mL	18,000 IU/0.72 mL
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- ◆ Built-in safety mechanism that lets the needle guard automatically slide over needle postinjection



Important Safety Information

FRAGMIN® Injection is not intended for intramuscular administration.

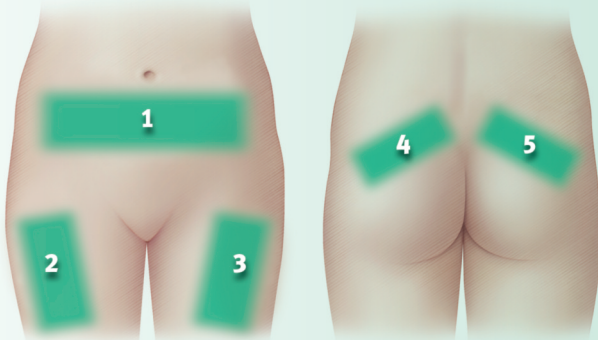
Handling and Administration

- ◆ Patients must be sitting or lying down
 - Administration must be by deep SC injection
 - FRAGMIN must not be administered by intramuscular injection
- ◆ When the area around the navel or thigh is injected, using the thumb and forefinger, you **must** lift up a fold of skin while giving the injection
- ◆ Use a 45- to 90-degree angle of insertion for the entire length of the needle

- ◆ FRAGMIN may be injected in the following areas:
 - The U-shaped area around the navel (1)
 - The upper outer side of the thigh (2,3)
 - The upper outer quadrangle of the buttocks (4,5)

Please see the complete Important Safety Information, including **Boxed WARNING for spinal/epidural hematomas**, on pages 2 to 3.

- ◆ Do not attempt to push syringe through plastic
- ◆ Peel foil to remove syringe
- ◆ While removing the syringe from the package, hold the syringe assembly by the open sides of the syringe, not the plunger or finger flange
- ◆ Plunger should only be handled upon injection
- ◆ Pull the needle shield straight off so needle does not bend
- ◆ Keep the needle pointing up until ready to inject
- ◆ Inspect the medicine to ensure it is clear and has nothing floating in it



The injection site should be varied daily.

Handling and Administration (cont'd)

When using prefilled fixed-dose syringes:

1. To ensure delivery of the full dose, the air bubble **should not** be expelled from the prefilled syringe before injection.
2. Hold the syringe by the open sides of the device and remove the needle shield.
3. Insert the needle into the injection area as described previously.
4. Depress the plunger of the syringe while holding the finger flange **until the entire dose has been given.**
5. The needle guard will **not** be activated unless the **entire** dose has been given.
6. Next, remove the needle from the body. Let go of the plunger and allow the syringe to move up inside the device until the entire needle is guarded.
7. The syringe assembly should be discarded in approved containers.



Syringe shown is not actual size.

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When using graduated syringes:

1. Hold the syringe by the open sides of the device and remove the needle shield.
2. With the needle pointing up, **prepare the syringe by expelling the air bubble** and then continuing to push the plunger to the desired dose or volume, discarding the extra solution in an appropriate manner.
3. Insert the needle into the injection area as described previously.
4. Depress the plunger of the syringe while holding the finger flange **until the entire dose remaining in the syringe has been given.**
5. The needle guard will **not** be activated unless the **entire** dose has been given.
6. Next, remove the needle from the body. Let go of the plunger and allow the syringe to move up inside the device until the entire needle is guarded.
7. The syringe assembly should be discarded in approved containers.

Please note: When using multiple-dose vials, after the first penetration of the rubber stopper, the multiple-dose vials should be stored at room temperature for up to 2 weeks. Discard any unused solution after 2 weeks.



Syringe shown is not actual size.

Call the FRAGMIN Hotline
1-866-61-EISAI
(1-866-613-4724)

or visit the Web site
www.fragmin.com

Eisai Assistance Program

- ◆ Provides information on payor-specific policies and can address other questions
- ◆ Coverage and payment depend on a patient's individual insurance plan
- ◆ Helps qualified indigent, underinsured, and uninsured patients

Patient Educational Resources

- ◆ Fragmin.com
 - Step-by-step injection instructions
 - FAQs on disease states and associated risks
 - Safety information

Important Safety Information

The most commonly reported side effect is hematoma at the injection site.

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