

Prior Authorization DRUG Guidelines

**FRAGMIN® (Dalteparin)**

Effective Date: 7/28/05

Date Developed: 7/19/05 by C. Wilhelmy MD

Last Approval Date: 1/26/16, 1/24/17, 1/23/18, 1/22/19, 2/18/20

Fragmin is a low molecular weight heparin analog which is similar to Lovenox. While dalteparin has been shown to inhibit both factor Xa and factor IIa (thrombin), the antithrombotic effect of dalteparin is characterized by a higher ratio of antifactor Xa to antifactor IIa activity (ratio = 4).

**Pre-Authorization Criteria:**

Fragmin is used for the prevention of deep vein thrombosis which may lead to pulmonary embolism, in patients requiring abdominal surgery who are at risk for thromboembolism complications (eg, patients >40 years of age, obesity, patients with malignancy, history of deep vein thrombosis or pulmonary embolism, and surgical procedures requiring general anesthesia and lasting >30 minutes); prevention of DVT in patients undergoing hip-replacement surgery; patients immobile during an acute illness; acute treatment of unstable angina or non-Q-wave myocardial infarction; prevention of ischemic complications in patients on concurrent aspirin therapy

.MONITORING PARAMETERS — Periodic CBC including platelet count; stool occult blood tests; monitoring of PT and PTT is not necessary

1. Recommended Dosing Regimen and Authorization Limit:

Drug	Dosing Regimen	Authorization Limit
Hip fracture or replacement	<u>Fragmin:</u> Preoperative varies, Postoperative 5,000 IU/day	<u>Fragmin:</u> 14 days
Abdominal surgery	<u>Fragmin:</u> 2500- 5000 IU QD	<u>Fragmin:</u> 5-10 days

High risk surgery/major gynecologic surgery or surgery with malignancy	<u>Fragmin:</u> 5000 IU QD	<u>Fragmin:</u> 7-10 days or until discharge
Acute medical illness	<u>Fragmin:</u> 5000 IU QD	<u>Fragmin:</u> 7-14 days until illness resolves and/or ambulatory
Acute spinal cord injury	<u>Fragmin:</u> 5000 IU QD	<u>Fragmin:</u> Continue to the end of rehabilitation phase of therapy
Recurrent DVT on oral anticoagulation or oral therapy precluded	<u>Fragmin:</u> 200 IU/kg QD	Indefinite <u>Fragmin:</u> max 18,000 IU/day
Unstable angina/non-Q wave MI	<u>Fragmin:</u> 120 IU/kg Q 12 H	<u>Fragmin:</u> max 10,000 IU/ Q 12H; 5-8 days
Pregnancy (prophylaxis)	<u>Fragmin:</u> 5000 IU QD	<u>Fragmin:</u> 6 weeks post partum
Extended treatment of symptomatic VTE in patients with cancer	<u>Fragmin:</u> Month 1: 200 IU/kg QD Month 2: 150 IU/kg QD	<u>Fragmin:</u> max 18,000 IU/day  Safety and efficacy beyond six months have not been evaluated
Pediatric patients treatment	<u>Fragmin:</u> 129 IU/kg QD	Consult literature for appropriate duration based on intended use

Pediatric patients prophylaxis	<u>Fragmin:</u> 92 IU/kg QD	Consult literature for appropriate duration based on intended use
--------------------------------	--------------------------------	---

**ADMINISTRATION** — For deep SubQ injection only. May be injected in a U-shape to the area surrounding the navel, the upper outer side of the thigh, or the upper outer quadrangle of the buttock. Apply pressure to injection site; do not massage. Use thumb and forefinger to lift a fold of skin when injecting dalteparin to the navel area or thigh. Insert needle at a 45- to 90-degree angle. The entire length of needle should be inserted. Do not expel air bubble from fixed-dose syringe prior to injection. Air bubble (and extra solution, if applicable) may be expelled from graduated syringes.

**PRODUCT AVAILABILITY:**

Fragmin: Single-dose prefilled syringe: 2,500 IU/0.2 mL, 5,000 IU/0.2 mL, 7,500 IU/0.3 mL, 10,000 IU/0.4 mL, 12,500 IU/0.5 mL, 15,000 IU/0.6 mL, 18,000 IU/0.72 mL.

Single-dose graduated syringe: 10,000 IU/1 mL. Multiple dose vial: 95,000 IU/3.8mL, 95,000 IU/9.5 L.

**CONTRAINDICATIONS** — Hypersensitivity to dalteparin or any component of the formulation; thrombocytopenia associated with a positive in vitro test for antiplatelet antibodies in the presence of dalteparin; hypersensitivity to heparin or pork products; patients with active major bleeding; patients with unstable angina or non-Q-wave MI undergoing regional anesthesia; not for I.M. or I.V. use

**WARNINGS / PRECAUTIONS** — Patients with recent or anticipated neuraxial anesthesia (epidural or spinal anesthesia) are at risk of spinal or epidural hematoma and subsequent paralysis. Consider risk versus benefit prior to neuraxial anesthesia. Risk is increased by concomitant agents which may alter hemostasis, as well as traumatic or repeated epidural or spinal puncture. Patient should be observed closely for bleeding if dalteparin is administered during or immediately following diagnostic lumbar puncture, epidural anesthesia, or spinal anesthesia.

Not to be used interchangeably (unit for unit) with heparin or any other low molecular weight heparins. Use with caution in patients with known hypersensitivity to methylparaben or propylparaben. Use with caution in patients with history of heparin-induced thrombocytopenia. Monitor platelet count closely. Rare thrombocytopenia may occur. Consider discontinuation of dalteparin in any patient developing significant thrombocytopenia. Monitor patient closely for signs or symptoms of bleeding. Certain patients are at increased risk of bleeding. Risk factors include bacterial endocarditis; congenital or acquired bleeding disorders; active ulcerative or angiodysplastic GI diseases; severe uncontrolled hypertension; hemorrhagic stroke; or use shortly after brain, spinal, or ophthalmology surgery; in patient treated concomitantly with platelet inhibitors; recent GI bleeding; thrombocytopenia or platelet defects; severe liver disease; hypertensive or diabetic retinopathy; or in patients undergoing invasive procedures.

Use with caution in patients with severe renal failure (has not been studied). Safety and efficacy in pediatric patients have not been established. Rare cases of thrombocytopenia with thrombosis have occurred. Multidose vials contain benzyl alcohol and should not be used in pregnant women. Heparin can cause hyperkalemia by affecting aldosterone. Similar reactions could occur with LMWHs. Monitor for hyperkalemia.

#### DRUG INTERACTIONS

Drugs which affect platelet function (eg, aspirin, NSAIDs, dipyridamole, ticlopidine, clopidogrel) may potentiate the risk of hemorrhage.

Thrombolytic agents increase the risk of hemorrhage.

Warfarin: Risk of bleeding may be increased during concurrent therapy. Dalteparin is commonly continued during the initiation of warfarin therapy to assure anticoagulation and to protect against possible transient hypercoagulability.

#### PREGNANCY RISK FACTOR — B

PREGNANCY IMPLICATIONS — Multiple-dose vials contain benzyl alcohol (avoid in pregnant women due to association with fetal syndrome in premature infants).

LACTATION — Excretion in breast milk unknown/use caution

#### REFERENCES

1. Braunwald, E, Antman, EM, Beasley, JW, et al. ACC/AHA 2002 Guideline Update for the Management of Patients With Unstable Angina and Non-ST-Segment Elevation Myocardial Infarction - Summary Article: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on the Management of Patients With Unstable Angina). *J Am Coll Cardiol* 2002; 40(7):1366-74. Available at: <http://www.acc.org/clinical/guidelines/unstable/incorporated/index.htm>. Accessed May 20, 2003.
2. . Frostfeldt, G, Ahlberg, G, Gustafsson, G, et al. Low Molecular Weight Heparin (Dalteparin) as Adjunctive Treatment of Thrombolysis in Acute Myocardial Infarction - A Pilot Study: Biochemical Markers in Acute Coronary Syndromes (BIOMACS II), *J Am Coll Cardiol*, 1999, 33:627.
3. Invasive Compared With Noninvasive Treatment in Unstable Coronary-Artery Disease: FRISC II Prospective Randomised Multicentre Study. Fragmin® and Fast Revascularisation During Instability in Coronary Artery Disease Investigators. *Lancet* 1999; 354:708.
4. Klein, W, Buchwald, A, Hillis, SE, et al. Comparison of Low Molecular-Weight Heparin With Unfractionated Heparin Acutely and With Placebo for 6 Weeks in the Management of Unstable Coronary Artery Disease. Fragmin® in Unstable Coronary Artery Disease Study. *Circulation* 1997; 96:61.
5. Kontny, F, Dale, J, Abildgaard, U, et al. Randomized Trial of Low Molecular Weight Heparin (Dalteparin) in Prevention of Left Ventricular Thrombus Formation and Arterial Embolism After Acute Anterior Myocardial Infarction: The Fragmin® in Acute Myocardial Infarction (FRAMI) Study. *J Am Coll Cardiol* 1997; 30:962.
6. . Long-Term Low-Molecular-Mass Heparin in Unstable Coronary-Artery Disease: FRISC II Prospective Randomised Multicentre Study., Fragmin®, Fast Revascularization During Instability in Coronary Artery Disease, Investigators. *Lancet*, 1999, 354:701.

7. Low-Molecular-Weight Heparin During Instability in Coronary Artery Disease, Fragmin® During Instability in Coronary Artery Disease (FRISC) Study Group. Lancet 1996; 347:561.
8. Nagge, J, Crowther, M, Hirsh, J. Is Impaired Renal Function a Contraindication to the Use of Low-Molecular Weight Heparin. Arch Intern Med 2002; 162:2605.
9. Wallentin, L. ASSENT 3 PLUS. [Paper presented at] American Heart Association 75th Scientific Sessions, November 17-20, 2002; Chicago, Ill.
10. Wong, GC, Giugliano, RP, Antman, EM. Use of Low-Molecular-Weight Heparins in the Management of Acute Coronary Artery Syndromes and Percutaneous Coronary Intervention. JAMA 2003; 289:331.
11. Zed, PJ, Tisdale, JE, Borzak, S. Low-Molecular-Weight Heparins in the Management of Acute Coronary Syndromes. Arch Intern Med 1999; 159:1849.
12. Fragmin prescribing information, Pfizer, March 2010.

Select Drug Information from [Lexi-Comp Online™](http://www.lexi-comp.com)  
 Copyright (1978 to present) Lexi-Comp, Inc.

©2013 UpToDate® • [www.uptodate.com](http://www.uptodate.com)  
 Epocrates 2013 – [www.epocrates.com](http://www.epocrates.com)

**Revision History:**

Date Reviewed/Updated: 10/4/11 by A. Reeves MD  
 Date Reviewed/No Updates: 4/2/12; 1/16/13 by A. Reeves MD  
 Date Approved by P&T Committee: 7/28/05; 10/25/11; 4/24/12; 1/29/13  
 Date Reviewed/No Updates: 1/28/14 by C. Sanders MD  
 Date Approved by P&T Committee: 1/28/14  
 Date Reviewed/No Updates: 1/13/15 by C. Sanders, MD  
 Date Approved by P&T Committee: 1/27/15  
 Date Reviewed/Updated: 3/12/15 by C. Sanders, MD; R. Sterling, MD  
 Date Approved by P&T Committee: 1/26/16  
 Date Reviewed/No Updates: 1/24/17 by C. Sanders, MD; R. Sterling, MD  
 Date Approved by P&T Committee: 1/24/17  
 Date Reviewed/No Updates: 1/23/18 by C. Sanders, MD; R. Sterling, MD  
 Date Approved by P&T Committee: 1/23/18  
 Date Reviewed/No Updates: 1/22/19 by C. Sanders, MD; R. Sterling, MD  
 Date Approved by P&T Committee: 1/22/19  
 Date Reviewed/No Updates: 2/18/20 by H. Taekman, MD; R. Sterling, MD  
 Date Approved by P&T Committee: 2/18/20

Revision Date	Content Revised (Yes/No)	Contributors	Review/Revision Notes
---------------	--------------------------	--------------	-----------------------

1/24/17	No	Catherine Sanders, MD; Robert Sterling, MD	Annual review
1/23/18	No	Catherine Sanders, MD; Robert Sterling, MD	Annual review
1/22/19	No	Catherine Sanders, MD; Robert Sterling, MD	Annual review
2/18/20	No	Howard Taekman, MD; Robert Sterling, MD	Annual review