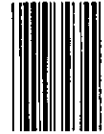


foi



* 5243139 *



* A *

5243139 A

{Part of Complete Approval Document 5226341A} Fragmin
(Pharmacia and Upjohn) 03/30/1999 Supplemental Approval
[Prophylaxis of Deep Vein Thrombosis]: S8 Approval Letter; Final
Labeling

This document was provided by: FOI Services, Inc

704 Quince Orchard Road • Suite 275
Gaithersburg MD 20878-1751 USA
Phone: 301-975-9400
Fax: 301-975-0702
Email: infofoi@foiservices.com

Do you need additional U.S. Government information?

Since 1975, FOI Services, Inc has specialized in acquiring government files using the Freedom of Information Act. We have millions of pages of unpublished documentation already on file and available for immediate delivery.

Many of the documents you need are available for immediate downloading at:

www.foiservices.com

Unless specified otherwise, all of FOI Services' documents have been released by the U.S. Government under the provisions of the Freedom of Information Act and are therefore available to the general public. FOI Services, Inc. does not guarantee the accuracy of any of the information in these documents; the documents will be faithful copies of the information supplied to FOI Services, Inc.

Food and Drug Administration
Rockville MD 20857

NDA 20-287/S-008

Pharmacia & Upjohn
Attention: James H. Chambers
7000 Portage Road
Kalamazoo, Michigan 49001-0199

MAR 30 1999

Dear Mr. Chambers:

Please refer to your supplemental new drug application dated April 16, 1997, received April 17, 1997, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Fragmin® (dalteparin sodium injection).

We acknowledge receipt of your submissions dated May 9, June 11 and 12, August 13, November 21, 1997, and February 25, March 19, September 8, and November 6, 1998. Your submission of November 6, 1998 constituted a complete response to our April 15, 1998 action letter.

This supplemental new drug application provides for the use of Fragmin® for prophylaxis of deep vein thrombosis (DVT), which may lead to pulmonary embolism, in patients undergoing hip replacement surgery.

We have completed the review of this supplemental application, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the enclosed labeling text. Accordingly, the supplemental application is approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the package insert).

Please submit 20 copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FPL for approved supplement NDA 20-287/S-008." Approval of this submission by FDA is not required before the labeling is used

In addition, please submit three copies of the introductory promotional materials that you propose to use for this product. All proposed materials should be submitted in draft or mock-up form, not final print. Please submit one copy to this Division and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising, and Communications, HFD-40
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

If a letter communicating important information about this drug product (i.e., a "Dear Health Care Practitioner" letter) is issued to physicians and others responsible for patient care, we request that you submit a copy of the letter to this NDA and a copy to the following address:

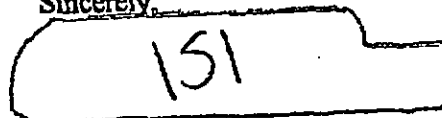
MEDWATCH, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20857

Please submit one market package of the drug product when it is available.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, contact Karen Oliver, Regulatory Health Project Manager, at (301) 827-7310.

Sincerely,



Lilia Talarico, M.D.
Director
Division of Gastrointestinal and Coagulation Drug
Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

Enclosure: Package Insert Text

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: 020287/S008

PRINTED LABELING

FRAGMIN®
dalteparin sodium injection

For Subcutaneous Use Only

SPINAL/EPIDURAL HEMATOMAS

When neuraxial anesthesia (epidural/spinal anesthesia) or spinal puncture is employed, patients anticoagulated or scheduled to be anticoagulated with low molecular weight heparins or heparinoids for prevention of thromboembolic complications are at risk of developing an epidural or spinal hematoma which can result in long-term or permanent paralysis

The risk of these events is increased by the use of indwelling epidural catheters for administration of analgesia or by the concomitant use of drugs affecting hemostasis such as non steroidal anti-inflammatory drugs (NSAIDs), platelet inhibitors, or other anticoagulants. The risk also appears to be increased by traumatic or repeated epidural or spinal puncture.

Patients should be frequently monitored for signs and symptoms of neurological impairment. If neurological compromise is noted, urgent treatment is necessary.

The physician should consider the potential benefit versus risk before neuraxial intervention in patients anticoagulated or to be anticoagulated for thromboprophylaxis (also see WARNINGS, Hemorrhage and PRECAUTIONS, Drug Interactions)

DESCRIPTION

FRAGMIN Injection (dalteparin sodium injection) is a sterile, low molecular weight heparin. It is available in single-dose, prefilled syringes and a multiple-dose vial. With reference to the WHO First International Low Molecular Weight Heparin Reference Standard, each syringe contains 2500 (16 mg dalteparin sodium) or 5000 (32 mg dalteparin sodium) anti-Factor Xa international units (IU) in 0.2 mL. Each 9.5 mL vial contains 10,000 (64 mg dalteparin sodium) anti-Factor Xa IU per 1 mL, for a total of 95,000 anti-Factor Xa IU per vial.

Each prefilled syringe also contains Water for Injection and sodium chloride, when required, to maintain physiologic ionic strength. The prefilled syringes are preservative free. Each multiple-dose vial also contains Water for Injection and 14 mg of benzyl alcohol per mL as a preservative. The pH of both formulations is 5.0 to 7.5.

Dalteparin sodium is produced through controlled nitrous acid depolymerization of sodium heparin from porcine intestinal mucosa followed by a chromatographic purification process. It is composed of strongly acidic sulphated polysaccharide chains (oligosaccharide, containing 2,5-anhydro-D-mannitol residues as end groups) with an average molecular weight of 5000 and about 90% of the material within the range 2000-9000. The molecular weight distribution is

Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

Real-Time Litigation Alerts



Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

Advanced Docket Research



With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

Analytics At Your Fingertips



Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

LAW FIRMS

Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

FINANCIAL INSTITUTIONS

Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS

Sync your system to PACER to automate legal marketing.