Department of Health and Human Services
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Office of Surveillance and Epidemiology
Office of Pharmacovigilance and Epidemiology

Pediatric Postmarketing Pharmacovigilance Review

Date:	March 9, 2026
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Product Name:	Fragmin (dalteparin sodium)
Pediatric Labeling Approval Date:	May 16, 2019
Application Type/Number:	NDA 020287
Applicant:	Pfizer, Inc
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EXECUTIVE SUMMARY

This review evaluates FDA Adverse Event Reporting System (FAERS) reports for Fragmin (dalteparin sodium) in pediatric patients less than 18 years of age. The Division of Pharmacovigilance (DPV) conducted this review in accordance with the Pediatric Research Equity Act (PREA). This review focuses on United States (U.S.) serious unlabeled adverse events associated with dalteparin sodium in pediatric patients.

Fragmin (dalteparin sodium) is a low molecular weight heparin that was initially FDA approved on December 22, 1994. Dalteparin sodium is currently indicated for:

- Prophylaxis of ischemic complications in unstable angina and non-Q-wave myocardial infarction when concurrently administered with aspirin therapy.
- Prophylaxis of deep vein thrombosis, which may lead to pulmonary embolism, in patients who are at risk for thromboembolic complications due to hip replacement surgery, abdominal surgery, or severely restricted mobility during acute illness.
- Extended treatment of symptomatic venous thromboembolism (VTE) in adult patients with cancer.
- Treatment of symptomatic VTE in pediatric patients 1 month of age and older.

This pediatric postmarketing safety review was prompted by pediatric labeling on May 16, 2019, that expanded the use of dalteparin sodium for the treatment of symptomatic VTE in pediatric patients aged 1 month and older.

DPV reviewed all U.S. serious FAERS reports with dalteparin sodium in pediatric patients less than 18 years of age from December 22, 1994, through January 20, 2026, and identified nine reports; however, all reports were excluded from further discussion.

There were no new safety signals identified, no increased severity of any labeled adverse events, and no deaths directly associated with dalteparin sodium in pediatric patients less than 18 years of age.

DPV did not identify any new pediatric safety concerns for dalteparin sodium at this time and will continue routine pharmacovigilance monitoring for dalteparin sodium.

1 INTRODUCTION

This review evaluates FDA Adverse Event Reporting System (FAERS) reports for Fragmin (dalteparin sodium) in pediatric patients less than 18 years of age. The Division of Pharmacovigilance (DPV) conducted this review in accordance with the Pediatric Research Equity Act (PREA). This review focuses on United States (U.S.) serious unlabeled adverse events associated with dalteparin sodium in pediatric patients.

1.1 PEDIATRIC REGULATORY HISTORY

Fragmin (dalteparin sodium) is a low molecular weight heparin that was initially FDA approved on December 22, 1994. Dalteparin sodium is currently indicated for:

- Prophylaxis of ischemic complications in unstable angina and non-Q-wave myocardial infarction when concurrently administered with aspirin therapy.
- Prophylaxis of deep vein thrombosis, which may lead to pulmonary embolism, in patients who are at risk for thromboembolic complications due to hip replacement surgery, abdominal surgery, or severely restricted mobility during acute illness.
- Extended treatment of symptomatic venous thromboembolism (VTE) in adult patients with cancer.
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This pediatric postmarketing safety review was prompted by pediatric labeling on May 16, 2019, that expanded the use of dalteparin sodium for the treatment of symptomatic VTE in pediatric patients aged 1 month and older.

1.2 RELEVANT LABELED SAFETY INFORMATION

The Fragmin (dalteparin sodium) labeling contains the following safety information excerpted from the Highlights of Prescribing Information and the *Pediatric Use* subsection. For additional dalteparin sodium labeling information, please refer to the full prescribing information.[1]

WARNING: SPINAL/EPIDURAL HEMATOMAS

See full prescribing information for complete boxed warning.

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**
- **Optimal timing between the administration of FRAGMIN and neuraxial procedures is not known**

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.

----------CONTRAINDICATIONS----------

- Active major bleeding
- History of heparin induced thrombocytopenia or heparin induced thrombocytopenia with thrombosis
- Hypersensitivity to dalteparin sodium
- In patients undergoing Epidural/Neuraxial anesthesia, do not administer FRAGMIN
    - As a treatment for unstable angina and non-Q-wave MI
    - For prolonged VTE prophylaxis
- Hypersensitivity to heparin or pork products

----------WARNINGS AND PRECAUTIONS----------

- Hemorrhage: Use caution in conditions with increased risk of hemorrhage
- Thrombocytopenia: Monitor thrombocytopenia of any degree closely
- Benzyl Alcohol Preservative: Do not use multiple-dose formulations in neonates and infants as they contain benzyl alcohol
- Laboratory Tests: Periodic blood counts recommended

----------ADVERSE REACTIONS----------

Most common adverse reactions (>1%) are: bleeding (including hemorrhage), thrombocytopenia (Type I), hematoma at the injection site, pain at the injection site, transient elevation of transaminases.

----------USE IN SPECIFIC POPULATIONS----------

8.4 Pediatric Use

The safety and effectiveness of FRAGMIN for the treatment of symptomatic venous thromboembolism (VTE) in patients have been established in pediatric patients aged 1 month and older.

Use of FRAGMIN for this indication is supported by evidence from well-controlled studies in adults with additional pharmacokinetic, pharmacodynamic, efficacy, and safety data from two separate studies in pediatric patients aged 1 month and older with symptomatic VTE. The frequency, type and severity of adverse reactions observed were generally consistent with those observed in adults.

Use preservative-free FRAGMIN in neonates and infants.

Serious adverse reactions including fatal reactions and the "gasping syndrome' occurred in premature neonates and low-birth weight infants in the neonatal intensive care unit who received benzyl alcohol preserved medications. In these cases, benzyl alcohol dosages of 99 to 234 mg/kg/day produced high levels of benzyl alcohol and its metabolites in the blood and urine (blood levels of benzyl alcohol were 0.61 to 1.378 mmol/L). Additional adverse reactions included gradual neurological deterioration, seizures, intracranial hemorrhage, hematologic abnormalities, skin breakdown, hepatic and renal failure, hypotension, bradycardia, and cardiovascular collapse. Preterm, low-birth weight infants may be more likely to develop these reactions because they may be less able to metabolize benzyl alcohol.

When prescribing FRAGMIN multiple-dose vials in infants consider the combined daily metabolic load of benzyl alcohol from all sources including FRAGMIN multiple-dose vials (FRAGMIN contains 14 mg of benzyl alcohol per mL) and other drugs containing benzyl alcohol. The minimum amount of benzyl alcohol at which serious adverse reactions may occur is not known.

The long-term effects of treatment with FRAGMIN in pediatric patients, including effects on growth and bone metabolism, are unknown.

2 METHODS AND MATERIALS

DPV searched the FAERS database with the strategy described in Table 1.

Table 1. FAERS Search Strategy[*]

Date of search	January 21, 2026
Time period of search	December 22, 1994[†] - January 20, 2026
Search type	RxLogix Pediatric Focused Review Alert – DPV
Product terms	Product Active Ingredient: dalteparin sodium; dalteparin
MedDRA search terms (Version 28.1)	All Preferred Terms

[*] See Appendix A for a description of the FAERS database.
[†] U.S. approval date for dalteparin sodium.
Abbreviation: MedDRA=Medical Dictionary for Regulatory Activities

3 RESULTS

3.1 SELECTION OF U.S. SERIOUS PEDIATRIC CASES IN FAERS

Our FAERS search retrieved nine U.S. serious[a] pediatric reports for patients less than 18 years old from December 22, 1994, through January 20, 2026, including one report with the outcome of death. We excluded all nine reports from the case series for the reasons described below:

[a] For the purposes of this review, the following outcomes qualify as serious: death, life-threatening, hospitalization (initial or prolonged), disability, congenital anomaly, required intervention, or other serious important medical events.

- Transplacental exposure (n=3)
- Adverse event more likely due to concomitant medications or comorbidities (n=2, including 1 death)
- Unassessable[b] (n=4)

One excluded U.S. FAERS report described a fatal outcome due to pediatric inflammatory multisystem syndrome temporally associated with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection.[c]

3.2 SUMMARY OF U.S. FATAL PEDIATRIC CASES (N=0)

There are no fatal pediatric adverse event cases for discussion.

3.3 SUMMARY OF U.S. SERIOUS NON-FATAL PEDIATRIC CASES (N=0)

There are no non-fatal pediatric adverse event cases for discussion.

4 DISCUSSION

DPV reviewed all U.S. serious FAERS reports with dalteparin sodium in pediatric patients less than 18 years of age from December 22, 1994, through January 20, 2026, and identified nine reports; however, all reports were excluded from further discussion.

There were no new safety signals identified, no increased severity of any labeled adverse events, and no deaths directly associated with dalteparin sodium in pediatric patients less than 18 years of age.

5 CONCLUSION

DPV did not identify any new pediatric safety concerns for dalteparin sodium at this time and will continue routine pharmacovigilance monitoring for dalteparin sodium.

6 REFERENCES

1. Fragmin (dalteparin sodium) [package insert]. New York, NY; Pfizer, Inc. 2024.

[b] Unassessable reports are those that cannot be assessed for causality because there is insufficient information reported (i.e., unknown time to event, concomitant medications and comorbidities, clinical course and outcome), the information is contradictory, or information provided in the report cannot be supplemented or verified.
[c] Also known as the multisystem inflammatory syndrome in children.

7 APPENDICES

7.1 APPENDIX A. FDA ADVERSE EVENT REPORTING SYSTEM (FAERS)

The FDA Adverse Event Reporting System (FAERS) is a database that contains information on adverse event and medication error reports submitted to FDA. The database is designed to support FDA's postmarketing safety surveillance program for drug and therapeutic biological products. The informatic structure of the database adheres to the international safety reporting guidance issued by the International Council on Harmonisation. Adverse events and medication errors are coded to terms in the Medical Dictionary for Regulatory Activities terminology. The suspect products are coded to valid tradenames or active ingredients in the FAERS Product Dictionary.

FAERS data have limitations. First, there is no certainty that the reported event was actually due to the product. FDA does not require that a causal relationship between a product and event be proven, and reports do not always contain enough detail to properly evaluate an event. Further, FDA does not receive reports for every adverse event or medication error that occurs with a product. Many factors can influence whether an event will be reported, such as the time a product has been marketed and publicity about an event. Therefore, FAERS data cannot be used to calculate the incidence of an adverse event or medication error in the U.S. population.