

Eisai Sharps Disposal Plan

Background

Eisai Inc. (Eisai or “the company”) takes environmental management and safety seriously and has long supported programs that protect our environment. Eisai established formal environmental policies in 2002 and created its worldwide Environmental Management and Safety Committee specifically to address concerns of the company and the neighborhoods in which it lives.

Sound environmental policy is central to maintaining Eisai’s *human health care (hhc)* mission. During the course of our research, discovering, and developing new and innovative treatments for debilitating diseases, Eisai uses chemicals, compounds, and materials that could be hazardous if not properly handled. Eisai and all its employees abide by federal and state laws and regulations, and internal rules and procedures that regulate the handling of certain classes of these chemicals and compounds, and other hazardous materials. The company views global environmental protection as an important component of its business operations and strives to protect the environment. Eisai not only complies with local, state, federal, and international laws, regulations and agreements concerning environmental protection, it also implements voluntary standards that exceed these requirements. Because there are a variety of standards, we believe it is essential to focus on voluntary efforts in the area of environmental stewardship.

Eisai understands the impact a pharmaceutical company can have on its surrounding environment as a result of its research and development activities. Accordingly, Eisai conducts its business in a manner that is as environmentally safe and friendly as possible. Historically, Eisai has striven to voluntarily dispose of its pharmaceutical waste through incineration whenever possible. Eisai also ensures that the company abides by Food and Drug Administration (FDA) Standards for Good Manufacturing Practices.

Eisai Practices Regarding Sharps: Self-Retractable Syringes

A great example of Eisai’s attention to patient safety and the environment can be found with Eisai’s agent, Fragmin[®] (dalteparin sodium injection). (Please see “Fragmin[®]: Important Safety Information”, Appendix B. FRAGMIN[®] Prescribing Information can be seen [here](#).) Since the company began marketing Fragmin[®] in 2005, Eisai has provided a self-retractable needle. The self-retractable needle technology helps protect both patients and others from being stuck by a needle not properly disposed of in a sharps container. This self-retractable needle encompasses “anti-needlestick” technology that renders it a passive device. Patients or healthcare professionals administering Fragmin[®] do not need to proactively prompt the needle sheath. (The sheath covers the needle to protect the patient and others from “sticks.”) With the Fragmin[®] syringe, a protective sheath automatically encompasses the needle in one action once the drug has been fully administered. With the Fragmin[®] syringes a patient can inject with one hand and the safety sheath is automatically employed in one action. This “anti-needlestick” technology is designed to save healthcare workers, waste management workers, and patients from unwanted “sticks” that can result in many months of waiting for blood testing to ensure they have not contracted an illness. Eisai also believes that empty vials must be disposed

of properly to prevent illegal re-use, and/or an environmental impact due to residual amounts of the drug product still in the vial.

Eisai supports patient education on safe medication disposal. We support the guidelines outlined by the federal Food and Drug Administration (FDA), the Drug Enforcement Agency (DEA), and the White House Office of National Drug Control Policy (ONDCP). These guidelines support safe disposal in household trash (by mixing the medications with undesirable substances such as kitty litter or coffee grounds, sealing them in a plastic bag and disposing of them the trash and disposing the bottle in trash separately after blacking out identifiable information), taking advantage of any local drug take back programs, or flushing of the medication only when the FDA recommends it on the approved labeling.

Plan

Providing for Effective Safe Needle Disposal

Eisai works daily to fulfill its *human health care* mission, which is achieved when we can provide access to safe, effective medicines to patients in need. Safety weighs heavily on Eisai's decisions when providing all its products, which is why we currently use the passive self-retraction needle for the administration of Fragmin[®].

While the vast majority of Fragmin[®] patients receive their drug therapies in a hospital or clinical setting, the company continues its efforts, as appropriate, to ensure patients understand how to dispose of home-generated sharps waste.

Education and Outreach

Patients

Currently, Eisai offers educational communications regarding proper administration and disposal to patients through Eisai's web site (www.eisai.com/us [under the "About Eisai Inc.—Environmental Health and Safety" link on the top of the page]), which provides effective instructions on how to safely dispose of the self-retractable needles used in the administration of Fragmin[®] into a disposal container. The purpose of this web site is to instruct visitors on how to safely dispose of syringes in disposal containers, and after the containers are full, dispose of the container. The web page also informs visitors about the California ban on disposing sharps in landfills, and provides information about appropriate sites to dispose of the containers according to the law.

Healthcare Practitioners

The company works with appropriate professional associations, when necessary, not only to educate physicians about safe sharps disposal and Eisai's plan in this regard, but patients as well. Educating healthcare practitioner organizations about Eisai's plan may ultimately enhance patient initiative because patients may be more apt to follow the plan if a trusted healthcare practitioner is giving guidance.

Eisai makes specific recommendations on its web site (www.eisai.com/us) under the “Environmental, Health and Safety” link for healthcare practitioners. The “environmental, health, and safety” page is focused exclusively on requirements or recommendations for disposal and we work to inform practitioners on the most appropriate means to instruct their patients to dispose of sharps containers.

Government Officials

When appropriate, Eisai may notify the state and local waste management departments about its plan to help patients dispose of sharps medical waste. This notification includes a contact name referring any inquiries regarding Eisai’s actions to the most appropriate company personnel. In such a case, government officials would also be directed to Eisai’s web page on sharps disposal and environmental, health, and safety.

Community Involvement

Eisai has a link on its web site permitting patients and others the opportunity to offer suggestions about how Eisai might improve its waste disposal plans. Eisai reviews these suggestions as it continues to monitor its plan for the disposal of sharps waste.

Eisai Contact Information

For any suggestions or inquiries regarding this sharps disposal plan, please contact the following person:

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Senior Manager, State Government Affairs
Sacramento, CA 95831
916-397-4734
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Appendix A:

The only prescription drug Eisai manufactures and distributes that is administered via a sharps device at home is Fragmin[®]. Fragmin[®] is administered through a passive self-retractable needle.

Provided Plan Elements	Company Activity
Patient Education	<p>Eisai continues to educate patients in a manner reflecting appropriate means of communication and use, including:</p> <ul style="list-style-type: none"> • Via the “Environmental Health and Safety“ link on Eisai.com/us, Eisai: <ul style="list-style-type: none"> - Includes a web page for patients regarding sharps disposal. - Explains the importance of proper sharps disposal for safety and the environment. - Provides contact information of additional groups that may have information on the issue. - Explains that in some states, such as in California, there is a ban on sharps in landfills and inform patients of the types of facilities at which it is appropriate to dispose of containers.
Local and state Coordination	<ul style="list-style-type: none"> • When appropriate, Eisai sends letters or electronic communication to waste management personnel of state and local programs informing them of its activities. If sent, these communications provide information regarding Eisai’s web site page for sharps disposal and environmental, health, and safety issues.
Consumer/Community Involvement	<ul style="list-style-type: none"> • Eisai has placed a link on its web site permitting patients or others the opportunity to offer the company suggestions on ways to improve the plan. Eisai reviews these suggestions as it continues to monitor this plan for collecting and disposing of sharps waste. • Eisai’s web site explains the California Code banning sharps waste from landfills and where it is best to dispose of sharps containers. • Eisai works with appropriate professional associations, when necessary, such as the physician and pharmacy trade associations, to ensure there will be a commitment from trusted healthcare practitioners in order to provide patient education on a safe manner of disposal at the provider level. The Eisai.com/us web site has been modified to ensure it has the most appropriate information addressing issues for healthcare practitioners.

Appendix B:

FRAGMIN[®]:

Please see FRAGMIN[®] Prescribing Information [here](#).

Indications

FRAGMIN[®] is a low molecular weight heparin (LMWH) indicated for:

- Prophylaxis of ischemic complications of unstable angina and non-Q-wave myocardial infarction
- Prophylaxis of deep vein thrombosis (DVT) in abdominal surgery, hip replacement surgery or medical patients with severely restricted mobility during acute illness
- Extended treatment of symptomatic venous thromboembolism (VTE) to reduce the recurrence in patients with cancer. In these patients, the FRAGMIN[®] therapy begins with the initial VTE treatment and continues for six months.

Limitations of Use

- FRAGMIN[®] is not indicated for the acute treatment of VTE.

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
- 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.

- 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.
- The optimal timing between the administration of FRAGMIN[®] and neuraxial procedures is not known. To reduce the potential risk of bleeding associated with concurrent use of FRAGMIN[®] and epidural or spinal anesthesia/analgesia or spinal puncture, consider the pharmacokinetic profile of FRAGMIN[®].
 - Should the physician decide to administer anticoagulation in the context of epidural or spinal anesthesia/analgesia or lumbar puncture, frequent monitoring must be exercised to detect any signs and symptoms of neurological impairment such as midline back pain, sensory and motor deficits (numbness or weakness in lower limbs), bowel and/or bladder dysfunction. Instruct patients to report immediately if they experience any of the above signs or symptoms. If signs or symptoms of spinal hematoma are suspected, initiate urgent diagnosis and treatment including consideration for spinal cord decompression even though such treatment may not prevent or reverse neurological sequelae.
- 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[®] 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/mm³. 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/mm³.

- 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.
- Each multiple-dose vial of FRAGMIN[®] contains benzyl alcohol as a preservative. Benzyl alcohol has been reported to be associated with a fatal “Gaspings 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[®]. Anti-Factor Xa may be used to monitor the anticoagulant effect of FRAGMIN[®], such as in patients with severe renal impairment or if abnormal coagulation parameters or bleeding occurs during FRAGMIN[®] therapy.
- The most commonly reported side effect is hematoma at the injection site.
- Allergic reactions (i.e., pruritus, rash, fever, injection site reaction, bullous 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.