U.S. Food and Drug Administration
Protecting and Promoting *Your* Health

Drug Safety Communications

Updated recommendations to decrease risk of spinal column bleeding and paralysis in patients on low molecular weight heparins

Safety Announcement

[11-6-2013] The U.S. Food and Drug Administration (FDA) is recommending that health care professionals carefully consider the timing of spinal catheter placement and removal in patients taking anticoagulant drugs, such as enoxaparin, and delay dosing of anticoagulant medications for some time interval after catheter removal to decrease the risk of spinal column bleeding and subsequent paralysis after spinal injections, including epidural procedures and lumbar punctures. These new timing recommendations, which can decrease the risk of epidural or spinal hematoma, will be added to the labels of anticoagulant drugs known as low molecular weight heparins, including Lovenox and generic enoxaparin products and similar products.

Health care professionals and institutions involved in performing spinal/epidural anesthesia or spinal punctures should determine, as part of a preprocedure checklist, whether a patient is receiving anticoagulants and identify the appropriate timing of enoxaparin dosing in relation to catheter placement or removal. To reduce the potential risk of bleeding, consider both the dose and the elimination half-life of the anticoagulant:

- For enoxaparin, placement or removal of a spinal catheter should be delayed for at least 12 hours after administration of prophylactic doses such as those used for prevention of deep vein thrombosis. Longer delays (24 hours) are appropriate to consider for patients receiving higher therapeutic doses of enoxaparin (1 mg/kg twice daily or 1.5 mg/kg once daily).
- A postprocedure dose of enoxaparin should usually be given no sooner than 4 hours after catheter removal.
- In all cases, a benefit-risk assessment should consider both the risk for thrombosis and the risk for bleeding in the context of the procedure and patient risk factors.

Epidural or spinal hematomas are a known risk of enoxaparin in the setting of spinal procedures and are already described in the *Boxed Warning* and the *Warnings and Precautions* sections of the labels for Lovenox and generic enoxaparin products. However, these serious adverse events continue to occur (see Data Summary). To address this safety concern, FDA worked with the manufacturer of Lovenox, Sanofi-Aventis, to further evaluate this risk and to update the *Warnings and Precautions* section of the Lovenox label with these additional timing

recommendations. The labels for generic enoxaparin products will also be revised accordingly, as will those of other low molecular weight heparin-type products.

Before undergoing an epidural or spinal procedure, patients should inform their health care professional if they are taking any anticoagulant drugs. When undergoing these types of procedures, patients should alert their health care professional immediately if they experience any symptoms such as numbness, tingling, leg weakness or paralysis, or loss of control over their bladder or bowels.

It is important to note that all anticoagulants carry the risk of causing spinal bleeding when used in conjunction with epidural/spinal anesthesia or spinal puncture. We are continuing to evaluate the safety of other anticoagulants to determine if additional label changes are needed.

Facts about enoxaparin (Lovenox)

- A blood-thinning drug used to prevent blood clots in the leg veins in patients who are on bed rest or who are having hip replacement, knee replacement, or abdominal surgery. It is often used along with another anticoagulant drug called warfarin to treat blood clots in the leg.
- Also used in combination with aspirin to reduce complications from heart attacks
- Comes in a syringe for injection

Additional Information for Patients

- If you will have epidural or spinal anesthesia, a spinal puncture, or an epidural injection for pain while receiving a blood-thinner such as enoxaparin (Lovenox or its generics), there is a risk for having bleeding around your spine that could cause you to become paralyzed.
- Tell your health care professional if you are taking any blood-thinning drugs, such as warfarin (Coumadin), anagrelide (Agrylin), aspirin or nonsteroidal anti-inflammatory drugs (ibuprofen, naproxen), cilostazol (Pletal), clopidogrel (Plavix), dipyridamole (Persantine), eptifibatide (Integrilin), prasugrel (Effient), sulfinpyrazone (Anturane), ticlopidine (Ticlid), or tirofiban (Aggrastat).
- After a spinal procedure, alert your health care professional immediately if you experience any symptoms such as numbness, tingling, leg weakness or paralysis, or loss of control over your bladder or bowels.
- Talk to your health care professional if you have any questions or concerns about enoxaparin or other anticoagulants.
- Report side effects from enoxaparin to the FDA MedWatch program, using the information in the "Contact FDA" box at the bottom of this page.

Additional Information for Health Care Professionals

- Cases of epidural or spinal hematomas continue to be reported with the use of enoxaparin (Lovenox or its generics) and other low molecular weight heparins and spinal/epidural anesthesia or spinal puncture procedures, resulting in long-term or permanent paralysis.

- Health care professionals and institutions involved in performing spinal/epidural anesthesia or spinal punctures should determine, as part of a preprocedure checklist, whether a patient is receiving anticoagulants and identify the appropriate timing of enoxaparin or other anticoagulant dosing in relation to catheter placement/removal.
- To reduce the potential risk of bleeding associated with the concurrent use of enoxaparin and epidural or spinal anesthesia/analgesia, the placement and removal of the catheter is best performed when the anticoagulant effect of enoxaparin is low, considering the dose of anticoagulant and its elimination half-life. Although no prospective trials of this timing have been performed to date, additional guidance is being provided now for considerations that may reduce the risk.
- Placement or removal of a catheter should usually be delayed for 12 hours after administration of deep vein thrombosis (DVT) prophylactic doses of enoxaparin, whereas patients receiving higher doses of enoxaparin (1 mg/kg twice daily or 1.5 mg/kg once daily) will require longer delays (24 hours). The subsequent enoxaparin dose should usually be given no sooner than 4 hours after catheter removal.
- In all cases, a benefit-risk assessment should consider both the risk for thrombosis and the risk for bleeding in the context of the procedure and patient risk factors.
- If anticoagulation is administered in the setting of epidural/spinal anesthesia, monitor patients frequently to detect any signs and symptoms of neurological impairment, such as midline back pain, sensory and motor deficits such as numbness or weakness in lower limbs, and bowel and/or bladder dysfunction.
- Counsel patients to alert their health care professional immediately if they experience any of the above signs or symptoms.
- If signs or symptoms of spinal hematoma are suspected, urgent diagnosis and treatment including spinal cord decompression should be initiated.
- All anticoagulants carry the risk of causing epidural or spinal hematomas when used in conjunction with epidural/spinal anesthesia or spinal puncture.
- Report adverse events involving enoxaparin to the FDA MedWatch program, using the information in the "Contact FDA" box at the bottom of this page.

Data Summary

The manufacturer of Lovenox, Sanofi-Aventis submitted to FDA 170 cases of spinal or epidural hematoma associated with Lovenox thromboprophylaxis and neuraxial anesthesia (spinal or epidural) or spinal puncture reported between July 20, 1992 (which precedes FDA-approval of Lovenox on March 29, 1993), and January 31, 2013. FDA reviewed these reports and found that 100 cases contained a confirmed diagnosis of spinal or epidural hematoma (by computed tomography [CT], magnetic resonance imaging [MRI], clinical symptoms/signs or surgical findings) or clear mention of spinal or epidural anesthesia, spinal puncture, or epidural anesthesia.

Among the 100 cases, the frequencies of certain risk factors for spinal or epidural hematoma were as follows:

Risk factors*	N
Patient factors	
Female sex	72
Elderly (≥65 years)	70
Abnormalities of spinal cord or vertebral column	20
Patients at increased risk of hemorrhage†	47
Renal insufficiency	7
Anesthetic factors	
Traumatic needle/catheter placement	26
Epidural technique	54
Indwelling epidural catheter during Lovenox administration	36
Lovenox dosing factors	
Immediate preoperative administration (<12 hours)	5
Intraoperative administration	7
Early postoperative administration (<12 hours)	17
Administration close to indwelling catheter removal (<12 hours)	1
Twice daily administration (vs. once daily administration)	48
Higher Lovenox dose than that in the label	1
Concomitant medications affecting hemostasis (antiplatelet, anticoagulant, NSAIDs, etc.)	43

*More than one risk factor could be found in a single case.

†Patient characteristics that increase risk of hemorrhage include: hypertension; malignancies; post-trauma or surgeries; rheumatoid arthritis; Crohn's disease; chronic atrial fibrillation treated with anticoagulant; and gastrointestinal bleeding.