

er. This is especially true for nonsymptomatic patients. “Several trials now show that in people without symptomatic heart disease, fixing the heart first doesn’t make much of a difference in how well they do in surgery.”

The guidelines also emphasize continuing antiplatelet therapy as soon as possible after urgent noncardiac surgery, especially in patients with drug-eluting coronary stents.

Dr. Fleisher said that the large amount of new data gathered in recent months led his group to postpone publication of the recommendations, but that in the future, he hopes to be able to publish more

frequent, focused updates, especially in reference to  $\beta$ -blockers.

The authors concluded by highlighting areas that require further study. “Although randomized trials have examined the effect of perioperative  $\beta$ -blockers on cardiac events surrounding surgery, and observational studies have shown the benefit of statins during the perioperative period, further evidence is needed with regard to the length of time medical therapy needs to be initiated before noncardiac surgery to be effective,” including management of antiplatelet drugs perioperatively, they wrote. ■

## NT-proBNP ‘Excellent’ Predictor

VIENNA — Preoperative N-terminal prohormone-B-type natriuretic peptide level is a strong and independent predictor of postoperative cardiac event risk in patients undergoing a wide range of non-coronary vascular surgery, Dr. Olaf Schouten reported at the annual congress of the European Society of Cardiology.

In a prospective study in 419 consecutive patients undergoing aortic aneurysm repair, lower-extremity peripheral bypass operations, or carotid surgery, patients with a preoperative NT-proBNP greater than

300 pg/mL had a 5.6-fold increased risk of a postoperative cardiac event, compared with those with a lesser value, even after adjustment for baseline cardiac risk factors and the type of vascular surgery, said Dr. Schouten, a vascular surgeon at Erasmus University, Rotterdam, the Netherlands.

Postoperative cardiac events—defined as the 30-day composite of death, MI, or troponin release—occurred in 20% of the 419 patients. The highest-risk form of vascular surgery was aortic aneurysm repair.

—Bruce Jancin

3. Remove the syringe from the injection site keeping your finger on the plunger rod (see Figure C).

Figure C



4. Orient the needle away from you and others, and activate the safety system by firmly pushing the plunger rod. The protective sleeve will automatically cover the needle and an audible “click” will be heard to confirm shield activation (see Figure D).

Figure D



5. Immediately dispose of the syringe in the nearest sharps container (see Figure E).

Figure E



#### NOTE:

- The safety system can only be activated once the syringe has been emptied.
- Activation of the safety system must be done only after removing the needle from the patient’s skin.
- Do not replace the needle shield after injection.
- The safety system should not be sterilized.

Activation of the safety system may cause minimal splatter of fluid. For optimal safety activate the system while orienting it downwards away from yourself and others.

**Intravenous (Bolus) Injection Technique:** For intravenous injection, the multiple-dose vial should be used. Lovenox should be administered through an intravenous line. Lovenox should not be mixed or co-administered with other medications. To avoid the possible mixture of Lovenox with other drugs, the intravenous access chosen should be flushed with a sufficient amount of saline or dextrose solution prior to and following the intravenous bolus administration of Lovenox to clear the port of drug. Lovenox may be safely administered with normal saline solution (0.9%) or 5% dextrose in water.

#### CONTRAINDICATIONS

- Active major bleeding.
- Thrombocytopenia associated with a positive *in vitro* test for anti-platelet antibody in the presence of enoxaparin sodium.
- Known hypersensitivity to enoxaparin sodium (e.g., pruritus, urticaria, anaphylactoid reactions) [see *Adverse Reactions* (6.2)].
- Known hypersensitivity to heparin or pork products.
- Known hypersensitivity to benzyl alcohol (which is in only the multi-dose formulation of Lovenox).

#### WARNINGS AND PRECAUTIONS

##### Increased Risk of Hemorrhage

Cases of epidural or spinal hematomas have been reported with the associated use of Lovenox and spinal/epidural anesthesia or spinal puncture resulting in long-term or permanent paralysis. The risk of these events is higher with the use of post-operative indwelling epidural catheters or by the concomitant use of additional drugs affecting hemostasis such as NSAIDs [see *boxed Warning, Adverse Reactions* (6.2) and *Drug Interactions* (7)].

Lovenox should be used with extreme caution in conditions with increased risk of hemorrhage, such as bacterial endocarditis, congenital or acquired bleeding disorders, active ulcerative and angiodysplastic gastrointestinal disease, hemorrhagic stroke, or shortly after brain, spinal, or ophthalmological surgery, or in patients treated concomitantly with platelet inhibitors.

Major hemorrhages including retroperitoneal and intracranial bleeding have been reported. Some of these cases have been fatal.

Bleeding can occur at any site during therapy with Lovenox. An unexplained fall in hematocrit or blood pressure should lead to a search for a bleeding site.

#### LOVENOX®

#### (enoxaparin sodium injection)

##### Percutaneous coronary revascularization procedures

To minimize the risk of bleeding following the vascular instrumentation during the treatment of unstable angina, non-Q-wave myocardial infarction and acute ST-segment elevation myocardial infarction, adhere precisely to the intervals recommended between Lovenox doses. It is important to achieve hemostasis at the puncture site after PCI. In case a closure device is used, the sheath can be removed immediately. If a manual compression method is used, sheath should be removed 6 hours after the last IV/SC Lovenox. If the treatment with enoxaparin sodium is to be continued, the next scheduled dose should be given no sooner than 6 to 8 hours after sheath removal. The site of the procedure should be observed for signs of bleeding or hematoma formation [see *Dosage and Administration* (2.1)].

##### Use of Lovenox with Concomitant Medical Conditions

Lovenox should be used with care in patients with a bleeding diathesis, uncontrolled arterial hypertension or a history of recent gastrointestinal ulceration, diabetic retinopathy, and hemorrhage.

##### History of Heparin-induced Thrombocytopenia

Lovenox should be used with extreme caution in patients with a history of heparin-induced thrombocytopenia.

##### Thrombocytopenia

Thrombocytopenia can occur with the administration of Lovenox.

Moderate thrombocytopenia (platelet counts between 100,000/mm<sup>3</sup> and 50,000/mm<sup>3</sup>) occurred at a rate of 1.3% in patients given Lovenox, 1.2% in patients given heparin, and 0.7% in patients given placebo in clinical trials.

Platelet counts less than 50,000/mm<sup>3</sup> occurred at a rate of 0.1% in patients given Lovenox, in 0.2% of patients given heparin, and 0.4% of patients given placebo in the same trials.

Thrombocytopenia of any degree should be monitored closely. If the platelet count falls below 100,000/mm<sup>3</sup>, Lovenox should be discontinued. Cases of heparin-induced thrombocytopenia with thrombosis have also been observed in clinical practice. Some of these cases were complicated by organ infarction, limb ischemia, or death [see *Warnings and Precautions* (5.4)].

##### Interchangeability with Other Heparins

Lovenox cannot be used interchangeably (unit for unit) with heparin or other low molecular weight heparins as they differ in manufacturing process, molecular weight distribution, anti-Xa and anti-IIa activities, units, and dosage. Each of these medicines has its own instructions for use.

##### Pregnant Women with Mechanical Prosthetic Heart Valves

The use of Lovenox for thromboprophylaxis in pregnant women with mechanical prosthetic heart valves has not been adequately studied. In a clinical study of pregnant women with mechanical prosthetic heart valves given enoxaparin (1 mg/kg twice daily) to reduce the risk of thromboembolism, 2 of 8 women developed clots resulting in blockage of the valve and leading to maternal and fetal death. Although a causal relationship has not been established these deaths may have been due to therapeutic failure or inadequate anticoagulation. No patients in the heparin/warfarin group (0 of 4 women) died. There also have been isolated postmarketing reports of valve thrombosis in pregnant women with mechanical prosthetic heart valves while receiving enoxaparin for thromboprophylaxis. Women with mechanical prosthetic heart valves may be at higher risk for thromboembolism during pregnancy, and, when pregnant, have a higher rate of fetal loss from stillbirth, spontaneous abortion and premature delivery. Therefore, frequent monitoring of peak and trough anti-Factor Xa levels, and adjusting of dosage may be needed [see *Use in Specific Populations* (8.6)].

##### Benzyl Alcohol

Lovenox multiple-dose vials contain benzyl alcohol as a preservative. The administration of medications containing benzyl alcohol as a preservative to premature neonates has been associated with a fatal “Gasping Syndrome”. Because benzyl alcohol may cross the placenta, Lovenox multiple-dose vials, preserved with benzyl alcohol, should be used with caution in pregnant women and only if clearly needed [see *Use in Specific Populations* (8.1)].

##### Laboratory Tests

Periodic complete blood counts, including platelet count, and stool occult blood tests are recommended during the course of treatment with Lovenox. When administered at recommended prophylaxis doses, routine coagulation tests such as Prothrombin Time (PT) and Activated Partial Thromboplastin Time (aPTT) are relatively insensitive measures of Lovenox activity and, therefore, unsuitable for monitoring. Anti-Factor Xa may be used to monitor the anticoagulant effect of Lovenox in patients with significant renal impairment. If during Lovenox therapy abnormal coagulation parameters or bleeding should occur, anti-Factor Xa levels may be used to monitor the anticoagulant effects of Lovenox [see *Clinical Pharmacology* (12.3)].

##### ADVERSE REACTIONS

##### Clinical Trials Experience

Because clinical studies are conducted under widely varying conditions, adverse reaction rates observed in the clinical studies of a drug cannot be directly compared to rates in the clinical studies of another drug and may not reflect the rates observed in practice.