Drug Guideline Title: Enoxaparin

Approved by: ICU Director
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Replaces Existing Drug Guideline: enoxaparin 2004

1. Introduction

The risk addressed by this policy:

Patient Safety

The Aims / Expected Outcome of this policy:

Enoxaparin should be administered safely and appropriately without any adverse side effects

Related Standards or Legislation

NSQHS Standard 1 Governance
National Standard 4 Medication Safety

Related Policies

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2. Policy Statement:

- All care provided within Liverpool Hospital will be in accordance with infection control, manual handling and minimization and management of aggression guidelines.
- Medications are to be prescribed and signed by a medical officer/authorized nurse practitioner (NP) unless required during an emergency.
- All drugs administered during an emergency (under the direction of a medical officer/authorized nurse practitioner) are to be documented during the event, then prescribed and signed following the event.
- Medications are to be given at the time prescribed (as close to the time as is possible when multiple drugs require ‘same time’ administration and, when the nurse is caring for more than one patient, recognition is given to a possible short delay to administration – antibiotics and other lifesaving drugs are to be prioritized) and are to be signed by the administering nurse.
• Parenteral medication prescriptions and the drug are to be checked with a second registered or endorsed enrolled nurse prior to administration. The “rights of drug administration” must be followed: right: patient, drug, dose, route, administration, time, reason for the drug, documentation, education and evaluation/outcome.
• Adverse drug reactions are to be documented and reported to a medical officer.
• Medication errors are to be reported using the hospital electronic reporting system: IIMS.
• Guidelines are for adult patients unless otherwise stated.
• Baseline FBC, PT, APTT, INR, EUC, CMP is necessary for all patients requiring low molecular weight heparin.

3. Principles / Guidelines

Actions 4,5,6
• Enoxaparin is an anticoagulant and antithrombotic. It is formed by depolymerisation of heparin to form a low molecular weight heparin.
• Its anticoagulant effect is by several actions on the coagulation pathway through binding to antithrombin III.
• The antithrombotic activity is related to inhibition of thrombin generation and inhibition of two main coagulation factors: factor Xa and thrombin.
• It also induces a sustained release of the tissue factor pathway inhibitor

Indications 1,4,5,9
• Prevention of venous thromboembolism in patients undergoing surgery, critically ill patients who are unwell and bed bound.
• Treatment of deep vein thrombosis.
• Treatment of unstable angina and non-Q wave myocardial infarction, with concurrent administration of aspirin.
• Treatment of acute ST-segment elevation MI (STEMI), with concurrent use of thrombolytic.
• Enoxaparin is the low molecular weight heparin currently prescribed in the ICU as the primary pharmacological prophylaxis in the following patients only unless discussed with the ICU staff specialist:
  ⇒ Hip replacements, total knee replacements.
  ⇒ Multi trauma patients who do not have multi organ failure or high risk of bleeding,
  ⇒ Spinal injuries after consultation with neurosurgeons

Contraindications 1,6
• Allergy to enoxaparin sodium, heparin or low molecular weight heparins.
• Acute bacterial endocarditis.
• Conditions with a risk of uncontrolled bleeding, bleeding disorders, focal lesions, haemorrhagic stroke (subarachnoid haemorrhage), active ulcerative disorders.
• Thrombocytopenia associated with positive in vitro test for antiplatelet antibodies.
• It is not used in patients with renal impairment, patients over 100 kg or less than 55 kg without discussion with the ICU Staff Specialist.

Precautions 6,7
• Heparin induced thrombocytopenia.
• Hepatic insufficiency, severe renal and hepatic disease.
• Uncontrolled arterial hypertension.
• History of gastrointestinal ulceration.
• Impaired haemostasis, concurrent platelet therapy.
• Recent ischaemic stroke.
• Diabetic retinopathy, recent neurological or ophthalmic surgery.
Significant Interactions $^{6,7}$

- It is not recommended to administer with agents affecting haemostasis: anticoagulants, thrombolytics, NSAIDs, systemic salicylates, aspirin, ticlopidine, dextran, clopidogrel, antiplatelet agents, glucocorticoids

Adverse Effects $^{6,7}$

- Haemorrhage.
- Thrombocytopaenia, thrombocytosis.
- Asymptomatic and reversible increases in liver transaminases.
- Skin irritation, systemic allergic reactions.
- Injection site reaction including skin necrosis – discontinue.

Before starting treatment

- Baseline full blood count is recommended and assessment of PT, aPTT, electrolytes, urea and serum creatinine concentration. A haematologist should be consulted if there are significant baseline abnormalities of full blood count, PT and/or aPTT.
- Estimate calculated creatinine clearance (CrCL). The eGFR (estimated glomerular filtration rate) is calculated by the pathology laboratories but may not be accurate at extremes of body weight, children, frail older people or with acute changes in kidney function. If in doubt CrCL should be calculated using the COCKCROFT–GAULT EQUATION which is available as an online calculator in powerchart (eMR).
- For patients with venous thromboembolism, cease antiplatelet agents unless it is specifically intended to continue these, and the benefit outweighs the risk.

Presentation

Enoxaparin pre-filled syringes:
- 20mg in 0.2 mL; 40mg in 0.4 mL; 60mg in 0.6 mL; 80mg in 0.8 mL; 100mg in 1.0 mL.

Administration Guidelines $^{4,5,6,7,10}$

- Care is required particularly in older patients, low body weight, patients on antiplatelet agents, and in the presence of impaired renal function.
- Do not administer intramuscularly.
- The subcutaneous injection of enoxaparin should be alternated between the left and right anterolateral abdominal wall using a different site for each injection. Do not rub the injection site after administration.
- Do not expel the air bubble from the syringe before the injection to avoid the loss of drug when using the 20 and 40 mg prefilled syringes.
- The whole length of the needle should be introduced vertically into the thickness of a skin fold held gently between the operator’s thumb and finger. This skin fold should be held throughout the duration of the injection.
- When using the 60, 80 and 100 mg graduated prefilled syringes, the volume to be injected should be measured precisely according to the dosage recommended.

A. Prophylaxis for venous thrombosis.

- High risk patients to receive enoxaparin 40mg in 0.4 mL, administered subcutaneously once daily. Therapy should continue for 7 – 10 days until risk has diminished.
- Moderate risk patients to receive enoxaparin 20mg in 0.2 mL, administered subcutaneously once daily. Therapy should continue for 7 – 10 days until risk has diminished.
B. Surgical patients.
- High risk patients to receive enoxaparin 40mg in 0.4 mL, administered postoperatively at 12 hours, subcutaneously.
- Dose is 40mg once daily, subcutaneously; continue until risk of DVT has diminished (usually 7-10 days)
- Prolonged thromboprophylaxis: enoxaparin 40mg in 0.4 mL once daily can be continued for up to 35 days postoperatively.

C. Prophylaxis for venous thromboembolism in Medical Patients.
- Enoxaparin 40mg in 0.4 mL subcutaneously daily for 6 to 11 days.

D. Treatment of DVT (deep venous thrombosis).
- Enoxaparin 1mg/kg of 100mg in 1.0mL, every 12 hours subcutaneously. Administered for 5 to 7 days or until a therapeutic oral anticoagulant effect is achieved (add warfarin usually within 72 hours to achieve an INR of 2-3).

E. Treatment of unstable angina and non-Q wave myocardial infarction.
- Enoxaparin 1mg/kg every 12 hours subcutaneously with the administration of concurrent oral aspirin. Duration for a minimum of 2 days and a maximum of 8 days.

F. Treatment of STEMI
- Enoxaparin 1mg/kg of 100mg in 1.0mL every 12 hours subcutaneously with the administration of concurrent oral aspirin. Administer between 15 minutes before and 30 minutes after start of fibrinolytic therapy for 8 days or until discharge.

G. Elderly Patients
- Enoxaparin 0.75mg/kg every 12 hours subcutaneously (maximum dose of 75mg subcutaneously)

Clinical Considerations
- The pre-filled syringe contains no antimicrobial agent and is for single-use only.
- Low molecular weight products are not interchangeable.
- Enoxaparin is renally excreted and accumulates in renal failure. Care is required particularly in older patients, low body weight, patients on antiplatelet agents, and in the presence of impaired renal function.
- Calculated creatinine clearance rate (CrCL) may overestimate renal function in very obese or oedematous patients.
- Formal assessment of renal function is recommended in these patients.
- Monitor anti-Xa levels to measure the anticoagulant effect of enoxaparin. aPTT is insensitive to enoxaparin.
- If the patient has had a recent surgical procedure, the surgeon involved should be consulted before the commencement of LMWH therapy.
- Patients receiving enoxaparin in conjunction with epidural/spinal anaesthesia are at risk for haematoma. Extreme vigilance must be used to detect signs such as observe...
for signs of midline back pain, sensory and motor deficits (numbness or weakness in lower limbs), bowel and/or bladder dysfunction.

- Patients should be instructed to inform their nurse/doctor immediately if they experience any of the above signs or symptoms.
- If signs or symptoms of spinal haematoma are suspected, urgent diagnosis and treatment including spinal cord decompression should be initiated.
- Platelet counts should be measured before initiation of therapy and then regularly during treatment. If there is a drop of 30 to 50% of the initial value, discontinue therapy immediately, perform antibody testing, and consider use of an alternate drug.

Considerations for enoxaparin use with High Risk Bleeding Procedures, Vascular Access and Epidural Catheter Insertion and Removal

- High bleeding risk procedure should where possible be avoided within 24-36 hours of a dose of enoxaparin and potentially longer if there is significant renal impairment.
- Vascular access sheaths should remain insitu for 6-8 hours after the administration of enoxaparin and doses withheld for 6-8 hours after removal of the sheath.
- No enoxaparin is to be administered within 12 hours of insertion or removal of an epidural/spinal catheter.
- In patients receiving pre-operative anticoagulant, insertion of epidural catheter should be delayed for at least 8-12 hours after a subcutaneous dose of twice daily enoxaparin, or at least 18 hours after a once daily dose of enoxaparin.

Monitoring

- Blood should be taken 4 hours (3 - 5 hours) after a dose of Enoxaparin for peak anti-Xa levels. Routine monitoring of anti-Xa levels is not required, but has been utilized in patients with obesity and/or renal insufficiency.
- For twice daily dosing, the therapeutic peak range is 0.6 - 1.0 units/mL.
- For once daily dosing, the peak anti-Xa activity should be 1 - 2 units/mL (Limited literature exist on once daily dosing compared to every 12 hours dosing).
- A full blood count should be checked daily for patients on LMWH therapy, to exclude heparin-induced thrombocytopenia, check for a fall in haemoglobin which may suggest bleeding.
- If thrombocytopaenia develops then LMW heparin therapy should be urgently reviewed and appropriate investigations instituted in consultation with a Haematologist.
- The possibility of a retroperitoneal bleed should be considered in the absence of another identified cause of pain in the back, leg, or abdomen. A full blood count and anti-Xa activity should be performed and reviewed as soon as possible including urgent medical assessment and imaging of the abdomen.
- Where the therapeutic intention is anticoagulation for venous thromboembolism, non-steroidal anti-inflammatory drugs (NSAIDs), aspirin and antiplatelet agents should be ceased to reduce the risk of bleeding, unless there is a specific indication for continued antiplatelet therapy, such as coronary stents. Consult Cardiologist.

Management of bleeding on Low Molecular Weight Heparin (LMWH)

- Although protamine only partially reverses the effect of LMWH, it does appear to reduce bleeding. The dose of protamine depends on the dose of enoxaparin injected.
- The suggested dosage of protamine is:
  - 1 mg protamine for each 100 anti-Xa units or per 1mg of enoxaparin given in the previous 8 hours (this is because 1 mg enoxaparin = 100 anti-Xa units)
  - A second dose of 0.5 mg protamine per 100 anti-Xa units (1mg) of enoxaparin LMW heparin can be considered if severe bleeding continues.
  - If the last dose of LMW heparin was > 8 hours, a smaller dose should be given (e.g. 0.5 mg protamine per mg of enoxaparin). 
- Protamine may not be beneficial if the last dose of LMW heparin was > 12 hours ago and renal function is normal.
4. **Performance Measures**
All incidents are documented using the hospital electronic reporting system: IIMS and managed appropriately by the NUM and staff as directed.

5. **References / Links**
10. SWSLHD_GL2015_004_Anticoagulation: Heparin (LMWH, UFH) and Warfarin

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