Low molecular weight heparin

use in primary care

Enoxaparin (Clexane) is a low molecular weight heparin (LMWH) used in the treatment of acute coronary syndromes and in the treatment and prevention of thromboembolic disorders.

Access to enoxaparin, has recently been widened, and GPs may become increasingly involved in its use. For many conditions, treatment with enoxaparin is started in hospital, however GPs may be involved in its initiation as well as the continuation of treatment.

In acute deep vein thrombosis without pulmonary embolism, enoxaparin can be used in the out-of-hospital setting (in conjunction with warfarin) because it can be administered by subcutaneous injection and generally does not require routine laboratory monitoring.

Initiation of enoxaparin

Contraindications to enoxaparin

Enoxaparin is contraindicated for people with an allergy to enoxaparin or other LMWHs as well as for people with active bleeding and conditions with a high risk of haemorrhage such as recent haemorrhagic stroke.[1]

It is also contraindicated if platelet count is less than, or equal to 50×10^9/L, in bacterial endocarditis, uncontrolled or severe hypertension, severe hepatic or renal disease, angiodysplasia or following recent eye or CNS surgery (less than one month prior).

Prior to commencing enoxaparin

Prior to commencing therapy with enoxaparin it is recommended that all patients:[2]

1. Are weighed
2. Have their creatinine clearance calculated using the Cockcroft- Gault formula. The eGFR calculated by the laboratory can be used as an indicator of renal impairment but the creatinine clearance equation should be used to guide dosage adjustment

Subsidised enoxaparin on special authority

Enoxaparin is available fully subsidised via special authority for pregnant women who require treatment with a low molecular weight heparin or for the treatment of venous thromboembolism where the patient has a malignancy.

It is also available fully subsidised via special authority for one month:

- For the short-term treatment of venous thromboembolism prior to establishing a therapeutic INR with oral anticoagulant treatment
- For the prophylaxis and treatment of venous thromboembolism in high risk surgery
- To enable cessation/re-establishment of existing warfarin treatment pre/post surgery
- For the prophylaxis and treatment of venous thromboembolism in acute coronary syndrome surgical intervention
- To be used in association with cardioversion of atrial fibrillation

3. Have blood tests to make sure they have a normal coagulation profile (INR, APTT), platelet count and normal liver function

Enoxaparin dosing

See Table 1 for dosing volumes.

Patients without renal impairment:[1]

Prophylaxis of venous thromboembolism: 40 mg daily

Treatment of venous thromboembolism:* 1.5 mg/kg once daily or 1 mg/kg twice daily

* Significant pulmonary embolus is usually treated with twice daily dosing.

Patients with renal impairment:

Prophylaxis of venous thromboembolism: 20 mg daily

Treatment of venous thromboembolism: An initial standard dose of enoxaparin based on the patient's actual body weight is used so that an effective concentration is achieved rapidly. However, for patients with reduced renal function (i.e. creatinine clearance less than 30 mL/min), subsequent doses require adjustment because of the risk of over-coagulation and bleeding.

For patients with creatinine clearance less than 30 mL/min enoxaparin should be dosed at 1 mg/kg once daily.[2]

Patients who are at extremes of weight

Dosing based on body weight is acceptable up to 150 kg, however there is evidence that a dose based on lean body weight may be more appropriate.[4] Once daily treatment is not recommended in patients over 100 kg (maximum syringe size is 150 mg).

Enoxaparin administration

Do not expel the air bubble from the syringe before the injection. The volume to be injected should be measured precisely by holding the syringe needle down to dispel any excess enoxaparin without expelling the air bubble.[1]

The whole length of the needle should be introduced vertically (at a 90° angle to the skin) into a skin fold gently held between the thumb and forefinger. The skin fold should be held throughout the duration of the injection.[1]

Monitoring of enoxaparin may be appropriate for those who are underweight or overweight and for those with impaired renal function

Anti-factor Xa may be used to monitor the anticoagulant effect of enoxaparin in patients with significant renal impairment or those at extremes of weight (e.g. below 45 kg or above 150 kg).[1] However anti-factor Xa monitoring is best managed by a specialist because it is not routinely available and results can be difficult to interpret.[2]

Adverse effects of enoxaparin

Haemorrhage

The risk of a significant bleed when using low molecular weight heparins is increased with:[5]

- Reduced creatinine clearance
- Number of enoxaparin doses received
- Increasing age
- Female gender
- Low body weight (< 45kg)
- Concurrent use of other drugs that affect haemostasis including aspirin, clopidogrel, warfarin or NSAIDs
- Previous peptic ulcer disease

Table 1: Volumes of Clexane required for each prescribed dose

120 mg and 150 mg syringes		80 mg and 100 mg syringes	
Syringe concentration is 150 mg/mL, each graduation is 0.02 mL = 3 mg		Syringe concentration is 100 mg/mL so each graduation is 0.025 mL = 2.5 mg	
Doses should be rounded to the nearest multiple of 3 mg		Doses should be rounded to the nearest 2.5 mg (or possibly 5 mg)	
Dose (mg)	**mL**	**Dose (mg)**	**mL**
150	1.00 (use 150 mg syringe)	**100**	1.00 (use 100 mg syringe)
147	0.98	97.5	0.975
144	0.96	95	0.95
141	0.94	92.5	0.925
138	0.92	90	0.90
135	0.90	87.5	0.875
132	0.88	85	0.85
129	0.86	82.5	0.825
126	0.84	**80**	0.80 (use 80 mg syringe)
123	0.82	77.5	0.775
120	0.80 (use 120 mg syringe)	75	0.75
117	0.78	72.5	0.72 5
114	0.76	70	0.70
111	0.74	67.5	0.675
108	0.72	65	0.65
105	0.70	62.5	0.625
102	0.68	60	0.60

Impaired renal function and prolonged use of enoxaparin were found to be significant predictors of bleeding in one New Zealand study. The authors suggested that current guidelines for dosing adjustment in renal impairment may be inadequate to minimise bleeding risk.[6] Consider discussing treatment with a specialist for patients who have impaired renal function or require prolonged treatment with enoxaparin.

A patient who has received LMWH and is clinically bleeding, may be administered protamine in hospital. While protamine reverses approximately 70% of the activity of LMWH, it does reduce clinical bleeding. If enoxaparin was given within eight hours, then a dose of 1 mg of protamine per 1 mg of enoxaparin is given. Smaller doses are recommended if it is greater than eight hours since enoxaparin was administered (0.5 mg protamine for 1 mg enoxaparin).[3]

Heparin-induced thrombocytopenia

Heparin-induced thrombocytopenia (HIT) is diagnosed when HIT antibodies are detected in conjunction with any of the following events: a decrease in platelet count of

greater than or equal to 50%, venous or arterial thrombosis, skin reactions occurring at heparin injection sites or acute systemic (anaphylactoid) reactions that occur after IV heparin bolus administration.[7]

HIT occurs rarely with the use of LMWH, occurring three fold less frequently than with heparin.[3] The frequency of HIT is highly variable and is influenced by: the reason the patient is receiving heparin (the risk is greatest post-surgery followed by use for medical patients, and lowest when used during pregnancy), duration of heparin exposure and gender (the risk is greater for females than males).

For people who are at higher risk of HIT (e.g. post-surgery, prolonged exposure, female) platelet count should be checked before initiation of enoxaparin, then regularly (every three to five days) during the initial stage of treatment. If HIT has not developed within the first month of treatment it is unlikely to occur.

For people at low risk of HIT, less frequent (or no) platelet count monitoring may be appropriate. All patients receiving enoxaparin should be instructed to contact their GP promptly if signs or symptoms of venous thromboembolism (the most common complication of HIT) occur or painful skin lesions develop at the injection sites.[7]

ACKNOWLEDGMENT Thank you to **Dr Paul Harper**, Haematologist, Midcentral DHB, Palmerston North, for expert guidance in developing this article.

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