Document Number # QH-GDL-951:2015

Guideline for Anticoagulation and Prophylaxis Using Low Molecular Weight Heparin (LMWH) in Adult Inpatients

1. Purpose

This Guideline provides recommendations regarding best practice for anticoagulation treatment and prophylaxis of venous thromboembolism for adult inpatients in Queensland Health facilities using low molecular weight heparins.

2. Scope

This Guideline provides information for all Queensland Health employees (permanent, temporary and casual) and all organisations and individuals acting as its agents (including Visiting Medical Officers and other partners, contractors, consultants and volunteers).

This Guideline takes into account the medication restrictions outlined in the Queensland Health List of Approved Medicines.

Some Hospital and Health Services may have local guidelines where differing medication restrictions are in place. These are beyond the scope of this Guideline.

3. Related documents

Authorising Policy and Standard/s:

- Queensland Health List of Approved Medicines

Procedures, Guidelines and Protocols:

- Guidelines for Anticoagulation Using Warfarin
- Guidelines for Managing Patients on Dabigatran (Pradaxa®)
- Guideline for managing patients on a factor Xa inhibitor – Apixaban (Eliquis®) or Rivaroxaban (Xarelto®)

Forms and templates:

- Statewide Heparin Intravenous Infusion Order and Administration – Adult form

4. Guideline

4.1 Indications

The low molecular weight heparins (LMWH), dalteparin and enoxaparin, are approved for use in Australia through the Therapeutic Goods Administration (TGA) and are listed on the Pharmaceutical Benefits Scheme (PBS) (see Table A).

Table A: TGA approvals and indications on the PBS for dalteparin and enoxaparin*

Dalteparin	Enoxaparin
Prophylaxis against thromboembolic complications in the perioperative or postoperative period of surgery.	Prevention of thromboembolic disorders of venous origin in patients undergoing orthopaedic and general surgery.
	Prophylaxis of venous thromboembolism (VTE) in medical patients bedridden due to acute illness.
Prophylaxis against thrombotic complications during haemodialysis and treatment of acute deep vein thrombosis (DVT).	Prevention of thrombosis in extracorporeal circulation during haemodialysis.
	Treatment of established DVT.
Extended treatment of symptomatic VTE (proximal DVT and/or pulmonary embolism) to reduce the recurrence of VTE in patients with solid tumour cancers.	
Treatment of unstable coronary artery disease, i.e. unstable angina and non-ST-elevation myocardial infarction (also known as non-Q-wave myocardial infarction).	Treatment of unstable angina and non-Q-wave myocardial infarction (MI), administered concurrently with aspirin.
	Treatment of acute ST-segment Elevation Myocardial Infarction (STEMI) as an adjunctive to thrombolytic treatment, including patients to be managed medically or with subsequent percutaneous coronary intervention (PCI).

* Information correct as at 1 November 2016. Refer to TGA website or PBS schedule for current indications
TGA: http://www.tga.gov.au/industry/artg.htm
PBS: http://www.pbs.gov.au/pbs/home

Note: Dalteparin prefilled syringe 15,000 international units in 0.6 mL (10) and 18,000 international units in 0.72 mL (10) are only on the PBS for management of symptomatic venous thromboembolism in a patient with a solid tumour(s).

There is good evidence that LMWHs are at least as safe and effective as unfractionated heparin (UFH) for the management of VTE and acute coronary syndrome (ACS) when used appropriately. LMWHs have more predictable anticoagulant activity than UFH, and therapeutic drug monitoring is not routinely necessary.

In addition to the TGA approved indications and PBS listings, the Queensland Health List of Approved Medicines (LAM) outlines the indications and restrictions for use of dalteparin and enoxaparin in Queensland Health facilities (see Table B).

Table B: Queensland Health List of Approved Medicines (LAM) LMWH restrictions†

LMWH product	LAM restriction
Dalteparin	
prefilled syringe 2500 international units in 0.2 mL (10)	For adult use: for prophylaxis of venous thromboembolism (VTE)* and during haemodialysis.
prefilled syringe 5000 international units in 0.2 mL (10)	For adult use: for prophylaxis of VTE*; and during haemodialysis; and treatment of VTE.
prefilled syringe 7500 international units in 0.75 mL (10) 10,000 international units in 1 mL (10) 12,500 international units in 0.5 mL (10)	For adult use: during haemodialysis; and treatment of VTE.
Enoxaparin	
prefilled syringe 20 mg in 0.2 mL (10)	For use only in paediatric patients*
prefilled syringe 40 mg in 0.4 mL (10)	(NOTE: Use graduated 60mg prefilled syringe for other doses smaller than 60mg). For use only in: (a) paediatric patients* (b) haemodialysis (c) acute coronary syndrome (d) treatment of VTE (NOTE: In 2017, enoxaparin will no longer be LAM listed for treatment of VTE.)
prefilled syringe 60 mg in 0.6 mL (10) 80 mg in 0.8 mL (10) 100 mg in 1.0 mL (10)	For use only in: (a) paediatric patients* (b) haemodialysis (c) acute coronary syndrome (d) treatment of VTE (NOTE: In 2017, enoxaparin will no longer be LAM listed for treatment of VTE.)

† Information correct as at 1 November 2016. Refer to latest edition of LAM for current restrictions.
LAM: http://www.health.qld.gov.au/clinical-practice/guidelines-procedures/medicines/approved-list/default.asp

***** Plus TGA disclaimer: "When medicines are used in ways other than as specified in the TGA approved product information, documentation and evaluation should be undertaken with reference to QHMAC's note in the introductory pages of the LAM and the CATAG guiding principles for the quality use of off-label medicines (www.catag.org.au)".

4.2 Contraindications

LMWH should not be used in the following patients:

- Previous heparin-induced thrombocytopenia / thrombosis (HITT).
- Known hypersensitivity or adverse reaction to LMWH (dalteparin or enoxaparin).
- Severe renal impairment [Creatinine clearance (CrCl) less than 30 mL/min] except when used as an anticoagulant during haemodialysis or for VTE prophylaxis.
- Conditions in which anticoagulation is contraindicated:
    - active bleeding
    - severe, uncontrolled hypertension (e.g. systolic blood pressure above 180 mmHg and/or diastolic blood pressure above 110 mmHg)
    - active peptic ulceration

- abnormalities of haemostasis (e.g. thrombocytopenia, haemophilia)
- severe liver disease.

4.3 Patients at risk of bleeding

For patients at risk of bleeding, UFH is recommended instead of LMWH. UFH has a much shorter half-life than LMWH and its anticoagulant effect can be reversed rapidly and completely (as opposed to only partially reversed) with protamine (section 4.3.2). UFH may also be a better choice in situations where the diagnosis or potential contraindications are unclear and where the effect may need to be reversed later.

4.3.1 Risk factors for increased sensitivity to LMWH

The following factors can predispose patients to a higher risk of bleeding during LMWH therapy (particularly during therapeutic dosing):

- renal impairment. LMWHs have a large fraction excreted unchanged and therefore the dose needs to be altered for degree of renal failure; UFH is recommended with severe renal impairment (i.e. CrCl less than 30 mL/min)
- advancing age (especially patients older than 75 years)
- conditions that make estimation of renal function unreliable such as:
  - unstable renal function (e.g. sepsis, acute renal failure)
  - dialysis-dependent patients
  - extremes of body weight
    - underweight patients (i.e. less than 50 kg), especially the elderly with low body weight
    - overweight / obese patients (i.e. greater than or equal to 105 kg), especially morbidly obese with body mass index (BMI) over 35 kg/m^2
  - diseases of skeletal muscle (e.g. rhabdomyolysis)
- use of concomitant drugs that affect haemostasis (other anticoagulants, antiplatelet agents)
- recent surgery or trauma
- invasive procedures such as spinal injection or puncture (i.e. epidural analgesia or anaesthesia)
- cancer
- conditions in which anticoagulation is contraindicated (see section 4.2).

4.3.2 Management of over-anticoagulation and bleeding

For inpatients, LMWH therapy should be reviewed daily by a medical officer. If any bleeding occurs, LMWH should be withheld or stopped and consideration of the cause (including changed pharmacokinetics, drug interactions or incorrect dose) should be undertaken with appropriate action subsequently taken. If LMWH therapy is to continue, consider anti-factor Xa assay to assist with management (see section 4.7.4).

If bleeding is serious:

- Ensure adequate blood volume support and maintenance of good urine output.
- Consider protamine sulphate intravenous 1 mg per 100 units of dalteparin or 1 mg per 1 mg of enoxaparin (maximum 50 mg) over 10 minutes. If between 8-24 hours since last dose of LMWH, then dose of protamine should be halved (i.e. 0.5 mg per 100 units of dalteparin or 0.5 mg per 1 mg enoxaparin). If greater than 24 hours since last LMWH dose then protamine is not required. Although protamine is less effective in reversing the

anticoagulant effect of LMWH than UFH, it may be used to partially correct LMWH overdose (achieving up to 60% reversal of anti-factor Xa activity) in addition to supportive measures in critical clinical situations. Repeated doses of protamine sulphate may be required if ongoing bleeding.

Consider other rescue therapy measures. Consult a haematologist regarding other potential measures, such as blood products (platelets, packed red blood cells), recombinant Factor VIIa or desmopressin acetate.

4.4 Drug interactions

Close clinical monitoring is recommended (watch for signs of bleeding or anaemia) during concomitant administration of LMWH and the following agents, especially if risk factors (see section 4.3.1) are present:

- other anticoagulants* (e.g. warfarin, dabigatran, rivaroxaban, apixaban)
- antiplatelet agents (e.g. aspirin, clopidogrel, prasugrel, ticagrelor, ticlopidine, glycoprotein IIb/IIIa receptor inhibitors (e.g. abciximab, tirofiban))
- non-steroidal anti-inflammatory drugs (NSAIDs), especially long half-life agents such as naproxen, piroxicam.

* In general, there is no need to provide prophylactic anticoagulation with LMWH to someone already on anticoagulation therapy (except during initiation).

4.5 Initiating or re-starting

Before initiating or re-starting:

1. Organise baseline pathology tests (serum creatinine, full blood count, coagulation studies).
2. Obtain patient's weight (kg) and height (cm). **Do not guess**.
3. Calculate patient's baseline creatinine clearance (CrCl) as per Cockcroft-Gault equation. **Do not use eGFR** for LMWH dosing. However, CrCl can be calculated using the Medication Dosing Calculator available via desktop icon on Queensland Health computers or via QHEPS.
4. Check for contraindications (see section 4.2).
5. Check for co-prescribed or recently administered antiplatelet agents or anticoagulants (e.g. LMWH doses given in emergency department or at a referring hospital, IV heparin infusion, VTE prophylaxis medication, doses in the stat section on the front of the medication chart).
6. Assess risk factors for altered pharmacokinetics and increased risk of bleeding.

4.5.1 Switching from LMWH to heparin and vice versa

Table C: Switching from LMWH to heparin and vice versa

	Changing to → / Changing from ↓	Treatment	
		Heparin IV (refer to statewide *Heparin Intravenous Infusion Order and Administration Form – Adult*)	Dalteparin or enoxaparin subcutaneous
Treatment	Heparin IV		Wait 1 to 2 hours
	Dalteparin or enoxaparin subcutaneous	Start when next dose is due (minimum 10 hours) without bolus	
Prophylaxis	Heparin subcutaneous	As soon as diagnosis made	As soon as diagnosis is made
	Dalteparin or enoxaparin subcutaneous	As soon as diagnosis is made	Seek specialist advice*

* Dose adjustment may be needed depending on when last dose of prophylactic LMWH was administered.

4.6 Dosing

4.6.1 Therapeutic anticoagulation

Dose according to actual body weight (rounded down to the nearest 10 kg) and renal function as detailed in Tables D and E (see also the Medication Dosing Calculator available via desktop icon on Queensland Health computers or via QHEPS). Note the product strengths available on the Queensland Health List of Approved Medicines (see Table B, section 4.1).

For patients with extremes of body weight (i.e. less than 50 kg or BMI greater than 35 kg/m^2), UFH is recommended instead of LMWH. Obese patients exhibit variable subcutaneous absorption of LMWH and the optimal dosing method for these patients has not been established. The practice of dose 'capping' for obese patients may not be appropriate. If LMWH is required for obese patients, anti-factor Xa monitoring is recommended.

For patients being commenced on warfarin for long-term anticoagulation, refer to *Guidelines for anticoagulation using warfarin* (copies available at end of patient bed chart or on QHEPS). For deep vein thrombosis or pulmonary embolism warfarin should be initiated at the same time as, or shortly after commencement of, LMWH therapy and should overlap for a minimum of five days and until the International Normalised Ratio (INR) has been in target range for at least two consecutive days. Warfarin should not be initiated prior to LMWH therapy.

Treatment of Venous Thromboembolism (VTE)

Dosing recommendations for treatment of VTE with dalteparin or enoxaparin are outlined in Table D taking into account renal function. Caution should be taken if using LMWH with moderate renal impairment (CrCl 30–50 mL/min).

Table D: Treatment of Venous Thromboembolism (VTE)

CrCl (Cockcroft-Gault)	Dosing for therapeutic anticoagulation
Greater than 50 mL/min (normal renal function)	Dalteparin 100 units/kg subcut every 12 hours[#] **OR** Enoxaparin 1 mg/kg subcut every 12 hours **OR** 1.5 mg/kg subcut every 24 hours (NB: the 24-hourly regimen is **not recommended** for inpatients or for high risk patients)
30–50 mL/min (moderate renal impairment) Continue monitoring renal function and anti-factor Xa levels*	Dalteparin 100 units/kg subcut every 12 hours[#] **OR** Enoxaparin 1 mg/kg subcut every 12 hours
Less than 30 mL/min (severe renal impairment)	LMWH **not recommended**. Use UFH (refer to statewide *Heparin Intravenous Infusion Order and Administration Form – Adult*). If intravenous access is not possible, discuss with consultant
BMI greater than 35 kg/m^2 **and** CrCl greater than 30 mL/min	LMWH **not recommended**. Use UFH If treatment with LMWH is necessary: Dalteparin 100 units/kg subcut every 12 hours (seek specialist advice if calculated dose is greater than 15,000 units). Monitor anti-factor Xa levels as per Section 4.7.4 **OR** Enoxaparin 1 mg/kg subcut every 12 hours (seek specialist advice if calculated dose is greater than 150 mg). Monitor anti-factor Xa levels as per Section 4.7.4

***** Refer to section 4.7.2 regarding monitoring with renal impairment. Use intravenous UFH if anti-factor Xa measurements are unavailable or renal function is unstable (e.g. acute kidney failure) and in dialysis-dependent patients. Intravenous UFH should also be strongly considered where eGFR may be inaccurate such as diseases of skeletal muscle, severe liver disease, extremes of body weight (especially the elderly with low body weight).

[#] For cancer patients - Month 1: Dalteparin 200 units/kg subcut once daily for 30 days (max daily dose 18,000 units)
Months 2–6: Dalteparin 150 units/kg subcut once daily (max daily dose 18,000 units).

Treatment of Non-ST Elevation Myocardial Infarction (NSTEMI)

Review current medication list in case patient is already on treatment doses of anticoagulant. If the patient is not already on an anticoagulant, use enoxaparin **plus** dual antiplatelet therapy. Anticoagulation is continued until revascularisation (if performed). For patients treated conservatively anticoagulation should be given for at least 48 hours, or for the duration of hospitalisation up to eight days. Management of anticoagulation at the time of angiogram and vascular access should be guided by local protocols. Anticoagulation is usually discontinued after revascularisation / percutaneous coronary intervention (PCI) unless specified by the operator.

Dosing recommendations for treatment of NSTEMI with enoxaparin is outlined in Table E taking into account renal function. Caution should be taken if using LMWH with moderate renal impairment (CrCl 30–50 mL/min). Current evidence for use of dalteparin in acute coronary syndrome is limited and therefore, enoxaparin is the LMWH of choice.

Table E: Treatment of Non-ST Elevation Myocardial Infarction (NSTEMI)

CrCl (Cockcroft-Gault)	Dosing for therapeutic anticoagulation
Greater than 50 mL/min (normal renal function)	Enoxaparin 1 mg/kg subcut every 12 hours
30–50 mL/min (moderate renal impairment) Continue monitoring renal function and anti-factor Xa levels.*	Enoxaparin 1 mg/kg subcut every 12 hours
Less than 30 mL/min (severe renal impairment)	LMWH **not recommended**. Use UFH (refer to statewide *Heparin Intravenous Infusion Order and Administration Form* - Adult). If intravenous access is not possible, discuss with consultant

***** Refer to section 4.7.2 regarding monitoring with renal impairment. Use intravenous UFH if anti-factor Xa measurements are unavailable or renal function is unstable (e.g. acute kidney failure) and in dialysis-dependent patients. Intravenous UFH should also be strongly considered where eGFR may be inaccurate such as diseases of skeletal muscle, severe liver disease, extremes of body weight (especially the elderly with low body weight).

Treatment of ST Elevation Myocardial Infarction (STEMI)

Thrombolysis (pharmacoinvasive strategy)

Anticoagulation is generally given in addition to dual antiplatelet therapy—refer to local protocols. Check renal function prior to starting, then dose enoxaparin according to patient's age as follows:

- Patients younger than 75 years, 30 mg IV bolus immediately prior to thrombolysis followed within 15 minutes by 1 mg/kg subcut every 12 hours. Each of the first two subcutaneous doses should not exceed 100 mg (refer to enoxaparin doses in Table D for subsequent doses).
- Patients older than 75 years, no IV bolus is required. Start with 0.75 mg/kg subcut every 12 hours. Maximum dose of 75 mg for each of the first two subcutaneous doses.
- In patients with creatinine clearance of less than 30 mL/min, use UFH instead.

Anticoagulation is recommended in STEMI patients treated with thrombolytics until revascularisation (if performed) or for the duration of hospital stay up to eight days.

The majority of patients with STEMI will undergo inpatient coronary angiogram preferably 3–24 hours following thrombolysis (pharmacoinvasive strategy). Management of anticoagulation at the time of coronary angiogram and vascular access should be guided by local protocols and the operating interventional cardiologist. Anticoagulation is usually discontinued after revascularisation / PCI unless specified by the operator.

Primary percutaneous coronary intervention (primary PCI)

Intravenous anticoagulation in addition to antiplatelet therapy is recommended for all patients undergoing primary PCI. Anticoagulant therapy is selected according to both ischaemic and bleeding risks of the patient. Intravenous anticoagulation with UFH is recommended in primary PCI. Bivalirudin OR intravenous enoxaparin may be used as alternatives to UFH with use guided by local protocols/preferences.

Anticoagulation doses in Primary PCI:

1. UFH (70–100 units/kg IV bolus when no GPIIb/IIIa inhibitor is planned; 50–70 units/kg IV bolus with GPIIb/IIIa inhibitor); OR
2. Bivalirudin 0.75 mg/kg IV bolus followed by IV infusion of 1.75 mg/kg/hour for up to 4 hours after the procedure; OR
3. Enoxaparin intravenously 0.5 mg/kg.

4.6.2 Venous thromboembolism (VTE) prophylaxis

Every hospitalised patient should be risk assessed for VTE on admission and at regular intervals. Refer to locally endorsed VTE prophylaxis guidelines or guidelines recommended for use by the Hospital and Health Service (e.g. National Health and Medical Research Council VTE prophylaxis guidelines or *Prevention of Venous thromboembolism: Summary of Best Practice Recommendations for Australia and New Zealand*) for consideration of appropriate prophylaxis options and duration. Table F outlines VTE prophylaxis dosing and duration for LMWH only. Where LMWH is indicated for VTE prophylaxis, the Queensland Health List of Approved Medicines lists dalteparin, with use of enoxaparin reserved for children.

Table F: LMWH Prophylaxis of Venous Thromboembolism (VTE)

Indication*	**Dosing for VTE prophylaxis**
Risk of thrombosis (e.g. surgery, especially procedures associated with high risk of thrombosis such as abdominal, pelvic, thoracic, orthopaedic, major joints or curative surgery for cancer; prolonged surgery and / or immobilisation; previous VTE)	Dalteparin 5000 units subcut once daily for 5–10 days or until mobilised May be continued up to five weeks after hip replacement surgery **OR** Enoxaparin 40 mg subcut once daily for 7–10 days or until mobilised May be continued up to four weeks after total hip replacement
Renal impairment (creatinine clearance less than 30 mL/min)	Dalteparin 2500 units subcut once daily **OR** Enoxaparin 20 mg subcut once daily
Total body weight less than 50 kg	Seek specialist advice regarding these patient groups. Evidence for use of LMWH in extremes of body weight is limited and careful clinical observation is required. UFH is usually recommended due to level of experience with this medication and its reversibility. If LMWH necessary, consider appropriate dose taking into account body weight and BMI. Seek specialist advice if BMI is greater than 35 kg/m^2.
Total body weight greater than 105 kg	

***** Dalteparin is the preferred LMWH for VTE prophylaxis due to its lower cost and similar efficacy compared to enoxaparin. Use of dalteparin for VTE prophylaxis in medical patients is currently off-label; however, its LAM listing for this indication is supported by its registration in the United States and the United Kingdom for VTE prophylaxis in medical patients, as well as its registration for VTE prophylaxis in surgical patients in Australia.

Routine anti-factor Xa monitoring is not recommended for patients on LMWH for VTE prophylaxis. If any significant bleeding occurs, LMWH should be stopped and urgent consultant review organised.

4.7 Monitoring

4.7.1 Clinical review

LMWH therapy should be reviewed daily by a medical officer. If any bleeding occurs, the LMWH should be withheld or stopped and urgent consultant review organised (see section 4.3.2). Consider anti-factor Xa assay to assist with management (see section 4.7.4).

4.7.2 Renal function

As it is a significant risk factor for bleeding, renal function should be assessed at baseline and regularly throughout treatment, especially if moderate renal impairment (i.e. CrCl 30–50 mL/min). Consider anti-factor Xa assay to assist with management of patients with renal impairment (see section 4.7.4), especially for prolonged treatment (more than five days). Therapeutic anticoagulation with LMWH is not recommended in patients with unstable renal function or severe renal impairment (i.e. CrCl less than 30 mL/min)—use UFH instead. Use UFH if anti-factor Xa measurements are unavailable or renal function is unstable (e.g. acute kidney failure) and in dialysis-dependent patients. Intravenous UFH should also be strongly considered where eGFR may be inaccurate such as diseases of skeletal muscle, severe liver disease, extremes of body weight (especially the elderly with low body weight).

4.7.3 Platelets

Platelet count should be measured during LMWH treatment to monitor for heparin-induced thrombocytopenia / thrombosis (HITT). HITT is a rare (less than 1%) but well-recognised and potentially fatal complication of heparin therapy, usually occurring within 5–10 days after the start of therapy (may occur earlier if patient has been exposed to heparin within the last three months). Although the frequency of HITT is three-fold less with LMWHs than with UFH, monitoring is still recommended. Platelet count should be measured at baseline and then three times weekly from day 4 through to day 14, or until LMWH therapy is stopped (whichever occurs sooner). A platelet count drop of 30%–50% below baseline may indicate HITT. The diagnosis is confirmed with a positive serological test for specific heparin-associated antiplatelet antibodies. If HITT is suspected, cease LMWH and substitute an alternative anticoagulant agent (e.g. danaparoid) in consultation with a haematologist. If HITT is confirmed, this should be carefully documented and future use of UFH or LMWH avoided.

4.7.4 Anti-factor Xa assay for therapeutic anticoagulation

To assist with management of therapeutic anticoagulation, LMWH therapy may be monitored using an anti-factor Xa assay (reported as *Clexane assay* or *Fragmin assay* in AUSLAB / AUSCARE). Anti-factor Xa monitoring is not routinely necessary, but should be considered to guide dosing for certain patient groups including:

- pregnancy (NB: LMWH are Category C)
- renal impairment (CrCl less than 50 mL/min)—start monitoring within 48 hours
- extremes of body weight (as CrCl may be inaccurate)
    - underweight patients (less than 50 kg, especially the elderly with low body weight)
    - obese patients [greater than or equal to 105 kg, especially the morbidly obese (BMI over 35 kg/m^2)]
- prolonged treatment (more than five days), especially in patients with moderate renal impairment (i.e. CrCl 30–50 mL/min)
- thromboembolic event despite therapeutic anticoagulation (consider HITT).

Anti-factor Xa monitoring process

Steps for organising anti-factor Xa levels are:

- wait until the patient has received at least two doses of LMWH before collecting blood for anti-factor Xa monitoring
- blood should be collected four hours after a subcutaneous dose for a peak level
- use blue top (citrate) blood collection tubes
- arrange for levels during normal haematology laboratory hours (e.g. for a patient receiving doses at 0800 hours and 2000 hours, arrange a level for 1200 hours rather than 2400 hours)

Therapeutic ranges for anti-factor Xa monitoring are shown in Table G.

Table G: Therapeutic ranges for anti-factor Xa monitoring*****

LMWH	Therapeutic range	Target level
Dalteparin	0.5 to 1 units/mL peak level for 100 units/kg twice daily dosing	0.75 units/mL
	1 to 2 units/mL peak level for once daily dosing (cancer patients)	1.5 units/mL
Enoxaparin	0.5 to 1 units/mL peak level for 1 mg/kg twice daily dosing	0.75 units/mL
	1 to 2 units/mL peak level for 1.5 mg/kg once daily dosing in patients with normal renal function (not recommended for inpatients or high risk patients)	1.5 units/mL

* These therapeutic ranges and target levels are not clearly defined in literature. They have been based on expert clinical consensus following review of available literature at the time of last review.

Dosing adjustments are based on the following equation:

$$\text{New dose (mg)} = \frac{[\text{current dose (mg)} \times \text{target level}]}{\text{current peak level}}$$

Therapeutic range depends on indication, in addition to which LMWH and dosing regimen is used. Further advice on dose adjustment can be sought by discussion with consultant, haematologist or clinical pharmacist.

4.8 Peri-operative management

LMWH should be ceased before procedures associated with high risk of bleeding including cardiac surgery, neurosurgery, abdominal surgery, surgery involving a major organ, or in major surgery where complete haemostasis is required. Other procedures such as spinal / epidural anaesthesia may require complete haemostasis. Consult local guidelines or seek specialist advice (e.g. surgical, haematology, cardiology). Patient factors associated with an increased risk of bleeding are detailed in section 4.3.1.

4.8.1 Semi-acute, elective or minor procedure / surgery

- Assess the risk of bleeding (according to type of surgery and patient factors) against the risk of thrombosis as LMWH may not need to be discontinued for minor procedures.
- If there is a high risk of thrombosis, consider bridging anticoagulant therapy with UFH.
- If LMWH needs to be withheld, plan ahead. The risk of excessive bleeding during surgery is increased for up to 36 hours after LMWH administration, and protamine can only partially reduce this risk.

4.8.2 Urgent invasive procedure/surgery

- Stop LMWH. Refer to relevant local VTE prophylaxis guidelines if available.
- Consider delaying surgery, if appropriate, for up to 24–36 hours.
- Where surgery cannot be delayed, cross-match blood and consult with haematology regarding measures to control bleeding prior to and during surgery (refer to section 4.3.2 for management of bleeding).

4.8.3 Re-starting LMWH after surgery

- Decision to re-start LMWH after surgery depends on many factors including risk of bleeding versus thrombosis, treatment versus prophylaxis, haemostasis after surgery, type of anaesthetic and epidural.
- For patients undergoing minor procedures associated with a low risk of bleeding, LMWH therapy can usually be resumed 24 hours post-procedure.
- For patients undergoing major surgery or procedures with a high risk of bleeding, treatment doses of LMWH should be delayed for 48–72 hours after haemostasis has been secured.
- If the patient requires treatment doses of LMWH and there is a high risk of thrombosis, consider bridging anticoagulant therapy with UFH.

5. Review

This Guideline is due for review on: 1 July 2018

Date of Last Review: 1 November 2016

Supersedes: Queensland Health Dosing and Monitoring Guidelines for Enoxaparin 2008

6. Business Area Contact

Medication Services Queensland

Email: medicationsafety@health.qld.gov.au

Phone: 07 3328 9818

7. Definitions of terms

Term	Definition / Explanation / Details
ACS	Acute coronary syndrome
BMI	Body mass index
CrCl	Creatinine clearance
DVT	Deep vein thrombosis
HITT	Heparin induced thrombocytopenia / thrombosis
INR	International normalised ratio
LAM	Queensland Health List of Approved Medicines
LMWH	Low molecular weight heparin
NSAIDs	Non-steroidal anti-inflammatory drugs
NSTEMI	Non-ST elevation myocardial infarction
PBS	Pharmaceutical Benefits Scheme
PCI	Percutaneous coronary intervention
STEMI	ST elevation myocardial infarction
TGA	Therapeutic Goods Administration
UFH	Unfractionated Heparin
VTE	Venous thromboembolism

8. Approval and Implementation

Policy Custodian:

Andrew Jagels

Acting Director, Medication Services Queensland

Approving Officer:

Dr Jeannette Young

Chief Health Officer

Approval date: **30 November 2016**

Effective from: **21 December 2016**

Version Control

Version	Date	Prepared by	Comments
1	1 Jul 2014	Justin Lee	
2	1 Nov 2014	Sarah Mathers	Clinician feedback addressed
2	6 Jan 2015	Sarah Mathers	Updated LAM homepage link
3	1 Jul 2015	Sarah Mathers	Amendment to treatment of STEMI
4	1 Nov 2016	Sarah Mathers	Updated in line with LAM restrictions

Disclaimer

This guideline has been prepared to promote and facilitate standardisation and consistency of practice, using a multidisciplinary approach.

Information in this guideline is current at time of publication.

The Department of Health, Queensland Government does not accept liability to any person for loss or damage incurred as a result of reliance upon the material contained in this guideline.

Clinical material offered in this guideline does not replace or remove clinical judgement or the professional care and duty necessary for each specific patient case.

Clinical care carried out in accordance with this guideline should be provided within the context of locally available resources and expertise.

This guideline does not address all elements of standard practice and assumes that individual clinicians have the responsibility to:

- Discuss care with consumers in an environment that is culturally appropriate and which enables respectful confidential discussion. This includes the use of interpreter services where necessary.
- Advise consumers of their choice and ensure informed consent is obtained.
- Provide care within scope of practice, meet all legislative requirements and maintain standards of professional conduct.
- Apply standard precautions and additional precautions as necessary, when delivering care.
- Document all care in accordance with mandatory and local requirements.

Guideline for anticoagulation and prophylaxis using low molecular weight heparin

Published by the State of Queensland (Queensland Health), November, 2016

For further information contact Medication Safety Officer, Medicines Regulation and Quality, Locked Bag 21, Fortitude Valley BC Qld 4006, email MedicationSafety@health.qld.gov.au.