

**Consensus Guidelines for
Australian Clinicians for the
usage of anti-coagulants
during heparin-based product
shortages**

15 May 2008

**Department of Health and Ageing,
Canberra**

Table of Contents

Background	3
Aim of Consensus Guidelines	4
Clinical categories and priorities for heparin based product usage.....	4
Prioritisation schema according to clinical need.....	5
A staged response to a shortage of heparin based products	6
Stage 1	6
Stage 2	6
Stage 3	7
Appendix 1: Anticoagulation Guidelines in use in Australia.....	8
Appendix 2: Anticoagulants and Antithrombotics - Alternatives for Prophylaxis and Treatment.....	9
Appendix 3: Patient Prioritisation Schema in Event of a Shortage of Heparin Based Products	15
References	20

Background

On 22 April 2008 the Therapeutic Goods Administration (TGA) issued a recall of five batches of the anticoagulant Clexane (enoxaparin) due to the detection of an impurity in the affected batches. The impurity ‘over-sulphated chondroitin sulphate’ (OSCS) has been implicated in severe adverse reactions in the USA and Europe. In January, the USA reported 44 deaths and additional affected cases associated with exposure to unfractionated intravenous heparin produced by Baxter. More recent reports indicate that contaminated products have been linked to 81 deaths in the USA.

The TGA has required testing of all heparin based products in Australia since informed of the contamination by the US FDA in March; this resulted in identification of the five contaminated batches of Clexane. Australian pharmacists were advised in the recall to return any Clexane dispensed from affected batches to the manufacturer, and to quarantine any affected product not yet dispensed, on site, pending further advice from the TGA. There was also a TGA recall of contaminated heparinised saline product in March 2008.

No other heparin based products in Australia are currently affected. All of Australia’s unfractionated heparin is free from contamination. The alternative low molecular weight heparin product, Fragmin (dalteparin) and heparinised saline products available in Australia currently are also free from contamination.

Heparin based products are widely used across the public and private hospital sector and in the community, across elective and emergency surgical procedures, for prophylaxis and treatment of thromboembolic disorders and in investigative procedures.

The risk of adverse events associated with the contaminated Clexane is unknown. To date there have been NO reported adverse events with Clexane usage of the type seen in relation to the use of unfractionated heparin in the United States, that is, no reports of anaphylaxis-like reactions or deaths. The TGA does have ‘adverse drug reaction’ reports for all forms of heparin. The adverse events reported overseas have been associated with IV usage of the unfractionated heparin, not low molecular weight heparins. Clexane is mostly given SC with some IV usage. The adverse events seen overseas are also thought to be dose-related, that is, bolus dosing, repeated and intravenous dosing may confer greater risk of adverse events. More recently a study of the contaminant¹ has shown that the adverse effects are mediated by direct activation of kinin-kallikrein pathways; that is, they are anaphylaxis-like but not due to anaphylaxis. This is important, supporting the hypothesis that acute toxicity is dose dependent.

The presence of the contaminant has been traced to the raw materials used to produce the “approved pharmaceutical ingredient” (API), which is the starting point for manufacture of heparin based products. There are concerns that manufacturers may experience difficulty in sourcing uncontaminated API for future production. This, coupled with the recent recall of Clexane in Australia and recalls of contaminated Clexane and contaminated unfractionated heparin products overseas, has the potential to lead to a global shortage of heparin based products. The TGA is endeavouring to procure alternative supplies of heparin based products, however a shortage of these products in Australia is a possible scenario for which we need to plan now.

The TGA is monitoring the ongoing availability of heparin based products in Australia and providing regular updates to the Department of Health and Ageing to assist with contingency planning. As part of this planning, the TGA and the Department of Health and Ageing are working through the Australian Health Protection Committee (AHPC) with the Clinical Colleges, the AMA, the jurisdictions, and Australia’s clinical experts to manage optimally the clinical implications of a shortage of heparin based products. These guidelines have been

constructed on a consensus basis by this group to assist clinicians and their patients in rational decision-making.

The TGA and the Department will keep the medical profession and consumers informed about product availability as the situation unfolds.

Aim of the Consensus Guidelines

The AHPC group has constructed on a consensus basis and using the best available evidence-based information (Appendix 1, 2 and references) the following guidelines for usage in the event of a shortage of heparin based products in Australia. The Department of Health and Ageing will update regularly about the availability of stock and whether there is a need to shift to the prioritising strategies outlined below.

The principle underlying the strategies is that prioritisation is according to clinical need. That is, if supply diminishes, those patients most in need of anticoagulant will have the highest priority.

More formally, the aim of these guidelines in the event of a heparin based products shortage is:

- To extend the availability of all heparin based products by prioritisation of their usage according to clinical need across medical, surgical and investigative indications;
- By appropriate prioritisation and usage, ensure there are no increases in preventable morbidity and mortality; and
- To facilitate national consistency in the utilisation of heparin based products.

Clinical categories and priorities for heparin based product usage

The AHPC Group considers that there are three groups of patients in prioritising usage of heparin based products in the event of a shortage. These groups are

Group 1 - Patients requiring active treatment for acute thromboembolic disorders

For example:

- Treatment of venous thrombosis and pulmonary embolism
- Patients on anticoagulant therapy for thrombosis with a current history of cancer
- Management of acute coronary syndromes
- Embolic stroke patients

Group 2 - Patients requiring anticoagulant support for investigative and therapeutic procedures

For example:

- Conditions in which there is no alternative to heparin with risk of significant patient morbidity and mortality if heparin is not available.

For example:

- Haemodialysis patients. Haemodialysis cannot be performed without anticoagulation and patients will survive 4-5 days only without a haemodialysis session.
- Support for cardiopulmonary bypass procedures

- Conditions resulting in significant patient morbidity that may be relieved by endovascular techniques which require heparin cover to minimise risk of arterial or venous thrombosis

For example:

- limb ischaemia with rest pain,
 - elective abdominal aortic aneurysm
- Elective or semi elective procedures for non-life threatening but life limiting conditions requiring intra-arterial or intra-venous bolus heparin use such as performed for lower limb claudication (pain with walking or exercise). This group at lower priority in the event of a shortage is also likely to be the largest.

Within **Group 2**, some procedures may be performed acutely, semi-electively and electively, and their prioritisation in the event of a heparin based products shortage should be determined by the relevant craft group according to clinical urgency and other relevant factors. For example: coronary angiography.

Group 3 - High risk patients receiving thromboprophylaxis

For example:

- Patients undergoing major surgery particularly of the abdomen,
- Patients with congestive cardiac failure
- Patients with fractures of the lower limb
- Prophylaxis for pregnant women at risk of thromboembolism
- Patients having total hip or total knee arthroplasty (in the absence of sufficient supplies of fondaparinux as a substitute).

The AHPC group agrees that in the event of a shortage of heparin based products, usage across these three groups of patients should be prioritised according to clinical need as follows:

Prioritisation schema according to clinical need

- 1) Patient groups and indications where low molecular weight heparin products need to be used
- 2) Patient groups and indications where low molecular weight heparin products can be substituted with unfractionated heparin and/or warfarin and/or other anticoagulants such as fondaparinux
- 3) Patient groups and indications where anticoagulants can be substituted with alternative measures such as graduated compression stockings (GCSs) and mechanical calf compression
- 4) Patient groups and indications which can be deferred or delayed without risk to patient safety

From the evidence-based guidelines for antithrombotic and thrombolytic therapy used by Australian clinicians (Appendix 1) and other peer-reviewed publications, the AHPC group has assembled detailed information on alternative products and therapies and how they may be used, including substitution regimens (Appendix 2).

The prioritisation schema of heparin based products according to clinical need is outlined in further detail in Appendix 3.

A staged response to a shortage of heparin based products

The AHPC group agrees that in the event of a shortage of heparin based products, there should be a staged clinical response to ensure maximum extension of availability of remaining stocks and that they are prioritised according to clinical need.

The TGA and the Department of Health and Ageing will keep the health community updated on stock availability and the need to move to and through the Stages outlined below. In addition, the Department has asked jurisdictions to advise it if any jurisdiction begins to experience shortages (ie Stage 2) so a national response can be implemented.

The AHPC group considers that as at 15 May 2008 we are in Stage 1. Conceptually, Stage 0 would indicate return to normal supply arrangements and national stock.

Stage 1

Forward supply of uncontaminated Australian Clexane stocks greater than 6 weeks; alternative heparin-based products such as dalteparin, UFH and fondaparinux available, not contaminated.

- Avoid all usage of heparin based products which are not evidence-based, so called 'discretionary usage'. An example of 'discretionary usage' is anticoagulation in elective coronary angiography.
- Use available enoxaparin (Clexane) and the alternative low molecular weight heparin dalteparin (Fragmin), where clinically indicated and according to the evidence.
- For lower risk patients, consider using VTE preventive strategies such as early mobilisation, GCSs and mechanical calf stimulation, wherever possible.
- Consider substitution of low molecular weight heparin with alternatives such as unfractionated heparin and/or warfarin, and/or other suitable anticoagulant therapies such as Fondaparinux where the evidence suggests no disadvantage nor additional patient risk and there is no adverse impact on health service delivery, as discussed under **Stage 2** below.

Stage 2

Forward supply of uncontaminated Australian Clexane stocks less than 6 weeks; alternative heparin-based products such as dalteparin, UFH and fondaparinux available, not contaminated.

- Restrict usage of all heparin based products wherever possible to conserve stock for emergency and lifesaving indications. This will include postponing those elective surgical procedures which can be delayed safely and using alternatives for maintaining patency of intravascular catheters such as normal saline, where possible.

Note: Up to 15% of children in a tertiary facility receive heparin, most of which is in the form of flushes for critical line patency.

While available, use uncontaminated enoxaparin (Clexane) and the alternative low molecular weight heparin dalteparin (Fragmin), according to the Prioritisation Schema outlined in Appendix 3.

- For lower risk patients, use VTE preventive strategies such as early mobilisation, GCSs and mechanical calf stimulation wherever possible.
- Consider substituting enoxaparin with unfractionated heparin and/or warfarin, and/or other suitable anticoagulant therapies such as fondaparinux where possible, and according to the

best available guidelines (Appendix 1 and 2). Substitution should be according to the Prioritisation Schema outlined in Appendix 3. This will require assessment of any risk associated with the substitution, discussion with the patient and informed consent in some instances.

Clexane substitution with alternative therapies will require health services planning to accommodate different treatment and testing regimens including planned anticoagulation for high risk surgery, to accommodate hospital admission where patients were previously managed as outpatients such as for treatment of VTE, and clinical training and vigilance around an anticipated different profile of adverse events associated with Clexane substitutes. For example, many Australian doctors will have limited experience with unfractionated heparin usage and monitoring, in those clinical indications where LMWH is now the treatment of choice.

For patients needing anticoagulation in remote settings where testing is difficult, there are alternative regimens requiring minimal dose adjustment according to APTT outlined in the Appendices.

- Where possible, clinically appropriate and safe, shift patients to warfarin, since the supply of warfarin is not at risk. For example, elective hip and knee replacement surgery may be undertaken with planned anticoagulation using warfarin (rather than Clexane) as is standard practice in North America.

Stage 3

Uncontaminated Clexane remains unavailable; Australian stocks of Clexane less than 2 weeks; alternative heparin-based products available but stock shortages developing.

- Continue the above strategies of Clexane substitution with Fragmin, unfractionated heparin, fondaparinux and warfarin. Substitution should follow the Prioritisation Schema outlined in Appendix 3. Over time, availability of other heparin based products may become threatened as they are used across a broader range of indications and if world supply does not improve.
- Continue to restrict elective surgery where anticoagulation with heparin based products essential, where possible.
- Continue to use early mobilisation, GCSs in low risk patients and mechanical calf compression, where available.

If during Stage 3, the situation deteriorates with shortages of alternative products developing, the AHPC group will provide further advice to the Australian clinical community. The TGA will continue to closely monitor supply and provide updates on stock availability until the situation normalises.

Appendix 1

Anticoagulation Guidelines in use in Australia

1. Prevention of Venous Thromboembolism. The Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. Geerts WH, Pineo GF, Heit JA, Bergqvist D, Lassen MR, Colwell CW, Ray JG. *Chest* 2004;126:338S-400S.
2. Prevention and Treatment of Venous Thromboembolism. International Consensus Statement. *Intern Angiology* 2006; 25: 101 – 61.
3. Prevention of Venous Thromboembolism. Best Practice Guidelines for Australia and New Zealand. 4th edition, 2007.

Appendix 2

Anticoagulants and Antithrombotics: Alternatives for Prophylaxis & Treatment

Information in the following tables is drawn from the published literature and consensus opinion of Australian experts across the relevant craft groups available in the timeframe. As such, the information provides a guide to clinical usage, informed by the evidence, and must be considered in the context of each patient's clinical and other circumstances.

The best evidence from the published literature suggests there are (i) indications where LMWH is difficult to substitute with UFH or alternative anticoagulants (eg treatment of VTE in pregnancy), (ii) indications where intravenous or SC UFH can be safely and effectively substituted but will impact hospital protocols and service provision (eg medical inpatients, prophylaxis in general surgery), and (iii) indications where SC UFH is less effective than LMWH or not effective (eg orthopaedic surgery, abdominal cancer surgery).

The evidence base for effectiveness and safety of the non pharmacological measures for VTE prophylaxis is less robust than for pharmacological measures² and informed consent would be needed for surgery to proceed.

Pharmacological Anticoagulants and antithrombotics²	
Intravenous and subcutaneous (IV & SC)	
Unfractionated heparin (UFH)	Use in prophylaxis and treatment of thromboembolic disease. Can be used as IV bolus or infusion. Requires regular APTT to monitor anticoagulation. UFH can be given for VTE therapy via weight-adjusted dose SC, with minimal need for dose-adjustment according to APTT. Two regimens have been studied ^{3 4} Second daily FBC to monitor for HITTS. (NB: Expect 5 additional cases of HITTS per 1000 pts treated with UFH rather than LMWH.
Low molecular weight heparin Enoxaparin (Clexane) Dalteparin (Fragmin) Fondaparinux (synthetic product - Arixtra)	Use in prophylaxis and treatment of thromboembolic disease. Clexane used SC Fragmin SC (or rarely by IV infusion) Fondaparinux SC for major hip surgery and total knee replacement
Lepirudin (Refludan) Danaparoid(Organon)	For use in heparin-induced thrombocytopenic thrombosis (HITTS) (See note on additional risk of HITTS above)
Direct thrombin inhibitor Bivalirudin (Angiomax)	Indicated for use during percutaneous coronary intervention
Oral agents	
Warfarin (Coumadin, Marevan)	Long term prophylaxis and treatment of thromboembolic disease. Can be used for VTE prophylaxis after hip or knee replacement. Requires monitoring with regular INR, initially daily until stable and therapeutic.
Clopidogrel Dipyridamole (Persantin)	No role in venous disease and thromboprophylaxis Clopidogrel could be used in some middle and low priority interventional radiology procedures to reduce risk of acute arterial thrombosis. Not available on PBS for non-cardiac risk patients. If clopidogrel used, would require use of arterial closure devices in these pts to reduce risk of bruising or haemorrhage (eg Star Close device from Abbott, Angio Seal device from St Jude).

Pharmacological Anticoagulants and antithrombotics²	
Mechanical methods of prophylaxis²	
<p>Main mechanical methods include:</p> <ul style="list-style-type: none"> • Graduated compression stockings (GCSs) • Intermittent pneumatic compression (IPC) devices and • The venous foot pump (VFP) <p>Also:</p> <p>Inferior vena cava filters – uncommon use – only in specially selected patients and</p> <p>Intraoperative intermittent calf stimulators</p>	<p>Main advantage of mechanical methods is lack of bleeding potential.</p> <p>Therefore, primarily useful for pts with high bleeding risks or as an adjunct to pharmacological methods.</p> <p>Work by increasing venous outflow and/or reducing stasis within the leg veins.</p> <p>All three modalities reduce the risk of DVT in a number of patient groups but less study on them and generally, less efficacious than pharmacological methods for prevention of DVT.</p> <p>Essential to select the correct size of the device, apply properly, and ensure that only removed for only a short time each day. Nursing and physiotherapy initiatives should ensure that the devices do not impede ambulation.</p> <p>Note: Care with proper use of, and optimal compliance with, the mechanical device</p>
GCS (further detail)	<p>GCS reduce venous stasis in the limb by applying a graded degree of compression to the ankle and calf, with greater pressure being applied distally.</p> <p>GCS should be used routinely for surgical inpatients and are effective in decreasing risk of DVT, either alone, or in combination with pharmacological prophylaxis in high risk patients^{5 6}</p> <p>GCS should not be used in patients with peripheral arterial disease.</p>
IPC (further detail)	<p>Intermittent pneumatic leg compression has both local and systemic effects.</p> <ul style="list-style-type: none"> ▪ Prevents venous thrombosis by enhancing blood flow in the deep veins of the legs, thereby preventing venous stasis.⁷ ▪ Reduces plasminogen activator inhibitor-1 (PAI-1) levels via an unknown mechanism and consequently increases endogenous fibrinolytic activity. <p>May cause discomfort in some patients</p> <p>Should not be used in patients with overt evidence of ischaemia due to peripheral vascular disease.</p> <p>Contraindicated in patients who have been on bed rest or immobilized for more than 72 hours without prophylaxis, as may cause a newly formed clot to dislodge.</p>

Treatment and/or prophylaxis regimens/alternatives

Venous thrombo-embolic disorders²

Treatment of venous thromboembolism (DVT, PE)	Acute DVT, recommend initial treatment with LMWH or UFH for at least 5 days; warfarin together with LMWH or UFH on the first treatment day and discontinuation of heparin when the INR is stable and > 2.0 for two consecutive readings
	If IV UFH – continuous infusion with dose adjustment to achieve and maintain a therapeutic APTT prolongation - regular daily measurements required OR SC UFH - initial dose of 35,000 Units/24 h SC, with subsequent dosing to maintain the APTT in the therapeutic range OR Initial treatment with LMWH SC once or twice daily- routine monitoring with anti-factor Xa level measurements is not recommended
	Warfarin dose is adjusted to maintain the INR at a target of 2.5 (range, 2.0 to 3.0) with daily INR measurements

Acute Coronary Syndromes²

Treated by percutaneous intervention (primary angioplasty) - emergency Early intervention +/- GPIIb/IIIa inhibitor eg abciximab (Reopro)	IV bolus of UFH is used at the time of the procedure— usually 2 boluses in total. Monitoring with activated clotting time (ACT)
Delayed intervention	UFH or LMWH while patient is waiting for angioplasty, LMWH ceased 12 hours before angioplasty and UFH used at the time of angioplasty OR Infusion of UFH or SC Clexane until intervention or for 48–72 hours ⁸
Non emergency percutaneous intervention (primary angioplasty)	Bivalirudin for the duration of the procedure. Consider postponing elective angioplasty.
Treatment with fibrinolytic therapy (TPA/RPA)	In addition a bolus of IV UFH (5000 Units) + 48 hours of UFH infusion OR 60 Units/kg (max 4000 Units) followed by an initial infusion of 12 Units/kg/hr (max 1000 Units/hr), adjusted to APTT ⁸ OR 24-48 hours of Clexane (pts <75 years) Note: Anticoagulation NOT recommended after thrombolysis using non fibrin specific product such as streptokinase.
Fibrinolysis or PCI	Bivalirudin can be used in patients with HITTS

Pregnancy

<p>Patients requiring anticoagulation in pregnancy</p>	<p>SC Clexane or Fragmin.</p> <p>Risk of osteoporosis with long term UFH prophylaxis (up to 9 months) to mother and foetus.</p> <p>LMWHs have potential advantages over UFH during pregnancy because they cause less HITTS, have a longer plasma half-life and a more predictable dose response than UFH, with the potential for once-daily administration, and are likely associated with a lower risk of heparin-induced osteoporosis.</p> <p>UFH could be considered where there is an absolute need for anticoagulation and the risk of no anticoagulation outweighs the risk to the foetus.</p> <p>Warfarin</p> <p>Warfarin can be used in the mid-trimester according to established protocols if the risks and benefits are understood by the mother.</p> <p>Women should be changed from warfarin to heparin as early as possible but no later than 7 weeks of pregnancy (5 weeks post conception) to prevent the teratogenic effects of warfarin.</p> <p>After 12 weeks (10 weeks post conception) there are circumstances where warfarin can be reintroduced. Close monitoring of INR is essential.</p> <p>Warfarin is then discontinued at 34 weeks and heparin reintroduced.</p>
--	---

Critical Care

<p>Multiple trauma</p>	<p>LMWH is effective and superior to low dose heparin for patients who have suffered multiple trauma.</p> <p>LMWH prophylaxis should be started as soon as it has been considered safe to do so. Intermittent pneumatic compression has been recommended, when feasible, because it eliminates any risk for bleeding.</p>
<p>Patients at high risk for bleeding</p>	<p>Mechanical prophylaxis with GCS and/or IPC recommended until bleeding risk decreases</p>
<p>ICU patients who are at moderate risk for VTE (eg medically ill or postoperative patients)</p>	<p>Low dose UFH or LMWH prophylaxis</p>
<p>Patients who are at higher risk, such as that following major trauma or orthopedic surgery</p>	<p>LMWH prophylaxis recommended</p>

Elective Orthopaedic Surgery^{2,9}

Consider rescheduling if safe and appropriate	
Consider day-5 doppler in high risk patients	
Total hip replacement	<p>Clexane (enoxaparin) 30mg SC 12 hourly or 40mg SC daily. LMWH usually started post-op in Australia because of practice of admitting pts to hospital on day of procedure. Continue with Clexane for 4-5 weeks post operatively.</p> <p>OR</p> <p>Fondaparinux (2.5 mg started 6 to 8 h after surgery) and follow up with LMWH for 5 weeks</p> <p>OR</p> <p>Clexane as above, with adjusted-dose warfarin started after surgery (INR target, 2.5; INR range, 2.0 to 3.0) for the next 5 weeks (note requires regular laboratory testing of INR and usually takes some time to achieve stable level – 10-11 days)</p> <p>OR</p> <p>Low dose UFH in preoperative period with postoperative dose adjusted heparin to maintain APTT around the upper range of normal is safe and effective but is less practical than LMWH treatments.</p> <p>Follow up with warfarin for 5 weeks if indicated for VTE prophylaxis</p> <p>OR</p> <p>Warfarin, starting on eve of surgery and aiming for INR of 2-3 is suitable for elective hip replacement. Needs INR testing and dose adjustment.</p>
Hip fracture surgery	<p>Clexane (enoxaparin) 40mg SC daily or (Fragmin) dalteparin 5000 Units SC daily. LMWH usually started post-op in Australia because of practice of admitting pts to hospital on day of procedure. Continue with LMWH for 28-35 days post operatively.</p> <p>OR</p> <p>Fondaparinux, (2.5 mg started 6 to 8 h after surgery) and follow up with LMWH for 5 weeks</p> <p>OR</p> <p>LMWH as above, with adjusted-dose warfarin started after surgery (INR target, 2.5; INR range, 2.0 to 3.0) for the next 5 weeks (note requires regular laboratory testing of INR and usually takes some time to achieve stable level – 10-11 days)</p> <p>OR</p> <p>UFH 5000 Units SC tds. Follow up with warfarin for 5 weeks if indicated for VTE prophylaxis</p> <p>OR</p> <p>Warfarin, starting on eve of surgery and aiming for INR of 2-3 is suitable for HFS. Needs INR testing and dose adjustment</p>
Total knee replacement	<p>LMWH 30mg SC bd., for 7-14 days postoperatively</p> <p>OR</p> <p>Fondaparinux (2.5 mg started 6 to 8 h after surgery)</p> <p>OR</p> <p>Adjusted-dose warfarin started on the eve of surgery (INR target, 2.5; INR range, 2.0 to 3.0) for the next 5 weeks (note this requires regular laboratory testing of INR)</p> <p>OR</p> <p>UFH in preoperative period with postoperative dose adjusted heparin to maintain APPT around the upper range of normal in conjunction with GCS and IPC. UFH not recommended as sole prophylaxis.</p>
Arthroscopy	<p>Early mobilisation</p> <p>Pharmacological prophylaxis not required.</p>

General, Vascular, Gynaecologic and Urologic Surgery²

<p>Low risk general surgery, minor procedure, <40, no additional risk factors</p>	<p>Recommend against the use of specific prophylaxis other than early and persistent mobilization. Not required in caesarean section unless other risk factors for VTE present</p>
<p>Moderate-risk general surgery patients are those patients undergoing a non major procedure and are between the ages of 40 and 60 years or have additional risk factors, or those patients who are undergoing major operations and are < 40 years of age with no additional risk factors</p>	<p>Prophylaxis with UFH, 5,000 Units SC bd, OR LMWH, according to manufacturer's specifications (different for Fragmin and Clexane) combined with GCS and/or IPC</p>
<p>Higher-risk general surgery patients are those undergoing non major surgery and are > 60 years of age or have additional risk factors, or patients undergoing major surgery who are > 40 years of age or have additional risk factors.</p>	<p>Recommend thromboprophylaxis with UFH, 5,000 Units SC tds, OR LMWH, according to manufacturer's specifications (different for Fragmin and Clexane) combined with GCS and/or IPC</p>
<p>General surgery patients with a high risk of bleeding</p>	<p>Use of mechanical prophylaxis with properly fitted GCS and/or IPC, Commence pharmacological prophylaxis when bleeding risk decreases</p>

Renal dialysis

<p>Patients undergoing haemodialysis Typically, patients have 3-4 sessions of haemodialysis per week. There are an estimated 7 500 haemodialysis patients in Australia. These patients are high priority for heparin based products in the event of a shortage.</p>	<p>Anticoagulation is essential Clexane may be substituted with unfractionated heparin, Fragmin or fondaparinux (Arixtra). Home therapy patients will need retraining if shifted from Clexane to unfractionated heparin. Warfarin is NOT an alternative anticoagulant in haemodialysis.</p>
--	--

Appendix 3**Patient Prioritisation Schema if there is a Shortage of Heparin Based Products¹⁰**

Treatment Priority 1	Specialty	Medical Conditions and/or Procedures
<p>Usage of LMWH should continue for these pts – high priority</p> <p>Apart from the specific clinical indications listed, LMWHs should not otherwise be given unless patients require anti-coagulation and have adverse reactions to other anti-coagulants.</p>	<p>Paediatrics</p>	<p>CLEXANE ONLY (no Fragmin)</p> <p>Clexane is the drug of choice for outpatient anticoagulation in children</p> <p>UFH may be used for inpatients, line patency and dialysis.</p> <p>There is no experience in using Clexane for dialysis in children.</p>
	<p>Obstetrics and gynaecology</p>	<p>Maternal metal cardiac valves.</p> <p>Women with DVT/PE during pregnancy</p> <p>Women with previous DVT/PE with a proven thrombophilia during pregnancy</p> <p>Women with antiphospholipid syndrome for maternal and foetal benefits during pregnancy</p>

Treatment Priority 2	Specialty	Medical Conditions and/or Procedures
<p>Unfractionated heparin can be substituted for Clexane/Fragmin.</p> <p>Consider using fondaparinux.</p> <p>Where possible, patients should be moved to oral anticoagulants.</p>	<p>Emergency Department</p>	<p>Pulmonary embolus</p> <p>Deep vein thrombosis</p> <p>Acute Coronary Syndromes</p> <p>Multiple trauma patients</p> <p>Patients on anticoagulant therapy for thrombosis with a current history of cancer</p> <p>Embolic stroke patients</p>
	<p>Paediatrics</p>	<p>Congenital heart disease</p> <p>Scoliosis surgery</p> <p>Maintenance of line patency in children</p>
	<p>Internal Medicine</p>	<p>Atrial Fibrillation in the absence of acute embolic stroke</p> <p>Prophylaxis of pts with PHx of VTE or thrombophilic state</p> <p>High Risk medical inpatients (eg cardiac failure, chest infection). No data on warfarin usage for this group.</p> <p>Hyperthyroidism</p>
	<p>Cardiothoracic surgery</p>	<p>Cardiac valve replacement</p> <p>Cardiac surgery</p>
	<p>Vascular</p>	<p>Vascular surgery</p> <p>Cerebral aneurysm coiling or embolisation, embolisation of cerebral vascular malformations at risk of haemorrhage, acute upper or lower limb ischaemia with threatened loss of limb, aortic dissection not amenable to surgical repair, acute occlusion of arteries or veins requiring urgent revascularisation not suitable for surgical intervention.</p> <p>Endovascular techniques which require heparin cover to minimise risk of arterial or venous thrombosis causing significant pt morbidity eg ischaemic limb rest pain.</p>
	<p>Orthopaedic Surgery</p>	<p>Hip, pelvis and acetabular fractures.</p> <p>Single long bone fractures</p> <p>Primary and secondary joint arthroplasty</p>

Treatment Priority 2 (cont)	Specialty	Medical Conditions and/or Procedures
	General surgery	<p>Intra-abdominal malignancy surgery</p> <p>Moderate-risk urgent or semi-elective general surgery patients are those patients undergoing a non-major procedure and are between the ages of 40 and 60 years or have additional risk factors, or those patients who are undergoing major operations and are < 40 years of age with no additional risk factors</p> <p>Higher-risk urgent or semi-elective general surgery patients are those undergoing non major surgery and are > 60 years of age or have additional risk factors, or patients undergoing major surgery who are > 40 years of age or have additional risk factors.</p> <p>Urgent or semi-elective general surgery patients with a high risk of bleeding</p>
	HITH (Hospital in the Home)	<p>DVT patients, not outlined above</p> <p>Note: Where testing is difficult eg rural/remote patients, can use SC UFH regimen with minimal need for dose adjustment according to APTT.</p>
	Renal	<p>Haemodialysis.</p> <p>Note: Anticoagulation essential for this group and warfarin NOT an alternative.</p>
	Obstetrics and gynaecology	<p>High risk women and moderate risk women.</p> <p>Post natal immediate thromboprophylaxis</p> <p>Postpartum thromboprophylaxis:</p> <p>Six week postpartum thromboprophylaxis is used in the following groups and is usually daily Clexane:</p> <ul style="list-style-type: none"> • Women with DVT in current or previous pregnancy • Women with thrombophilia and previous DVT • Certain other high risk thrombophilias

Treatment Priority 3	Specialty	Medical Conditions and/or Procedures
<p>Use alternatives to heparin based products eg use other products or mechanical prophylaxis eg IPC</p>	<p>Internal Medicine</p>	<p>DVT prevention for medical inpatients. Use IPC or GCS.</p>
	<p>General Surgery</p>	<p>Low risk general surgery, minor procedure, <40 yrs, no additional risk factors</p>
	<p>Laparoscopic surgery</p>	<p>In general laparoscopic surgery is low risk for thrombosis. Thromboprophylaxis is not recommended apart from early mobilisation.²</p>
	<p>Intravascular catheters</p>	<p>Alternative products such as normal saline may be used for maintenance of intravascular catheters. NB However heparin is still required for maintenance of line patency in children.</p>
	<p>Obstetrics and Gynaecology</p>	<p>Caesarean section. Recommend use of graduated elastic compression stockings and intermittent pneumatic compression boots.¹¹ Available data suggest that the risk of VTE is higher after caesarean section (especially emergency surgery) than after vaginal delivery.¹² The presence of additional risk factors for pregnancy-associated VTE (for example, prior VTE, thrombophilia, age > 35 years, obesity, prolonged bed rest, and concomitant acute medical illness) may exacerbate this risk. Use of GCS during and after caesarean section is recommended in patients considered to be at moderate risk of VTE, with addition of LMWH or UFH prophylaxis in those thought to be at high risk.¹² However, data on benefits associated with these interventions are inconclusive. Laparoscopic gynaecological surgery with additional risk factors for VTE, use GCS or IPC.</p>

Treatment Priority 4	Specialty	Medical Conditions and/or Procedures
<p>Procedures and elective surgery which can be deferred safely</p>	<p>Vascular</p>	<p>Elective procedures for non-life threatening but life limiting conditions requiring intra-arterial or intra-venous bolus heparin use such as performed for lower limb claudication.</p>
	<p>General Surgery</p>	<p>Moderate-risk elective general surgery patients.</p> <p>Higher-risk elective general surgery patients.</p> <p>Elective general surgery patients with a high risk of bleeding.</p>

References

- 1 Kishimoto TK, Viswanathan K, Ganguly T et al. Contaminated Heparin Associated with Adverse Clinical Events and Activation of the Contact System. *N Engl J Med*, 2008, 10.1056/NEJMOA0803200
- 2 Geerts WH, Pineo GF, Heit JA, Bergqvist D et al. Prevention of Venous Thromboembolism. The Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. *Chest*, 2004; 126:338S-400S.
- 3 Kearon C, Ginsberg JS, Julian JA, Douketis J et al. Comparison of Fixed-Dose Weight-Adjusted Unfractionated Heparin and Low-Molecular-Weight Heparin for Acute Treatment of Venous Thromboembolism. *JAMA* 2006; 296: 935-42.
- 4 Prandoni P et al. Subcutaneous Adjusted-Dose Unfractionated Heparin vs Fixed-Dose Low-Molecular-Weight Heparin in the Initial Treatment of Venous Thromboembolism. *Arch Internal Med* 2004; 164: 1077-83.
- 5 Phillips SM, Gallagher M, Buchan H. Use graduated compression stockings postoperatively to prevent deep vein thrombosis. *Br Med J* 2008; 336: 943-4.
- 6 Amaragiri SV, Lees TA. Elastic compression stockings for prevention of deep vein thrombosis. *Cochrane Database Syst Rev* 2000;(3):CD001484.
- 7 Pineo GF. Prevention of venous thromboembolic disease :In *UpToDate*, January 2008
- 8 Acute Coronary Syndrome Guidelines Working Group. Guidelines for the management of acute coronary syndromes 2006. *Med J Aust*, 2006; 184 (8 Suppl): S1-S32
- 9 Deitelzweig SB, McKean SC, Amin AN et al. Prevention of venous thromboembolism in the orthopedic surgery patient. *Cleveland Clinic Journal of Medicine*, 2008. Vol 75,S3.
- 10 Consensus view of the AHPC group based on peer reviewed literature and expert clinical opinion.
- 11 Gates S, Brocklehurst P, Davis LJ. Prophylaxis for venous thromboembolic disease in pregnancy and the early postnatal period. *Cochrane Database Syst Rev*, 2002; (2):CD001689.
- 12 Bates SM, Greer IA, Hirsh J, Ginsberg JS. Use of Antithrombotic Agents During Pregnancy. The Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. *Chest*, 2004;126:627S-644S.