MIL

Oxford University Hospitals NHS
NHS Foundation Trust

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This Medicines Information Leaflet is produced locally to optimise the use of medicines by encouraging prescribing that is safe, clinically appropriate, and cost-effective to the NHS.

Prevention of hospital associated venous thromboembolism (VTE) in inpatients aged 16 years or more (excluding pregnancy and the puerperium)

For patients with suspected or confirmed COVID-19 please prescribe LMWH according to the dosing guidance

Oxford University Hospitals (OUH) local VTE prevention guidance is based on NICE NG89 'Venous thromboembolism in over 16s: reducing the risk of hospital-acquired deep vein thrombosis or pulmonary embolism'. The full Trust policy on VTE prevention can be accessed via this link. This MIL aims to provide a summary of this policy.

VTE risk assessment

All patients aged 16 or older admitted to OUH **must** be VTE risk assessed within **6 hours** of admission. They should be VTE risk assessed regularly throughout their stay, as clinical condition changes. Risk assessments should be documented and completed using the electronic VTE risk assessment form within EPR. Those identified as having a risk of VTE must be offered appropriate management *as soon as possible* after the risk assessment has been completed. All eligible patients should have appropriate VTE prevention measures administered within **14 hours** of admission.

Risk factors for thrombosis and bleeding and contraindications to mechanical thromboprophylaxis are listed on the electronic VTE risk assessment form and as part of the flow charts at the end of this guidance (appendix 1 and 2). The completed VTE risk assessment will provide a recommendation for appropriate thromboprophylaxis for your patient. It is imperative that this guidance is considered unless there is a clinical reason not to. In this case, the reason must be documented in the medical notes, and the patient should be re-assessed regularly as the clinical condition changes.

Measures to reduce VTE risk

- Patients should be counselled about their risk of VTE and provided with written and verbal information.
- Encourage people to mobilise as soon as possible.
- Maintain adequate hydration.
- Thromboprophylaxis should be commenced (if there are no contraindications) for those inpatients who are interrupting anticoagulant therapy.

Thromboprophylaxis

Thromboprophylaxis can consist of pharmacological and/or mechanical measures.

Mechanical thromboprophylaxis

For surgical patients, anti-embolism stockings (AES) and/or intermittent pneumatic compression (IPC) should be used unless contraindicated. Medical patients should not generally be prescribed mechanical thromboprophylaxis. Medical patients at high risk of VTE in whom pharmacological thromboprophylaxis is contraindicated may be considered for mechanical thromboprophylaxis at the physician's discretion: in these circumstances, there is greater evidence to support the use of IPC when compared to AES. Mechanical thromboprophylaxis must be prescribed on the drug chart and skin safety checks should be carried out at least every 8 hours and documented on EPR.

Pharmacological thromboprophylaxis

Dalteparin is the low molecular weight heparin (LMWH) of choice at OUH for pharmacological prophylaxis. The licensed dose of dalteparin is 5,000 units once daily. However, there is evidence to suggest dose banding based on weight (see **Table 1**) may provide more effective prophylaxis and should be considered in patients at the extremes of body weight.

Table 1: Weight based doses adjustments for dalteparin

Weight (kg)	Dose (units)
Less than 40	2,500 once daily
40-120	5,000 once daily
121-150	7,500 once daily
More than 150	5,000 twice daily

Dalteparin procedures/operations
Patients who have dalteparin withheld pending procedures/emergency surgery are at risk of missing recurrent doses if the procedure/surgery is cancelled or postponed. In this instance review thromboprophylaxis morning and evening.

Please ensure thromboprophylaxis is optimised peri-operatively. For interventional radiology guidelines see here.

Pre-procedure: Most procedures/operations can be carried out 12 hours after prophylactic dalteparin; for procedures without significant bleeding risk, prophylactic dalteparin does not necessarily need to be withheld.

Post-procedure: Prophylactic dalteparin should usually be administered 6-12 hours post-surgery (for example hip and knee replacement surgery), provided haemostasis is secure. For **high bleeding risk** surgery (for example spinal or neurosurgery) dalteparin should be delayed for 24-48 hours post operatively.

Some patients may require a more prolonged period without pharmacological thromboprophylaxis, if considered clinically appropriate by the senior clinician involved in the patient's care. This should be reviewed daily, and the decision documented in the medical notes.

Specific guidance for lumbar puncture: Prophylactic dalteparin should not be administered in the 12 hours prior to a lumbar puncture or insertion of an epidural, spinal or nerve infusion catheter. Prophylactic dalteparin should not be administered within 4 hours after a lumbar puncture or epidural catheter (or 24 hours afterwards if the insertion was traumatic/ there was a bloody tap).

Surgery and medications containing oestrogen

Advise patients to consider stopping oestrogen- containing oral contraceptives or hormone replacement therapy 4 weeks before elective surgery. (Please note: HRT does not need to stop if the oestrogen component is topical). If stopped, provide advice on alternative contraceptive methods. Cessation of oestrogen-containing contraceptives may not be necessary prior to minor procedures carried out under local anaesthesia which do not involve the pelvis or lower limbs and are not likely to result in immobility.

Monitoring
Routine monitoring of the anticoagulant effect of dalteparin is not normally required; however, it may be necessary in certain circumstances (consideration should be given to monitoring dose adjustments in patients with significant renal impairment).

Routine monitoring for heparin induced thrombocytopenia (HIT) is not required for patients receiving dalteparin, except for patients who have undergone cardiac surgery. In these patients, platelet counts should be monitored at baseline and every 2-4 days between days 4 to 14 of treatment.

Inhibition of aldosterone secretion by unfractionated or low molecular weight heparin can cause result in hyperkalaemia in susceptible patients (e.g., patients with diabetes, chronic renal failure, or acidosis, or those taking potassium sparing drugs). If such patients are given dalteparin for longer than 7 days, potassium should be monitored weekly whilst an inpatient.

Pharmacological prophylaxis in renal impairment
Dalteparin is renally cleared, so care is required when administering dalteparin to patients with severe renal impairment (GFR less than 20mL/min/1.73m^2). Limited data suggest that dose adjustment may not be required with short-term use (less than 10 days). For longer term use, accumulation can be measured by a heparin anti-Xa assay (citrate tube to coagulation laboratory). Peak (4 hours post dose) and trough (immediately pre-dose) should be measured. For thromboprophylaxis, peak levels should be in the region of 0.3 heparin anti-Xa units/mL with undetectable troughs. **Arbitrary dose reduction may result in sub-optimal provision of prophylaxis and may put the patient at increased risk of hospital associated VTE.** However, a dose reduction should be considered in those patients in whom accumulation is detected by heparin anti-Xa assay.

Pharmacological prophylaxis in dialysis patients
There is little data regarding the use of prophylactic dalteparin, and dosing regimens in dialysis patients. Dialysis patients are overall at increased risk of both thrombosis and bleeding. Following discussion with renal consultants at OUH, it has been agreed that inpatients at risk of thrombosis should be prescribed a standard dose of dalteparin unless contraindicated (in addition to routine anticoagulant for prevention of clotting in the extracorporeal circuit). If there is particular concern regarding bleeding risk, this should be discussed with the on-call renal consultant and reduced dosage considered on an individual basis, with documentation of this decision.

Coronary or peripheral artery disease (CAD or PAD)
For patients with CAD/PAD managed on rivaroxaban 2.5mg twice daily and aspirin 75mg OD, we recommend stopping rivaroxaban and replacing with dalteparin for the duration of inpatient thromboprophylaxis (or extended thromboprophylaxis, if indicated). Continue aspirin. Advice must be given to the patient to restart rivaroxaban once thromboprophylaxis is completed.

Alternatives to dalteparin
Heparins are derived from pigs which may be of concern to some people. Discuss the alternatives with people who have concerns about using animal products, considering their suitability, advantages, and disadvantages. Patients who have localized skin reactions to dalteparin may be prescribed an alternative agent e.g., enoxaparin in the first instance. Fondaparinux may be used if patients also develop localized skin reactions to LMWHs.

Fondaparinux
Fondaparinux is available for patients who are unable to receive LMWHs but who are eligible for pharmacological thromboprophylaxis (e.g., patients with a history of heparin induced thrombocytopenia, or those who decline LMWHs due to animal origin). The dose for prophylactic fondaparinux is 2.5mg subcutaneously once daily for most patients.
N.B. In patients with renal insufficiency (GFR 20-50mL/min/1.73m^2), the dose should be reduced to 1.5mg subcutaneously once daily. In patients with significant renal impairment (GFR less than 20mL/min/1.73m2), fondaparinux should be avoided. The half-life of prophylactic fondaparinux is 17-21 hours (age dependent) in patients with normal renal function. This should be considered if planning surgery.

Danaparoid
Danaparoid is also available for patients with a history of HIT, at a dose of 750units subcutaneously twice daily. Monitoring of anticoagulant effect is not normally required. In patients at extremes of body weight and those with renal insufficiency, danaparoid anti-Xa levels can be measured, and dose adjustments made if necessary. Steady state levels should be in the region of 0.15-0.35 danaparoid anti-Xa units/ml.

Unfractionated heparin
Unfractionated heparin is only indicated for use in certain specialist clinical areas and should not be used outside of those areas unless on the advice of a specialist.

Direct oral anticoagulants (DOACs)
Apixaban, dabigatran and rivaroxaban are oral agents licensed for extended thromboprophylaxis after elective hip or knee surgery.

Aspirin
Do not regard aspirin or other antiplatelet agents as adequate pharmacological thromboprophylaxis for VTE.

Patients with acute stroke
Separate guidance is available for the provision of thromboprophylaxis in acute stroke patients.

Pregnancy and the puerperium
Separate guidance is available for the risk assessment and provision of thromboprophylaxis to obstetric patients.

Palliative care patients
Do not routinely offer thromboprophylaxis to patients expected to die within the next week. This decision should be reviewed regularly for improvements or stability. For all other patients, including those under palliative care, use the VTE risk assessment to consider thromboprophylaxis, its potential risks and benefits. Seek the views of patients and their families and/or carers and the multidisciplinary team.

Extended (post discharge) thromboprophylaxis
Certain high-risk procedures carry a significant risk of VTE that continues post discharge, and as such extended thromboprophylaxis is indicated after these procedures (see **Table 3**). Duration depends on the indication and the agent used but must be supplied by the hospital. Please refer to the Dalteparin Primary Care Guidelines for details on local prescribing responsibilities.

Table 3: Extended thromboprophylaxis recommendations

Surgery	Thromboprophylaxis
Elective hip replacement	Prophylactic dalteparin for 35 days post operatively and anti-embolism stockings until discharge
Elective knee replacement	Prophylactic dalteparin for 14 days post operatively and anti-embolism stockings until discharge
Fragility fracture of the pelvis, hip or proximal femur	Prophylactic dalteparin for 35 days post operatively and anti-embolism stockings until discharge
Arthroscopic knee surgery, if total anaesthetic time greater than 90 minutes (or risk of thrombosis outweighs risk of bleeding). Other knee surgery (for example, osteotomy or fracture surgery) with total general anaesthetic time greater than 90 minutes	Prophylactic dalteparin for 14 days post operatively and anti-embolism stockings until discharge
Lower limb immobilisation	See lower limb immobilisation for patients eligible for prophylactic dalteparin.
Major abdominal cancer surgery	Prophylactic dalteparin for 28 days post operatively and anti-embolism stockings until discharge
Certain very high risk patients e.g. previous history of VTE may warrant extended thromboprophylaxis after lower risk procedures; or a longer duration of extended thromboprophylaxis after a high risk procedure.	Please contact haemostasis team via EPR for non-urgent advice.

Safe prescribing points

- **Risk assessment recommendations.** If you do not think that the 'recommended outcome' as per the risk assessment is appropriate for your patient, discuss this with a senior member of the MDT and document the decision in the medical notes.
- **It is essential to prescribe both pharmacological and mechanical thromboprophylaxis** (as indicated) after completion of the VTE risk assessment by initiating the VTE powerplan within the "Requests and Prescribing, Suggested Plan" tab.
- **Review VTE prevention measures** if the clinical situation changes. **This is particularly important pre and post procedure.**

References

1. UKCPA Medicines Q&A no. 326.2. What doses of thromboprophylaxis are appropriate for adult patients at the extremes of body weight? **SPS and UKCPA HAT Committee**, September 2020
2. Low Molecular Weight Heparins in Renal Impairment and Obesity: Available Evidence and Clinical Practice Recommendations Across Medical and Surgical Settings' *Nutescu,E.A. et al.* **Annals of Pharmacotherapy**, 2009 Vol. 31064-1083
3. Anticoagulating obese patients in the modern era *Patel, J.P. et al* **British Journal of Haematology**, 2011 Vol. 155137-149
4. Antithrombotic Therapy and Prevention of Thrombosis, 9th edition. American College of Chest Physicians Evidence-Based Clinical Practice Guidelines" *Guyett, GH et al* **Chest**, 2012 Vol. 1417S-47S
5. FSRH Guideline. Combined Hormonal Contraception Published January 2019, amended November 2020. https://www.fsrh.org/standards-and-guidance/documents/combined-hormonal-contraception/.
6. British National Formulary (BNF) Online. Contraceptives, hormonal. British *Medical Association and the Royal Pharmaceutical Society of Great Britain* London. Accessed 1/7/2020 via https://bnf.nice.org.uk/treatment-summary/contraceptives-hormonal.html.
7. Eikelboom JW, Connolly SJ, Bosch J, et al. Rivaroxaban with or without aspirin in stable cardiovascular disease. N Engl J Med 2017;377:1319-30.

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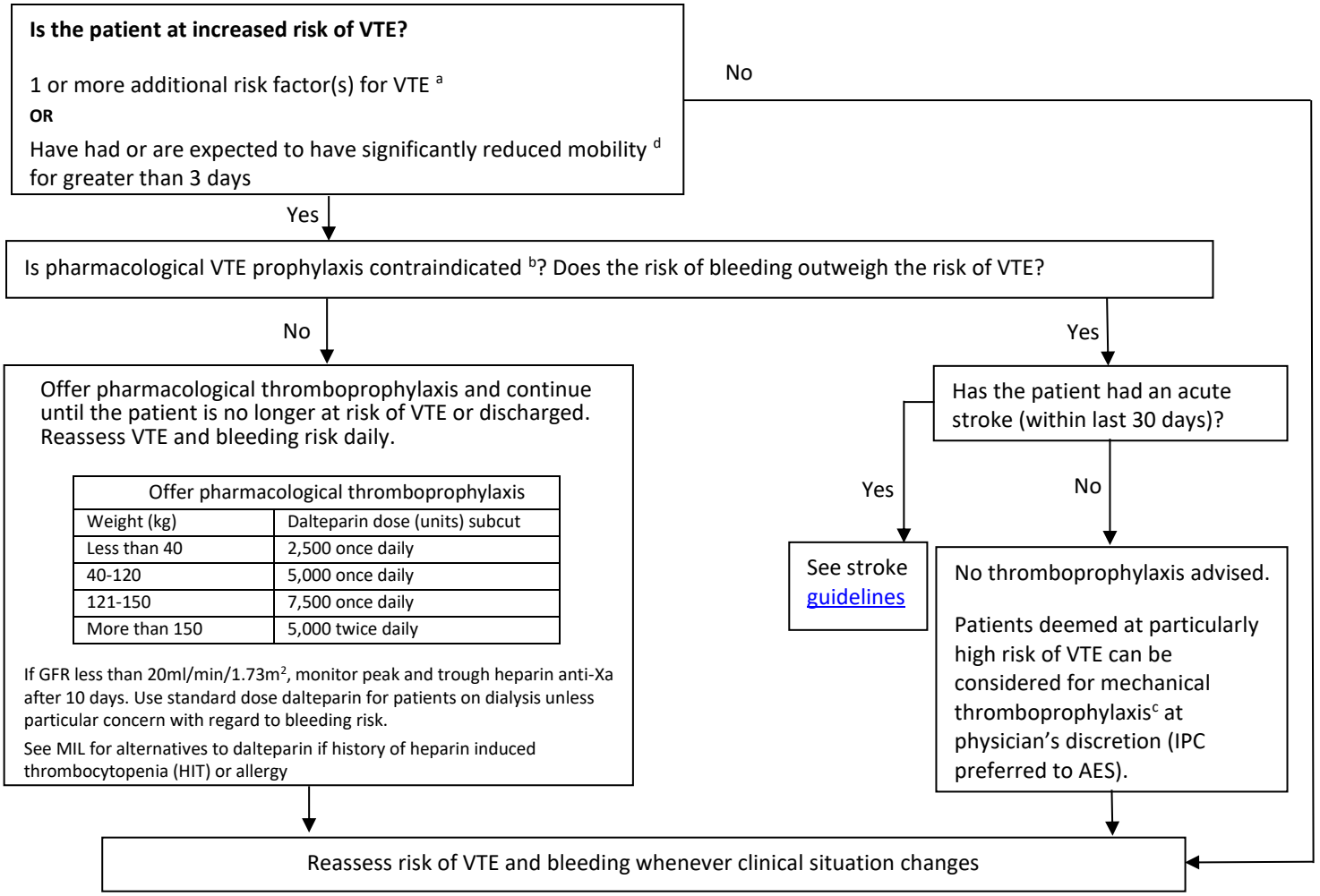
Appendix 1: VTE Prevention in Medical Inpatients Aged 16 Years or Above



Key:
AES- anti-embolism stockings; IPC-intermittent pneumatic compression; GFR – glomerular filtration rate (eGFR is a reasonable guide to GFR in most patients, but in patients at extremes of body weight GFR should be calculated using Cockcroft-Gault and ideal body weight); VTE- venous thromboembolism
d-significantly reduced mobility is defined in NICE CG89 as 'patients who are bed bound, unable to walk unaided or likely to spend a substantial proportion of their day in bed or chair'
e - Consider offering pharmacological VTE prophylaxis to patients in palliative care who have potentially reversible acute pathology. Do not routinely offer thromboprophylaxis to patients expected to die within the next week.

a Additional risk factors for VTE

- Age over 60 years
- Active cancer or cancer treatment
- Critical care admission
- Dehydration
- Known thrombophilia
- Obesity (BMI over 30kg/m^2)
- One or more significant medical comorbidities (for example): heart disease, metabolic endocrine or respiratory pathologies, acute infectious diseases, inflammatory conditions
- Personal history of VTE or first-degree relative with a history of VTE
- Use of hormone replacement therapy
- Use of oestrogen-containing contraceptive therapy
- Varicose veins with phlebitis
- Pregnancy or less than 6 weeks postpartum

b Risk factors for bleeding

- Active bleeding
- Acquired bleeding disorder (such as acute liver failure)
- Concurrent use of anticoagulants known to increase the risk of bleeding (such as warfarin with an INR 2 or more; direct/novel oral anticoagulants such as apixaban, rivaroxaban, edoxaban, dabigatran; or fondaparinux)
- Acute stroke
- Thrombocytopenia (platelets less than 75x10^9/l)
- Uncontrolled systolic hypertension (230/120mmHg or higher)
- Untreated inherited bleeding disorder (such as haemophilia and von Willebrands disease)
- Lumbar puncture/epidural/spinal anaesthesia within the next 12 hours
- Lumbar puncture/epidural/spinal anaesthesia within the previous 4 hours
- Other high risk bleeding procedure such as neurosurgery, spinal surgery or eye surgery

c Contraindications to mechanical thromboprophylaxis

Do not offer to patients who have:

- Suspected or proven peripheral arterial disease
- Peripheral arterial bypass grafting
- Peripheral neuropathy or other causes of sensory impairment
- Any local conditions in which AES may cause damage, for example fragile 'tissue paper skin' dermatitis, gangrene or recent skingraft
- Known allergy to material of manufacture
- Cardiac failure
- Severe leg oedema or pulmonary oedema from congestive heart failure
- Unusual leg size or shape
- Major limb deformity preventing correct fit
- Acute VTE

Do not offer AES to acute stroke patients, use IPC alone. Use caution and clinical judgement when applying AES over venous ulcers or wounds.

Appendix 2: VTE Prevention in Surgical Inpatients Aged 16 Years or Above

The patient is at increased risk of VTE if any of the following statements apply:

Surgical procedure with a total anaesthetic and surgical time greater than 90 minutes
Surgical procedure involving pelvis or lower limb with total anaesthetic and surgical time greater than 60 minutes
Acute surgical admission with inflammatory or intra-abdominal condition
Expected significant reduction in mobility
1 or more patient related VTE risk factor(s) [a]

Yes

Start mechanical thromboprophylaxis (e.g. AES and/or IPC (unless contraindicated)[c]. Continue until the patient no longer has significant reduced mobility.

No

No thromboprophylaxis is required.

Is pharmacological VTE prophylaxis contraindicated? Does the risk of bleeding outweigh the risk of VTE?[b]

No

Offer pharmacological thromboprophylaxis and continue until no significant reduction in mobility or discharged.
Reassess VTE and bleeding risk daily.

Offer pharmacological thromboprophylaxis	
Weight (kg)	Dalteparin dose (units) subcut
Less than 40	2,500 once daily
40-120	5,000 once daily
121-150	7,500 once daily
More than 150	5,000 twice daily

If GFR less than 20ml/min/1.73m^2, monitor peak and trough heparin anti-Xa after 10 days. See MIL for alternatives to dalteparin if history of heparin induced thrombocytopenia (HIT) or allergy.

Yes

Continue mechanical thromboprophylaxis alone.
Reassess bleeding and VTE risk daily.

Extended (post discharge) thromboprophylaxis.

This is indicated for certain high risk procedures. For dalteparin, the total duration of extended thromboprophylaxis as per SPC is:

Elective hip replacement – 35 days.
Fragility fracture pelvis/hip/proximal femur – 35 days
Elective knee replacement – 14 days.
Arthroscopic knee surgery and other knee surgery (e.g. osteotomy or fracture surgery) when GA time greater than 90 minutes – 14 days
Major abdominal cancer surgery – 28 days
Lower limb immobilisation- See lower limb immobilisation guidance for patients eligible
It may be indicated for certain high risk patients (e.g. previous history of VTE) after a lower risk procedure. For advice contact haematology.

Key: AES – anti-embolism stockings; IPC – intermittent pneumatic compression; GA – general anaesthetic; GFR – glomerular filtration rate (eGFR is a reasonable guide to GFR in most patients, but in patients at extremes of body weight GFR should be calculated using Cockcroft-Gault and ideal body weight); VTE – venous thromboembolism

d– 'significantly reduced mobility' is defined in NICE guidelines as 'patients who are bed bound, unable to walk unaided or likely to spend a substantial proportion of their day in bed or in a chair'

e - High VTE risk surgical patient- hip or knee arthroplasty, hip fracture surgery, major trauma and spinal cord injury, and surgery in patients with other significant (e.g. cancer, previous VTE) or multiple VTE risk factors

a Additional risk factors for VTE

- Age over 60 years
- Active cancer or cancer treatment
- Critical care admission
- Dehydration
- Known thrombophilia
- Obesity (BMI over 30kg/m^2)
- One or more significant medical comorbidities (for example): heart disease, metabolic endocrine or respiratory pathologies, acute infectious diseases, inflammatory conditions
- Personal history of VTE or first-degree relative with a history of VTE
- Use of hormone replacement therapy
- Use of oestrogen-containing contraceptive therapy
- Varicose veins with phlebitis
- Pregnancy or less than 6 weeks postpartum

b Risk factors for bleeding

- Active bleeding
- Acquired bleeding disorder (such as acute liver failure)
- Concurrent use of anticoagulants known to increase the risk of bleeding (such as warfarin with an INR 2 or more; direct/novel oral anticoagulants such as apixaban, rivaroxaban, edoxaban, dabigatran; or fondaparinux)
- Acute stroke
- Thrombocytopenia (platelets less than 75x10^9/l)
- Uncontrolled systolic hypertension (230/120mmHg or higher)
- Untreated inherited bleeding disorder (such as haemophilia and von Willebrands disease)
- Lumbar puncture/epidural/spinal anaesthesia within the next 12 hours
- Lumbar puncture/epidural/spinal anaesthesia within the previous 4 hours
- Other high risk bleeding procedure such as neurosurgery, spinal surgery or eyesurgery

c Contraindications to mechanical thromboprophylaxis

Do not offer to patients who have:

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- Peripheral arterial bypass grafting
- Peripheral neuropathy or other causes of sensory impairment
- Any local conditions in which AES may cause damage, for example fragile 'tissue paper skin' dermatitis, gangrene or recent skingraft
- Known allergy to material of manufacture
- Cardiac failure
- Severe leg oedema or pulmonary oedema from congestive heart failure
- Unusual leg size or shape
- Major limb deformity preventing correct fit
- Acute VTE

Do not offer AES to acute stroke patients, use IPC alone. Use caution and clinical judgement when applying AES over venous ulcers or wounds