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 see separate 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'. See the full Trust policy on VTE prevention. 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 **14 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

Enoxaparin sodium is the Low-Molecular Weight Heparin (LMWH) of choice in OUH. Enoxaparin is a biological medicine and as such should be prescribed by brand; Inhixa® will be supplied for all enoxaparin prescriptions. Each reference to enoxaparin in this document relates to Inhixa®.

Weight of patient

Doses of enoxaparin are weight-based. It is imperative that the patient is weighed and that the weight is documented on the patient's electronic record. In exceptional circumstances, when weighing the patient is not possible, the estimated weight must be documented. For patients with known fluid overload

(e.g. those requiring dialysis, nephrotic syndrome, liver or heart failure), dry weight should be used to dose the LMWH. Pharmacy will not dispense enoxaparin and nursing staff are at liberty to refuse to administer enoxaparin if there is no documented weight.

Table 1: Weight based doses adjustments for enoxaparin

Weight (kg)	Dose (mg) for CrCl above 30mL/min
Less than 50	20mg once daily
50-100	40mg once daily
101-150	60mg once daily
More than 150	40mg twice daily

Enoxaparin procedures/operations
Patients who have enoxaparin 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 enoxaparin; for procedures without significant bleeding risk, prophylactic enoxaparin does not necessarily need to be withheld.

Post-procedure: Prophylactic enoxaparin 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) enoxaparin 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 enoxaparin should not be administered in the 12 hours prior to a lumbar puncture or insertion of an epidural, spinal or nerve infusion catheter. For patients with creatinine clearance of 30mL/min or less, consider doubling the timing of puncture/catheter placement or removal to at least 24 hours. Prophylactic enoxaparin 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 (HRT) 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. See **Appendix 3** for further guidance

Monitoring
Routine monitoring of the anticoagulant effect of enoxaparin 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 enoxaparin 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 LMWH can 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 enoxaparin for longer than 7 days, potassium should be monitored weekly whilst an inpatient.

Pharmacological prophylaxis in renal impairment
Enoxaparin is renally cleared, so care is required when administering enoxaparin to patients with severe renal impairment (CrCl 15-30mL/min). There is evidence to suggest dose banding based on weight (see **Table 2**) may provide more effective prophylaxis.

Table 2: Weight based doses adjustments for enoxaparin in renal impairment

Weight (kg)	Dose (mg) for CrCl 15-30mL/min
Less than 50	20mg once daily
50-100	20mg once daily
101-150	40mg once daily
More than 150	60mg once daily

Pharmacological prophylaxis in patients with CrCl less than 15mL/min or on dialysis (including patients on peritoneal & haemodialysis, whether for AKI or CKD5D)
There are few data regarding the use of prophylactic enoxaparin, and dosing regimens in patients with CrCl less than 15mL/min or for those on dialysis. These patients are at increased risk of both thrombosis and

bleeding. Following consultation with the renal team at OUH, it has been agreed that inpatients at risk of thrombosis should be prescribed a set dose of enoxaparin 20mg once daily unless contraindicated (in addition to routine anticoagulant for prevention of clotting in the extracorporeal circuit). If these patients require an extended period of prophylactic enoxaparin (over 7 days), trough anti-Xa measurements at day 7 should be considered (aiming for trough levels less than or equal to 0.2IU/ml). If there is particular concern regarding bleeding risk, this should be discussed with the on-call renal consultant, 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 enoxaparin 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.

Patients who decline LMWH

Patients may decline LMWH for various reasons. Please see section below on 'alternatives to enoxaparin' and the administration policy for further information.

For patients who continue to decline LMWH despite being offered alternatives, please document this clearly in the medical notes.

Alternatives to enoxaparin

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 enoxaparin may be prescribed an alternative agent e.g. dalteparin in the first instance. Fondaparinux may be used if patients also develop localized skin reactions to LMWHs.

For those patients routinely prescribed therapeutic anti-coagulation (including secondary prevention doses of DOACs e.g. 2.5mg apixaban BD, 10mg rivaroxaban OD.) clinical teams should prescribe these anticoagulants in preference to VTE prevention doses of LMWH (clinical situation allowing).

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.
In patients with renal insufficiency (CrCl 20- 50mL/min), the dose should be reduced to 1.5mg subcutaneously once daily. In patients with significant renal impairment (CrCl less than 20mL/min), 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)

Clinical teams can consider alternative oral therapy (such as a low dose DOAC) in individual circumstances. **This is non-formulary and approval from MMTC is required prior to starting by completing this form.**

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.

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 Enoxaparin Primary Care Guidelines for details on local prescribing responsibilities.

Table 3: Extended thromboprophylaxis recommendations

For patients with a previous history of VTE who are not taking long term anticoagulation – we suggest 6 weeks of thromboprophylaxis. Please contact haemostasis team via EPR for non-urgent advice if you would like to discuss an individual's care

Surgery	Thromboprophylaxis
Elective hip replacement	Prophylactic enoxaparin for 35 days post operatively and mechanical thromboprophylaxis until discharge
Elective knee replacement	Prophylactic enoxaparin for 14 days post-operatively and mechanical thromboprophylaxis until discharge
Fragility fracture of the pelvis, hip or proximal femur, including arthroplasty for this indication	Prophylactic enoxaparin for 28 days post-operatively and mechanical thromboprophylaxis 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 enoxaparin for 14 days post operatively and mechanical thromboprophylaxis until discharge
Lower limb immobilisation	See **lower limb immobilisation MIL** for patients eligible for prophylactic enoxaparin.
Major abdominal cancer surgery	Prophylactic enoxaparin for 28 days post operatively and mechanical thromboprophylaxis until discharge

Pregnancy and the puerperium

Separate guidance is available for 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.

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.

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Prepared by: Vicki McDonnell, Lead Anticoagulation & Thrombosis Pharmacist, Dr Susie Shapiro, Consultant Haematologist and VTE Prevention Team

Updated by: Gurpreet Bahra, Specialist Anticoagulation and Thrombosis Pharmacist, Dr Nicola Curry, Consultant Haematologist and VTE Prevention Team.

With advice from: Dr Richard Haynes (Renal Consultant)

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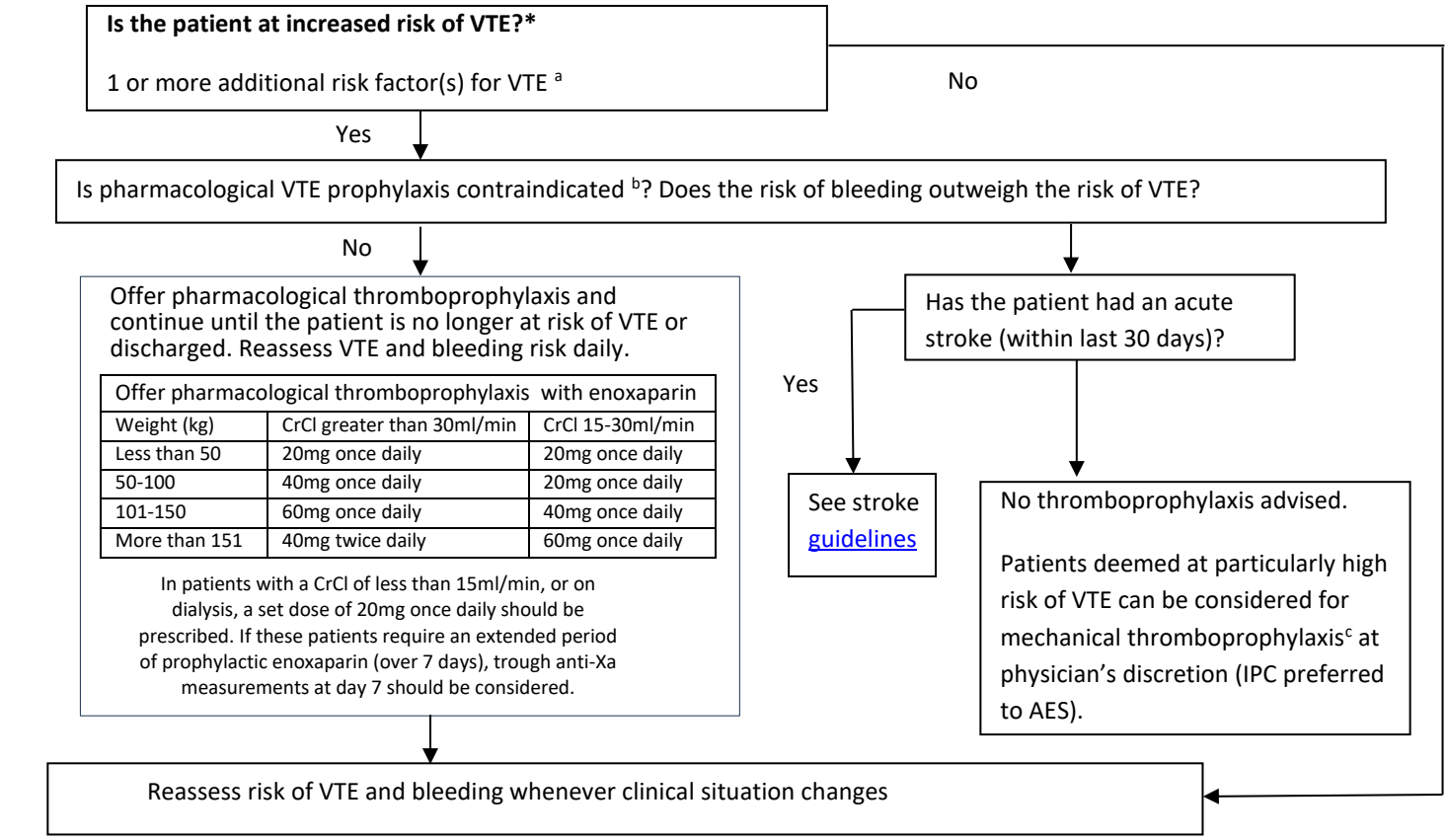
Appendix 1: VTE Prevention in Medical Inpatients Aged 16 Years or Above



Key:
AES- anti-embolism stockings; IPC-intermittent pneumatic compression; VTE- venous thromboembolism
*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 12-24 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 skin graft
- 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
1 or more patient related VTE risk factor(s) [a]

Yes → Start mechanical thromboprophylaxis (e.g. AES and/or IPC (unless contraindicated)[c].

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 discharged. Reassess VTE and bleeding risk daily

Offer pharmacological thromboprophylaxis with enoxaparin		
Weight (kg)	CrCl greater than 30ml/min	CrCl 15-30ml/min
Less than 50	20mg once daily	20mg once daily
50-100	40mg once daily	20mg once daily
101-150	60mg once daily	40mg once daily
More than 151	40mg twice daily	60mg once daily

If on VTEp for an extended period (over 7 days) then consider trough anti-Xa levels at day 7 for patients with CrCl less then 15mL/min or on dialysis. See MIL for alternatives to enoxaparin 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 enoxaparin, the total duration of extended thromboprophylaxis is:

Elective hip replacement – 35 days.
Fragility fracture pelvis/hip/proximal femur – 28 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; VTE – venous thromboembolism

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
- Have had or are expected to have significantly reduced mobility[d]

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 12-24 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:

- 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 skin graft
- 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 3: Surgery and medications containing oestrogen

Class of drug	Pre-operative		Post operative
Hormone replacement therapy (HRT)	**CONTINUE** In minor surgery without immobilisation **STOP** In major surgery with prolonged immobilisation, at least 4 weeks prior to surgery if on oral therapy Transdermal HRT can **CONTINUE** as limited evidence of adverse impact on VTE risk		Continue thromboprophylaxis if appropriate until discharge. HRT should be restarted ONLY after full mobilisation.
Oral contraceptives	**Combined oral contraceptives (COC)** **CONTINUE** Minor surgery (no immobilisation) **STOP** Major surgery/surgery to legs/prolonged immobilisation (alternative contraception arrangements to be made at least 4 weeks before)	**Progesterone only contraceptives (POC)** **CONTINUE** If on progesterone only contraceptive. Ensure thromboprophylaxis prescribed.	Restart COC at the first menses occurring at least 2 weeks after full mobilisation.