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Venous Thromboembolism (VTE)

Prevention protocol for adult patients

Version 1

26 September 2021

Aim and scope:
To standardize Venous Thromboembolism (VTE) risk assessment that delivers decision support to the point of care and standardize the clinical practice for VTE prevention to reduce morbidity and mortality related to thrombosis. The VTE prevention protocol developed to cover all related clinical specialties.

Targeted end users:
This protocol intended to be used by the physicians and other Health Care Providers working at MOH hospitals.

Targeted population:
All adult patients admitted to MOH hospitals.

Level of Evidence:
Review of best practice and expert opinion.

Disclaimer:
This living guidance is subject to updates with new emerging data or within 2 years.
The task force members have no conflict of interest. This protocol is not attached to any funding.

Scoring

VTE prevention protocols selected VTE and bleeding risk assessment based on:

- Modified Caprini tool for all cases except obstetric.
- Royal College of Obstetrics & Gynecology (RCOG) VTE and bleeding risk assessment tool for Obstetric cases only (Antenatal & Postnatal)

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Modified Caprini

RISK FACTORS			
1 score for each ❑ Age 41-60 years ❑ BMI > 25 Kg/m2 ❑ Minor surgery ❑ Swollen legs (current) ❑ Varicose veins ❑ Major Surgery (in the past month) ❑ lung disease (e.g., emphysema or COPD) ❑ Currently on bed rest or restricted mobility ❑ History of Inflammatory bowel disease ❑ Acute myocardial infarction ❑ Congestive heart failure (<1 month) ❑ Sepsis/ **Pneumonia** (<1month)/ ❑ History of unexplained or recurrent spontaneous abortion (>3) ❑ Pregnant or post-partum (<1 month) ❑ Oral contraceptives or hormone replacement	**2 score for each** ❑ Age: 61-74 years ❑ Arthroscopic Surgery ❑ Laparoscopy Surgery (>45 min) ❑ Major open Surgery (>45 min) ❑ Cancer (current or previous) ❑ Immobilizing Plaster cast ❑ Bed bound for more than 72hrs ❑ Central venous access	**3 score for each** ❑ Age≥ 75 years ❑ History of DVT/PE ❑ **Family history of VTE** ❑ Factor V Leiden ❑ Prothrombin 20210A ❑ Lupus anticoagulant ❑ Anticardiolipin antibodies ❑ Elevated serum homocysteine ❑ Heparin-induced thrombocytopenia ❑ Other congenital or acquired thrombophilia	**5 score for each** ❑ Hip, pelvis or leg fracture (within the past month) ❑ Stroke (within past month) ❑ Multiple trauma (within past month) ❑ Elective major lower extremity arthroplasty ❑ Acute Spinal cord injury – **paralysis** (within the past month)

Based on the calculation of scores from the selected risk factors the patient should fall in one of the following risk levels:

RISK LEVEL			
If total scores equal to 0 or 1: **Low** risk	If total scores equal to 2: **Moderate** risk	If total scores equal to 3 or 4: **High** risk	If total scores equal to or more than 5: **Highest** risk

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VTE prophylaxis based on Modified Caprini risk levels

I- For all MEDICAL and GENERAL SURGICAL conditions:

Category	Supportive Care	Pharmacotherapy	Precautions
• Low Risk	• Encourage ambulation if not restricted	• No thromboprophylaxis required	
• Moderate Risk	• Encourage ambulation if not restricted • Offer mechanical prophylaxis if pharmacological prophylaxis contraindicated	• Enoxaparin 40 mg SC once daily **OR** • Unfractionated Heparin 5000 Units SC BID or TID **OR** • Fondaparinux dose 2.5 mg SC q24h	If CrCl < 30ml/min, Enoxaparin 30 mg subcutaneously once daily and avoid Fondaparinux
• High Risk	• Encourage ambulation if not restricted **with or without** mechanical prophylaxis	• Enoxaparin 40mg SC once daily **OR** • Unfractionated Heparin 5000 Units SC TID **OR** • Fondaparinux dose 2.5 mg SC q24h	If CrCl < 30ml/min, Enoxaparin 30 mg subcutaneously once daily and avoid Fondaparinux
• Highest Risk	• Encourage ambulation if not restricted **with** mechanical prophylaxis	• Enoxaparin 40mg SC once daily **OR** • Unfractionated Heparin 5000 Units SC TID **OR** • Fondaparinux dose 2.5 mg SC q24h	If CrCl < 30ml/min, Enoxaparin 30 mg subcutaneously once daily and avoid Fondaparinux

Prophylactic Dose Anticoagulation based on BMI and CrCl:

CrCl (ml/min)	BMI (Kg/m²)	Enoxaparin	Fondaparinux	Unfractionated heparin (UFH)
>30	<40	40 mg SC q24h	2.5 mg SC q24h	5000 units SC q8-12h
	>40	40 mg SC q12h	5 mg SC q24h	7500 units SC q8h
<30	<40	7500 units SC q8h		
	>40	UFH 7500 units SC q8h		

Special consideration:

Oncology cases:

- Start prophylaxis early administration (postoperative, within 12 hours) or late administration (postoperative, after 12 hours) of antithrombotic prophylaxis in major surgical patients including cancer depending on bleeding risk
- Duration of anticoagulant for abdominal cancer surgery or previous VTE is **30 days**

Critical cases:

- For patient admitted to critical care units, routine assessment for VTE & bleeding risk is recommended and routine thrombo-prophylaxis is administered for at risk patients.
- For critical care patients who are at high-risk of bleeding, we recommend the optimal use of mechanical thromboprophylaxis with IPC at least until the bleeding risk decreases. When the high bleeding risk decreases.
- When the high bleeding risk decreases, we recommend that pharmacologic thromboprophylaxis be substituted for or added to the mechanical thromboprophylaxis.

II- ORTHOPEDIC Surgery:

Category	Supportive Care	Pharmacotherapy	Precautions
A. Elective hip replacement			
For patient undergoing elective total hip replacement (THR)		Recommended thromboprophylaxis either: **a. LMWH:** - At a usual high-risk dose 40 mg SC q24h initiated 12 h **before** surgery **OR** - At a usual high-risk dose 30 mg SC q24h initiated 12 to 24 h **after** surgery **OR** **b. Fondaparinux dose 2.5 mg SC q24h initiated 6-8 hr after surgery** **OR** **c. Apixaban 2.5** mg twice daily initiated 12-24 hr after surgery **OR** **d. Adjusted-dose VKA (Warfarin)** started preoperatively the evening of the surgical day ***(INR target 2.5, INR range: 2.0 – 3.0 for 35 days)***	
For patient undergoing THR who have a high risk of bleeding	Optimal use of a mechanical method with IPC	When the high bleeding risk decreases, pharmacologic thrombo-prophylaxis be substituted for or added to the mechanical thrombo-prophylaxis	Patients placed on mechanical prophylaxis after surgery because of a high risk of bleeding should have their risk of bleeding consistently reassessed, with pharmacologic prophylaxis started as soon as the bleeding risk is decreased
B. Elective Knee Replacement			
For patient undergoing total knee replacement (TKR)		Recommended thromboprophylaxis either: **a. LMWH:** - At a usual high-risk dose 30 mg SC q24h initiated 12 to 24 h after surgery **OR** **b. Fondaparinux dose 2.5 mg SC q24h initiated 6-8 hr after surgery** **OR** **c. Apixaban 2.5** mg twice daily initiated 12-24 hr after surgery **OR** **d. Adjusted-dose VKA (Warfarin**) started preoperatively of the evening of the surgical day ***(INR target 2.5, INR range: 2.0 – 3.0 for 35 days)***	
For patient undergoing TKR who have a high risk of bleeding	Optimal use of a mechanical method with IPC	When the high bleeding risk decreases, pharmacologic thrombo-prophylaxis be substituted for or added to the mechanical thrombo-prophylaxis to extend pharmacological prophylaxis beyond 10 days after discharge	
C. Hip Fracture Surgery (HFS)			

Category	Supportive Care	Pharmacotherapy	Precautions
For patient undergoing HFS		Routine thromboprophylaxis minimum 10 days up to 35 days is recommended: **a. Fondaparinux** 2.5 mg SC q24h initiated 6-8h after surgery OR **b. LMWH** 30mg SC q12h initiated 12-24hr after surgery OR **c. Adjusted dose VKA (Warfarin)** preoperatively (INR target. 2.5. INR range. 2.0 to 3.0)	
D. Elective Spine Surgery			
• Low risk	Encourage ambulation	No thromboprophylaxis required	
• Moderate Risk such as: - Advanced age - Malignancy - Neurological deficit - Previous VT - An anterior surgical approach	Optimal use of peri-operative IPC	The recommended thromboprphylaxis options: **a. Enoxaparin** 40 mg SC once daily OR **b. Unfractionated Heparin** 5000 Units SC or TID	VTE prophylaxis after elective spinal surgery can typically be initiated 12–24 hours postoperatively. Prophylaxis may need to be delayed if the surgical site remains open
• Highest Risk	Optimal use of a mechanical method (i.e. GCS and/or IPC)	The recommended thromboprophylaxis is one of the pharmacological thromboprophylaxis options combined with mechanical method: **a. Enoxaparin** 40 mg SC once daily OR **b. Unfractionated Heparin** 5000 Units SC or TID	
E. Knee arthroscopy			
• Low risk	Encourage ambulation	No thromboprophylaxis required	
• High risk (multiple risk factors or following a complicated procedure)	Early mobilization	The recommended thromboprophylaxis is one of the pharmacological thromboprophylaxis options combined with mechanical method: LMWH minimum of 10 days. **a. Enoxaparin** 40 mg SC once daily OR **b. Unfractionated Heparin** 5000 Units SC or TID	
F. Isolated Lower Extremity Injuries Distal to the Knee			
For patient with Isolated Lower Extremity Injuries Distal to the Knee		Routine use of thromboprophylaxis is **NOT** suggested	

III. UROLOGIC Surgery:

Category	Supportive Care	Pharmacotherapy	Precautions
For patient undergoing transurethral or other low risk procedures	Early mobilization	The recommendation is **against** the use of thromboprophylaxis	
For patient undergoing major open urologic procedures		The recommendation is to use **routine** thromboprophylaxis with: **Pharmacological prophylaxis** alone: **a. Enoxaparin** 40 mg SC once daily **OR** **b. Unfractionated Heparin** 5000 Units SC TID **OR** **Pharmacological plus mechanical prophylaxis**	Patients with very high risk for bleeding, we recommend the optimal use of mechanical thrombo-prophylaxis with GCS and/or IPC at least until the bleeding risk decreases. When the high bleeding risk decreases, we recommend pharmacologic thrombo-prophylaxis substituted for or added to the mechanical thrombo-prophylaxis.

IV. LAPRAROSCOPIC Surgery:

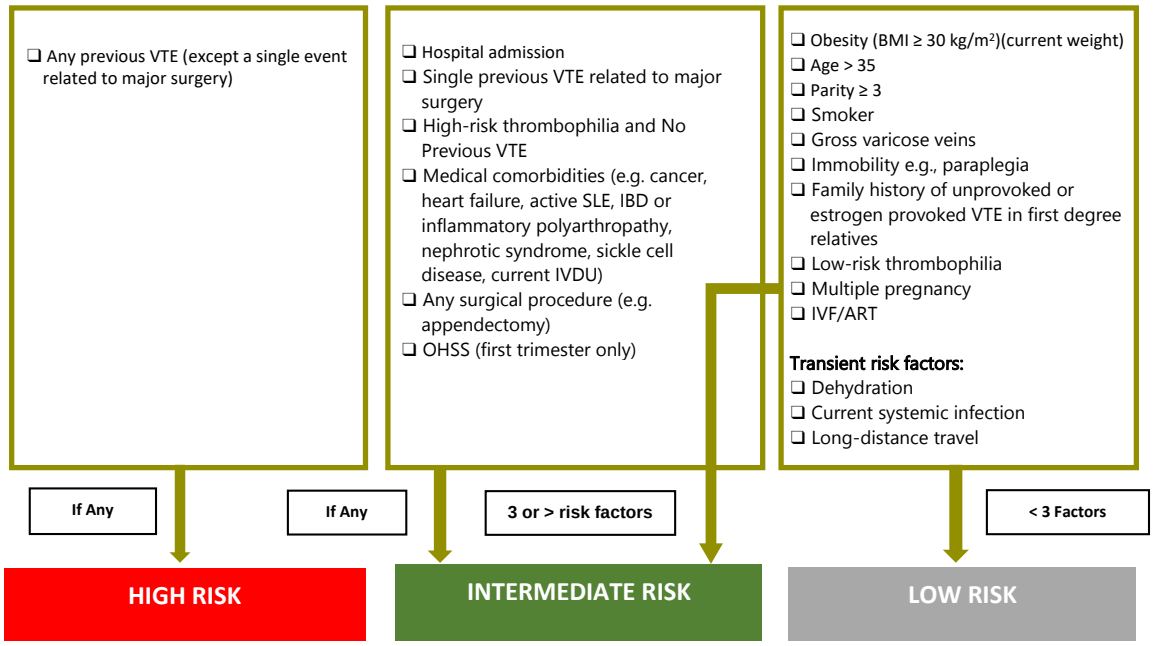
Category	Supportive Care	Pharmacotherapy	Precautions
For patient undergoing entirely laparoscopic procedures who don't have additional risk factors	Early mobilization	The recommendation is **against** the use of thromboprophylaxis	
For patient undergoing entirely laparoscopic procedures who don't have additional risk factors	Optimal use of a mechanical method (i.e., GCS and/or IPC)	The recommendation is the use of **routine** thromboprophylaxis with either: **Pharmacological prophylaxis** alone: **a. Enoxaparin** 40 mg SC once daily **OR** **b. Unfractionated Heparin** 5000 Units SC TID **OR** **Pharmacological plus mechanical prophylaxis**	

V. BARIATRIC Surgery:

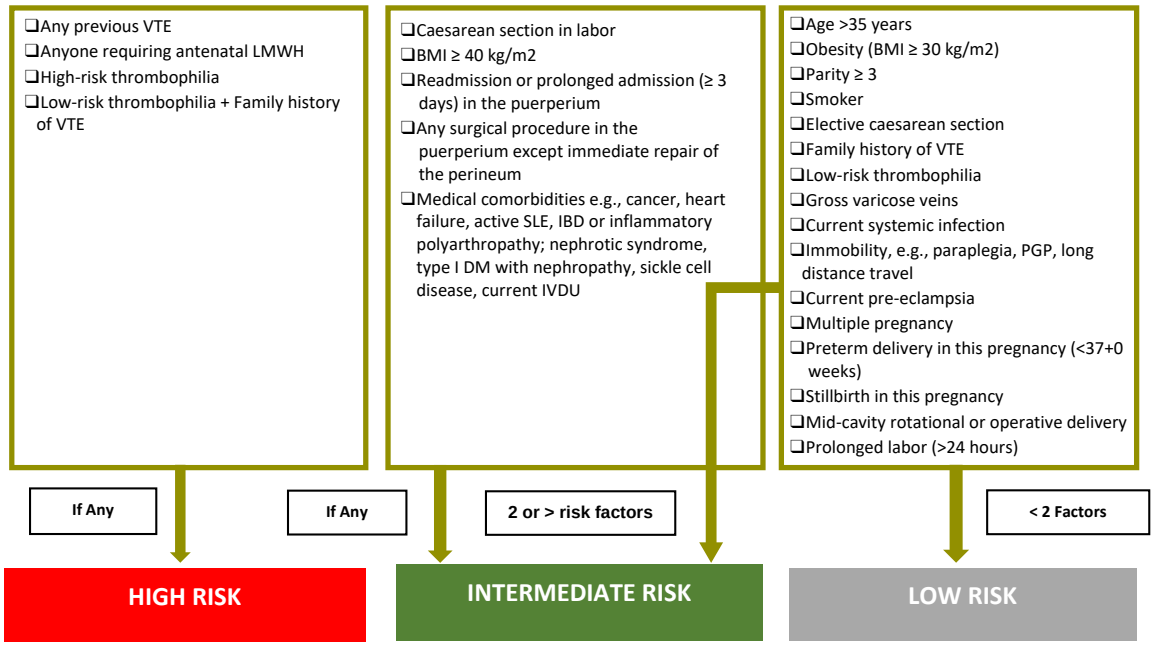
Category	Supportive Care	Pharmacotherapy	Precautions
For patient undergoing inpatient bariatric surgery	Optimal use of a mechanical method (i.e., GCS and/or IPC)	The recommendation is the use of **routine** thromboprophylaxis with either: **Pharmacological prophylaxis** alone: **a. Enoxaparin** 40 mg SC once daily **OR** **b. Unfractionated Heparin** 5000 Units SC TID **OR** **Pharmacological plus mechanical prophylaxis**	

RCOG VTE risk factors (refer to RCOG risk factor calculator):

VI. ANTENATAL:



VII. POSTNATAL:



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VTE Prophylaxis based on RCOG risk levels

Risk factors in pregnancy and the puerperium	
Pre-existing risk factors	**Score**
Previous VTE (except a single event related to major surgery)	4
Previous VTE provoked by major surgery	3
Known high-risk thrombophilia	3
Medical comorbidities e.g., cancer, heart failure; active systemic lupus erythematous, inflammatory polyarthropathy or inflammatory bowel disease; nephrotic syndrome; type I diabetes mellitus with nephropathy; sickle cell disease. current intravenous drug user	3
Family history of unprovoked or estrogen related VTE in first-degree relative	1
Known low-risk thrombophilia (no VTE)	1a
Age (> 35 years)	1
Obesity (body mass index [BMI] 30 0 kg/m2 or higher) either pre pregnancy or in early pregnancy	1 or 2b
Parity ≥ 3	1
Smoker	1
Gross varicose veins	1

Obstetric risk factors	Score
Previous VTE (except a single event related to major surgery)	4
Previous VTE provoked by major surgery	3
Known high-risk thrombophilia	3
Medical comorbidities e.g., cancer, heart failure; active systemic lupus erythematous, inflammatory polyarthropathy or inflammatory bowel disease; nephrotic syndrome; type I diabetes mellitus with nephropathy; sickle cell disease. current intravenous drug user	3
Pre-eclampsia in current pregnancy	1
ART/IVF (antenatal only)	1
Multiple pregnancy	1
Caesarean section in labor	2
Elective caesarean section	1
Mid-cavity or rotational operative delivery	1
Prolonged labor (> 24 hours)	1
PPH (> 1 liter or transfusion)	1
Preterm birth < 37+0 weeks in current pregnancy	1
Stillbirth in current pregnancy	1

Transient risk factors	Score
Any surgical procedure in pregnancy or puerperium except immediate repair of the 3 perinea, e.g., appendicectomy, postpartum sterilization	3
Hyperemesis	4
OHSS (first trimester only)	1
Current systemic infection	1
Immobility, dehydration	1

- If total score ≥ 4 antenatally, consider thromboprophylaxis from the first trimester.
- If total score 3 antenatally, consider thromboprophylaxis from 28 weeks.
- If total score ≥ 2 postnatally, consider thromboprophylaxis for at least 10 days.
- If admitted to hospital antenatally consider thromboprophylaxis.
- If prolonged admission (≥ 3 days) or readmission to hospital within the puerperium, consider thromboprophylaxis.

VTE prophylaxis for OBSTETRICS (Ante and Post-natal):

- Pharmacological thromboprophylaxis should be avoided, discontinued or postponed in women at risk of bleeding after careful consideration of the balance of risks of bleeding and thrombosis.
- LMWH is safe and easy to use postpartum and has the advantage of not requiring monitoring.
- For those women receiving LMWH antenatally (and therefore for 6 weeks postpartum) or for those requiring 10 days' postpartum thromboprophylaxis, it is the agent of choice.
- Experience of LMWH in the puerperium reports no problems during breastfeeding

Category	Supportive Care	Pharmacotherapy	Precautions
• **Low Risk**	- Early mobilization & avoid dehydration	- No thromboprophylaxis required	
• **Moderate Risk**	- Encourage ambulation - Intermittent pneumatic compression or Graduated compression stockings	The recommendation is the use of **routine** thromboprophylaxis with either: **a. Enoxaparin** SC once daily according to **current** weight as the following: **Weight** — **Enoxaparin** < 50 kg — ❑20 mg daily 50–90 kg — ❑40 mg daily 91–130 kg — ❑60 mg daily 131–170 kg — ❑80 mg daily > 170 kg — ❑0.6 mg/kg/ day **OR** **b. Unfractionated Heparin** 5000 Units SC BID or TID Antenatal prophylaxis from 28 weeks in pregnancy.	
• **High Risk**	- Encourage ambulation - Intermittent pneumatic compression or Graduated compression stockings	The recommendation is the use of **routine** thromboprophylaxis with either: **a. Enoxaparin** SC once daily according to **current** weight as the following: **Weight** — **Enoxaparin** < 50 kg — ❑20 mg daily 50–90 kg — ❑40 mg daily 91–130 kg — ❑60 mg daily 131–170 kg — ❑80 mg daily > 170 kg — ❑0.6 mg/kg/ day **OR** **b. Unfractionated Heparin** 5000 Units SC BID Antenatal prophylaxis from first trimester.	

Medication Related Information				
Medication	Contraindication	Major Drug Interactions	Required dose adjustment	Pregnancy
Unfractionated Heparin (UFH)	- Severe thrombocytopenia - Uncontrolled active bleeding; except when due to DIC	Apixaban Dabigatran Endoxaban Mifepristone Rivaroxaban Streptokinase Urokinase	**Renal impairment**: No specific recommendations are available **Hepatic impairment**: No specific recommendations are available **Geriatric**: No adjustment necessary; however, a higher incidence of bleeding has been reported in patients over 60 years of age, especially women, therefore lower doses of	Fetal risk cannot be ruled out

Medication Related Information				
Medication	Contraindication	Major Drug Interactions	Required dose adjustment	Pregnancy
			heparin may be indicated in these patients.	
Enoxaparin	- Active major bleeding - History of immune-mediated heparin-induced thrombocytopenia within the past 100 days or in presence of circulating antibodies - Hypersensitivity to benzyl alcohol (present in multi-dose formulation) - Hypersensitivity to enoxaparin sodium, heparin, or pork products	Apixaban Dabigatran Endoxaban Mifepristone Rivaroxaban Urokinase	**Renal impairment** (CrCl 30 to 80 mL/min): No adjustment necessary. **Renal impairment** (CrCl less than 30 mL/min): Unfractionated heparin recommended instead of low-molecular-weight heparin (LMWH); if LMWH is used, reduce usual recommended dose by 50%. **Renal impairment** (CrCl less than 30 mL/min) in prevention of DVT following abdominal surgery: 30 mg subQ once daily. **Renal impairment** (CrCl less than 30 mL/min) in prevention of DVT following hip or knee replacement surgery: 30 mg subQ once daily. **Renal impairment** (CrCl less than 30 mL/min) in prevention of DVT in medical patients during acute illness: 30 mg subQ once daily.	Fetal risk cannot be ruled out
Warfarin	- Blood dyscrasias - Cerebral aneurysms - CNS hemorrhage - Dissecting aorta - Eclampsia, preeclampsia, threatened abortion - Gastrointestinal, genitourinary, or respiratory tract ulcerations or overt bleeding - Hemorrhagic tendencies - Hypersensitivity to warfarin or any component of the product - Major regional or lumbar block anesthesia - Malignant hypertension - Pericarditis and pericardial effusion - Pregnancy, except in pregnant women with mechanical heart valves, who are at high risk of thromboembolism - Recent or potential surgery of central nervous system or eye - Recent or potential traumatic surgery resulting in large open surface Spinal puncture and other procedures with potential for uncontrollable bleeding Unsupervised and potentially noncompliant patients	Tamoxifen Streptokinase Urokinase Allopurinol Amiodarone Barbiturates Cholestyramine resin	**Renal impairment:** No adjustment necessary; monitor INR more frequently in patients with compromised renal function to maintain INR within the therapeutic range **Geriatric:** Consider using lower initial and maintenance dosage **Pregnancy, mechanical valve:** Warfarin to goal INR plus aspirin 75 mg to 100 mg/day during second and third trimesters; during first trimester, warfarin may be continued in patients who can achieve therapeutic INR with doses of 5 mg/day or less. Frequent monitoring required. Discontinue warfarin and initiate continuous infusion unfractionated heparin prior to planned vaginal delivery (guideline dosing)	Contraindicated
Fondaparinux	- Contraindicated in patients with a CrCl < 30 mL/min/1.73 m2 Body weight less than 50 kg in VTE prophylaxis - Active major bleeding	Apixaban Dabigatran Endoxaban Mifepristone Rivaroxaban	**Renal impairment (CrCl 30 to 50 mL/min):** Use with caution; may cause prolonged anticoagulation. **Hepatic impairment (mild to moderate):** No dosage adjustment required; however, observe closely for signs/symptoms of bleeding.	Fetal risk cannot be ruled out

Medication Related Information				
Medication	Contraindication	Major Drug Interactions	Required dose adjustment	Pregnancy
	- Thrombocytopenia associated with positive in vitro test for antiplatelet antibody in the presence of fondaparinux sodium - History of serious hypersensitivity reaction (eg, angioedema, anaphylactoid or anaphylactic reactions)		**Geriatric:** Pay particular attention to dosing directions and concomitant medications (especially anti-platelet medication). **Hemodiafiltration in patients with heparin-induced thrombocytopenia:** Initiate at 0.03 mg/kg post dialysis body weight, administered via the efferent line of the dialyzer; titrate in increments of 0.01 mg/kg post dialysis body weight based on post dialysis anti-Xa activity.	
Apixaban	- Contraindicated in patients with a CrCl < 25 mL/min/1.73 m2 SCr > 2.5 mg/dL - Active pathological bleeding - Severe hypersensitivity (eg, anaphylactic reactions) to apixaban	Rifampin, phenytoin, carbamazepine, St. John's wort) protease inhibitors, itraconazole, ketoconazole	50% dose reduction if receiving 5 or 10 mg twice daily with strong CYP3A4 and P-gp inhibitor (e.g., protease inhibitors, itraconazole, ketoconazole, conivaptan)	Fetal risk cannot be ruled out

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