University of Colorado Hospital
UNIVERSITY OF COLORADO HEALTH

Anticoagulation Pocket Cards

*Adapted from the ACCP Evidence-Based Clinical Practice Guidelines 9th Edition)***

Stewardship of Anticoagulant/Anti-thrombotic Medications

The following individuals/services are available to assist with thrombosis and/or bleeding issues within the designated times:

- The *Inpatient Anticoagulation – Thrombosis Management Service* is available from 7:00 am – 5:00 pm Monday-Friday, and 7:00 am to 2:30 pm weekends and holidays
- The *ACP Outpatient Anticoagulation Clinic* is available from 8 am to 5 pm Monday-Friday
- The hematology consult service is available 24 hours a day, 7 days a week by paging the hematology fellow on-call. Please consult the On-Call Schedule on the UCH HUB mainpage to identify the hematology fellow on-call.

Outpatient ACP Anticoagulation Clinic

Phone: 720-848-0577
Pager: 303-266-1069

Inpatient Anticoagulation-Thrombosis Management Service

Pager 303-266-0791

For patients established in one of these clinics, use contact information below:

UM- Lowry Anticoagulation Clinic ✓ Phone: 720-848-9521 ✓ Fax: 720-848-7143	UFM Boulder Anticoagulation Clinic ✓ Phone: 720-848-9200 ✓ Fax: 720-848-9202
Cardiology Anticoagulation Clinic ✓ Phone: 720-848-6533 ✓ Fax: 720-848-0469	CHF Anticoagulation Clinic ✓ Phone: 720-848-5300 ✓ Fax: 720-848-0476

**The Ninth ACCP Conference on Antithrombotic and Thrombolytic Therapy: Evidence-Based Guidelines. Chest 2012; 141:Number 2 (suppl):7S-801S

Transition of Care

If patient with clinically stable PE (Table 1) or documented DVT and lacks early discharge exclusion criteria (Table 2) then discharge patient through the VTE pathway (*see VTE discharge order set*)

Table 1
Pulmonary Embolism Severity Index

	PESI Score
Age (in years)	____
Male sex	+ 10
Current Cancer	+ 30
CHF (heart failure)	+ 10
Chronic Lung Disease	+ 10
Pulse > 110 / min	+ 20
Systolic BP < 100 mmHg	+ 30
RR > 30 / min	+ 20
Temp < 36° C	+ 20
Acute Altered LOC*	+ 60
O2 Sat < 90% **	+ 20

TOTAL SCORE = _____

> 85 = Not clinically stable for discharge (Class III, IV or V)

* defined as disorientation, lethargy, stupor or coma

** with or without supplemental oxygen

Table 2
Early Discharge Exclusion Criteria*

- Age < 18 yrs
- Pregnancy
- History of HIT (Heparin Induced Thrombocytopenia) or Heparin allergy
- Active clinically relevant bleeding
- Recent (< 2 weeks) surgery
- Recent (< 4 weeks) neurosurgery
- CrCl < 30 ml / min
- Other medical reason for hospital admission/stay
- PESI > 85 (see Table 1 for PE)
- Hypoxic and unable to get home oxygen
- Extension of acute VTE on anticoagulation therapy
- Unable or unwilling to administer LMWH at home and home health not available
- Unwilling or unable to follow-up as outpatient

If weight > 150 kg consult the Anticoagulation Management Service

** Early Discharge: Prior to minimum 5 day overlap of injectable anti-thrombin agent & warfarin*

- Patients chronically on warfarin should have follow up to established provider within 7 days.
- Patients newly started on warfarin should have follow up within 3 days.
- For patients on Medicine/Hospitalist Service, schedule appointment with the Outpatient Hematology and Thrombosis Clinic.

Physician to write prescription for injectables to cover completion of therapy; the minimum duration of overlap with injectable anti-thrombotic agent and warfarin is 5 days, regardless of the INR. After 5 days, the injectable anti-thrombotic agent should be discontinued *only* when the patient's INR is > 2 for 2 consecutive days. A minimum of 7 days of therapy for the injectable anticoagulant should be provided on the discharge prescription.

Management of Anticoagulant Related Bleeding – Anticoagulant Reversal

Decision Support and Consensus Guidelines – Anticoagulation Subcommittee

Key Points

- ***Most patients with excess anticoagulation and/or bleeding can be managed with supportive measures and withholding further anticoagulation***
- ***The following recommendations are based on low-level evidence and are intended to reflect the suggestions of the Anticoagulant Subcommittee. Decisions on the course of management may vary from patient to patient***
- ***Procoagulants are KNOWN to be Thrombogenic***
  - ***Providers are encouraged to exercise caution when considering procoagulant use in patients at high risk for thrombosis***
- ***For more information contact the Inpatient Anticoagulation-Thrombosis Management Service – Pager 303-266-0791, or the hematology fellow on-call***

Patients experiencing bleeding that requires management, but who are not currently receiving anticoagulation are referred to the following policies/guidelines for assistance as appropriate depending on the patient scenario:

- ***Massive Transfusion Protocol***
- ***UCH Pharmacy Department Guideline for recombinant Factor VIIa***
- ***Procurement and Dispensing of Clotting Factor Concentrates***

Definitions

Non-urgent:
Reversal is elective (procedures > 7 days away)

Urgent, without bleeding:
Reversal needed within hours

Urgent, with bleeding:
Emergency reversal

General Measures

- Hold further doses of anticoagulant, consider reversal/antidote
- Supportive treatment
  - Volume resuscitation
  - Inotropes as needed
- Transfusion
  - Red cells, platelets, FFP as needed
- Local or Surgical Hemostatic measures
- Investigate bleeding source

Available Reversal Agents

Agent	Dose	Comments
Vitamin K	1-10 mg IV/PO, not SQ or IM	• Infusion reactions rare; administer over 20-30 min • Takes 6 (IV) to 24 (PO) hours to reverse warfarin • Large doses can cause warfarin resistance on resumption (10-15 mg)
Protamine sulfate	12.5-50 mg IV	• Full reversal of unfractionated heparin • 60%-80% reversal of LMWH • No reversal of fondaparinux
Platelets	1 apheresis unit 5-8 whole blood units	• Raise platelet count by 30 x 10^9/L • Goal platelet count 50 - 100 x 10^9/L (indication dependent)
Frozen plasma (FFP)	10-30 mL/kg (1 unit = ~250ml)	• Replaces all coagulation factors, but cannot fully correct • Hemostasis usually requires factor levels~30%, Factor IX may only reach 20% • May need repeat dose after 6 hours • Large volume, takes hours to thaw and infuse
Prothrombin complex concentrates (PCC)	25-50 units/kg IV (25 units/kg preferred initial dose)	• Rapid INR correction in warfarin patients • Small volume infusion over 10-30 minutes • Risk of thrombosis 1.4% • Contraindicated with history of HIT • May need repeat dose after 12 hours • Consider adding FFP if 3-factor PCC used
Recombinant factor VIIa (rFVIIa)	15-90 units/kg (lower doses, such as 20 ug/kg, studied for AC reversal)	• Rapid infusion of small volume • Rapid INR correction of warfarin, but may not correct bleeding because only restores FVIIa • Risk of thrombosis 5-10% • May need repeat dose after 2 hours

Management of Anticoagulant Related Bleeding – Anticoagulant Reversal

Decision Support and Consensus Guidelines – Anticoagulation Subcommittee

Patient In Need Of Anticoagulant Reversal

Warfarin

Non urgent	Urgent (no bleeding)	Urgent (bleeding)
See UCH Anticoagulant Guidelines for Peri-operative management	- If procedure can be delayed 6-24 hours, vitamin K 5-10 mg PO/IV; otherwise - FFP or PCC prior to procedure. Repeat in 6-12 hours if INR high - Vitamin K 5-10 mg PO/IV if sustained reversal is desired	- General measures plus - Vitamin K 5-10 mg IV, repeat every 12 hours as needed plus - FFP 15-30 ml/kg *or* - PCC (Profilnine) 25 units/kg, repeat every 12 hours as needed

Unfractionated Heparin

Non urgent	Urgent (no bleeding)	Urgent (bleeding)
Hold 4 hours prior to procedure	- Consider Protamine Sulfate if delay not possible for high bleed risk procedure	- General measures plus - Protamine sulfate 1 mg for every 100 units heparin given in past 2-3 hours (max dose 50 mg)

LMWH (enoxaparin/dalteparin)

Non urgent	Urgent (no bleeding)	Urgent (bleeding)
See UCH Anticoagulant Guidelines for Peri-operative management	- Wait 12-24 hours if possible - Consider Protamine Sulfate if delay not possible for high bleed risk procedure	- General measures plus - Protamine sulfate 1 mg for every 1mg enoxaparin, or 100 units dalteparin, in previous 8 hours (max dose 50 mg) - Consider Factor VIIa 20 units/kg, repeat every 2 hours as needed

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Fondaparinux

Non urgent	Urgent (no bleeding)	Urgent (bleeding)
See UCH Anticoagulant Guidelines for Peri-operative management	- **Wait 12-24 hours if possible**	- **General measures plus** - **Consider Factor VIIa 20 units/kg, repeat every 2 hours as needed**

Dabigatran or Rivaroxaban

Note: Check aPTT (dabigatran) or Prothrombin Time (rivaroxaban). If tests are completely normal, unlikely drug is contributing to bleed and supportive measures for bleeding should be primary treatment. If elevated, even to a small degree, likely drug is present and contributing to bleed and reversal can be considered

Non urgent	Urgent (no bleeding)	Urgent (bleeding)
See Below – perioperative Management Guidelines	- See UCH Anticoagulant Guidelines for Peri-operative management	- General measures plus maintenance of adequate diuresis - Activated Charcoal (if within 2-3 hours of overdose) plus - Consider Dialysis (dabigatran only) plus - PCC (Profiline) 25 units/kg, repeat every 12 hours as needed (preferred for rivaroxaban). May consider adding FFP. or - Factor VIIa 20 units/kg, repeat every 2 hours as needed

Dabigatran

Estimated Renal Function	Half-life (hours)	Time of Discontinuation after last dose of dabigatran prior to an invasive procedure	
		Standard bleeding risk	Elevated bleeding risk
> 80 ml/min	**13**	**24 hours**	**2-4 days**
50-80 ml/min	**15**	**24 hours**	**2-4 days**
30-50 ml/min	**18**	**48 hours**	**4 days**
< 30 ml/min	**27**	**2-5 days**	**> 5 days**

Rivaroxaban

Estimated Renal Function	Half-life (hours)	Time of Discontinuation after last dose of rivaroxaban prior to an invasive procedure	
		Standard bleeding risk	Elevated bleeding risk
> 50 ml/min	**8**	**24 hours**	**48 hours**
30-50 ml/min	**9-10**	**48 hours**	**3-4 days**

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Warfarin Initiation and Monitoring

- Baseline INR within prior 48 hrs required for initiation of warfarin (Joint Commission Requirement)
- Most patients are started on 5mg per day. Patients that may be started on 2.5 mg per day include:

Liver dysfunction	Patients taking interacting drugs
Impaired nutrition	Thyrotoxicosis
Heart failure	Very elderly

- PT/INR should be checked daily when initiating warfarin therapy
- During initial titration, warfarin dosage adjustments should be made in small increments of no more than 15 – 20%
- Subsequent INR is checked every 3 to 7 days until warfarin dose is stabilized.

Warfarin Initiation Dosing Nomogram

Note – this nomogram is meant as a general guide. Acute care patients may have multiple factors (changes in diet or concomitant disease states, drug interactions, etc.) which may prompt dosing decisions that deviate from this protocol. Please contact the Inpatient or Outpatient Anticoagulation Management Services for help or more information

Day	INR	Dose
1		5mg
2	< 1.5 1.5 - 1.9 2.0 - 2.5 > 2.5	5 mg 2.5 mg 1 – 2.5 mg Hold
3	< 1.5 1.5 - 1.9 2.0 - 3 > 3	5 - 10 mg 2.5 - 5 mg 0 – 2.5 mg Hold
4	< 1.5 1.5-1.9 2-3 > 3	10 mg 5 – 7.5 mg 0 – 5 mg Hold
5	< 1.5 1.5-1.9 2-3 > 3	10 mg 7.5 - 10 mg 0 – 5 mg Hold
6	< 1.5 1.5-1.9 2-3 > 3	7.5 – 12.5 mg 5 – 10 mg 0 – 7.5 mg Hold

Cautions with Anticoagulation Therapy

Active bleeding	Excessive alcohol intake
Active peptic ulcer disease	Uncontrolled HTN
Thrombocytopenia	Hepatic dysfunction
Recent hemorrhagic stroke	History of falls
Dementia or severe cognitive impairment	Daily use of steroids/NSAIDS
Planned invasive procedure/ surgery	

Warfarin Initiation and Monitoring

Optimal Therapeutic Range and Duration of Warfarin		
DVT/PE	Goal INR	Duration:
• Primary event DVT/Acute PE, transient reversible risk factor	2.0-3.0	3 months
• Primary idiopathic proximal DVT/acute PE	2.0-3.0	3 months - Long term
• Primary idiopathic distal DVT	2.0-3.0	3 months
•Two or more DVT/PE (low bleeding risk)	2.0-3.0	Long term
•Two or more DVT/PE (lhigh bleeding risk)	2.0-3.0	3 months
• Antiphospholipid Antibody Syndrome	2.0-3.0	Long term
° no additional risk factor or lack of response to therapy	2.0-3.0	Long term
° Add'l risk factor or recurrent DVT/PE with therapeutic INR	2.5-3.5	Long term
• DVT/PE and cancer	LMWH x3-6mo then warfarin (2.0-3.0) or LMWH	Long term (or until cancer resolves)
• Superficial vein thrombosis	LMWH/Heparin or warfarin 2.0-3.0	4 weeks
Atrial Fibrillation		
• AF (see table below for risk factors)		
° no risk factors	No therapy or aspirin 75-325 mg/day	Long term
° ≥ 1 risk factor	2.0-3.0	Long term
• AF + mitral valve stenosis	2.0-3.0	Long term
• AF + prosthetic heart valves	Depends on valve type and position, see UCH anticoagulation guideline	

Consult the UCH Anticoagulation Therapy Guideline for goal INR values for other indications and references.

Stroke Risk Factors
Prior Stroke/TIA (2 points)
Age ≥75 (1 point)
History of HTN (1 point)
Diabetes (1 point)
Heart failure(1 point)

Meds ↑ warfarin effect	**Meds ↓ warfarin effect**
Amiodarone	Sucralfate
Fluoroquinolones	Carbamazepine
Fluconazole	Cholestyramine
Isoniazid	Dicloxacillin
Propafenone	Mesalamine
Omeprazole	Nafcillin
Metronidazole	Phenytoin
Levothyroxine	Rifampin
TMP/SMX	

↓ Warfarin Requirements	↑ Warfarin Requirements
Hyperthyroidism	High Vit K Diet
Fat malabsorbtion	Hypothyroidism
Age >65 years	Nephrotic syndrome
Diarrhea/steatorrhea	Tobacco
Cancer	Chronic EtOH abuse
High fever	
Acute alcohol use	
Stress	

Not an exclusive list. Review the literature for additional interactions.

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Heparin Continuous Infusion

*For patient specific questions on dosing unfractionated heparin, please page the Anticoagulation – Thrombosis Management Service (pager 303-266-0791)

Unfractionated Heparin

- Weight based dosing more rapidly achieves therapeutic and stable anticoagulation and is therefore the preferred dosing strategy
- Avoid bolus doses in the following patient populations:
    - Stroke
    - Neurosurgery
    - Patients who have received thrombolytic therapy
    - Patients post Percutaneous Coronary Intervention (PCI)

Weight-based dosing for Unfractionated Heparin

- Patients receiving ACS dosing (option 2) should have their ***initial*** doses capped at 5,000 unit bolus and 1,000 unit/hr initial infusion rate
    - In patients >80 kg calculate a corrected initial bolus and infusion rate dosing
        - Bolus: 5,000 units ÷ pt weight = corrected bolus dose (units/kg)
        - Infusion: 1,000 units ÷ pt weight = corrected infusion rate (units/kg/hr)
    - ACS infusion doses may be titrated > 1,000 units/hr based on aPTT
- There is no maximum initial dose in patients with VTE, regardless of weight

Unfractionated Heparin Order Form Information

- The order form is mandatory for all continuous infusion heparin orders that are being titrated to a therapeutic aPTT range, prescribers must choose:
    - Initial bolus dose (or no bolus)
    - Initial infusion dose
    - Goal aPTT range
    - Monitoring and titration strategy
- The goal aPTT ranges are designed per supporting data for each therapeutic indication:
    - The "Standard Dose Heparin Therapy" for DVT/PE
        - Goal correlates with therapeutic heparin levels (equivalent to 0.3-0.7 IU/mL by factor Xa inhibition).
    - The "Lower Dose Heparin Therapy" for ACS/MI and other indications
        - Goal represents an aPTT value ~ 1.5-2.5 times the patient's baseline aPTT value or upper limit of the UCH lab baseline aPTT standard
- Some indications for heparin therapy are not represented by these 2 dosing strategies
    - Prescribers may choose to write their own dose, aPTT goal range and titration strategy
    - If this method is utilized, a similar aPTT increment strategy should be used for titrating doses
        - The titration algorithm is not intended for adjusting heparin doses < 400 units/hour

Heparin Nomogram

(Please consult most recent heparin continuous order set for current recommended goal aPTT range)

☑ Check aPTT at baseline (If baseline aPTT value abnormal, contact house officer, consider consulting hematology)
☑ Check aPTT every 6 hours after heparin initiation and after any dosing change; change to every morning if ≥ 2 consecutive therapeutic aPTTs

Treatment of DVT/PE
Initial bolus (optional)= 80 units/kg
Initial infusion rate= 18 units/kg/hr

Standard Dose Heparin Therapy (DVT/PE Treatment) Goal aPTT Range is equivalent to Heparin Level of 0.3-0.7 units/mL		
☐ aPTT (seconds)	☐ aPTT (seconds)	Dose Adjustment (Max Dosing Weight = 100 kg)
< 40	< _____	Bolus 40 units / kg, Increase infusion by 3 units / kg / hr
40 – 54	____ - ____	Bolus 20 units / kg, Increase infusion by 2 units / kg / hr
55 – 71	____ - ____	Increase infusion by 1 unit / kg / hr
72 – 93	____ - ____	Goal Range. No Change
94 – 109	____ - ____	Decrease infusion by 1 unit / kg / hr
110 – 125	____ - ____	Hold infusion for 0.5 hour, Decrease infusion by 2 units / kg / hr
126 - 200	____ - ____	Hold infusion for 1 hour, Decrease infusion by 3 units / kg / hr
> 200	> _____	Send ***stat*** aPTT, contact MD, HOLD infusion until aPTT < 200 (check q4h), then Decrease infusion by 4 units/kg/hr

Treatment of ACS/MI, arterial thrombosis, A fib, other
If patient weight < 80 kg:
Initial bolus (optional)= 60 units/kg, Initial infusion rate: 12 units/kg/hr
If patient weight ≥ 80 kg: see order set for calculation

Lower Dose Heparin Therapy (ACS/MI, Stroke, Afib, Other) Goal aPTT Range is equivalent to 1.5-2.5 times baseline aPTT		
☐ aPTT (seconds)	☐ aPTT (seconds)	Dose Adjustment (Max Dosing Weight = 80 kg)
< 30	< _____	Increase infusion by 3 units/kg/hr
30 – 39	____ - ____	Increase infusion by 2 units/kg/hr
40 – 49	____ - ____	Increase infusion by 1 unit/kg/hr
50 – 80	____ - ____	Goal Range. No Change
81 – 90	____ - ____	Decrease infusion by 1 unit/kg/hr
91 – 100	____ - ____	Hold infusion for 0.5 hour, Decrease infusion by 2 units/kg/hr
101 – 200	> _____	Hold infusion for 1 hour, Decrease infusion by 3 units/kg/hr
> 200	> _____	Send ***stat*** aPTT, contact MD, HOLD infusion until aPTT < 200 (check q6h), then Decrease infusion

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Heparin Induced Thrombocytopenia (HIT)

- HIT: Immune mediated thrombocytopenia characterized by formation of antibodies to heparin-platelet activating factor 4 complex
- Immune mediated HIT typically occurs 5-10 days after starting heparin (can occur w/in 24 hrs if pt received heparin in last 100 days)
- ***Pre-test Probability Scoring (using the 4T score, see below) is a crucial step in the diagnosis and management of HIT***
- 4T Score: Add the corresponding points for the four "T" categories to obtain a total score for the patient (Maximum score = 8):
  6-8 High Probability of HIT 4-5 Intermediate Probability of HIT < 4 Low Probability of HIT
- ***Patients with a low probability score have a extremely low incidence of HIT (1%) and should continue to receive heparin***
- Patients with an intermediate or high probability score and suspected of HIT, should have a HIT antibody sent and be treated as appropriate.

Clinical Diagnosis and Pretest Probability Score			
Points	2	1	0
Thrombocytopenia	**> 50% platelet fall AND nadir > 20 AND no surgery within preceding 3 days**	**- > 50% fall BUT surgery within 3 days OR - any combination of platelet fall and nadir not meeting criteria for Score 2 or Score 0**	**- < 30% platelet fall - any platelet fall with nadir < 10**
Timing of platelet count fall consistent with HIT	**- platelet fall day 5-10 after heparin start - platelet fall within 1 day of heparin start AND exposure to heparin within 5-30 days**	**- consistent with platelet fall days 5-10 but unclear - platelet fall within 1 day of heparin start AND exposure to heparin within 31-100 days - platelet fall after day 10**	**Platelet fall < day 4 without exposure to heparin in past 100 days**
Thrombosis or other sequelae	**- confirmed new thrombosis - Skin necrosis at injection site - anaphylaxis to heparin bolus - adrenal hemmorrhage**	**- recurrent VTE in pts on therapeutic anticoagulant - suspected thrombosis (awaiting confirmation) - erythematous skin lesions at heparin injection site**	**Thrombosis suspected**
OTher cause for thrombocytopenia	**No alternative explanation available**	**<u>Possible other cause is evident</u> - sepsis without proven microbial source - thrombosytopenia associated with ventilator initiation - other**	**<u>Possible other cause is present</u> - within 72 hours of surgery - confirmed bacteremia/fungemia - chemo or radiation within 20 days - DIC form non-HIT cause - posttransfusion purpura - platelet count < 20 and other drug cause**

Tests:

- Heparin associated platelet antibodies (HAPA) - A negative HAPA test does not rule out the diagnosis of HIT with complete certainty (sensitivity > 90%), nor is a positive test diagnostic (specificity 50-90%)
- Serotonin release assay – Utilizes radiolabled 14C-Serotonin. When combined with HAPA, the test has a sensitivity and specificity of 100% and 97%, respectively. Lab outside UCH conducts test - may take up to 2 weeks to receive results.

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Treatment of HIT

- ***Discontinue all sources of heparin including flushes, heparin coated catheters, and enoxaparin or dalteparin. Do not administer platelet transfusions.***
- ***Oral anticoagulation (warfarin, dabigatran or rivaroxaban) should not be initiated until the patient's platelet count returns to baseline after treatment with a direct thrombin inhibitor. If the patient is currently on warfarin, immediate reversal with vitamin K is recommended.***
- Choose argatroban or bivalirudin therapy and initiate therapy at below recommended dosing. Begin infusion immediately, without waiting for levels of prior anticoagulant to return to baseline.

Bivalirudin (Angiomax®)	Argatroban
• Preferred in patients with hepatic insufficiency • Dosage adjustment for CrCl less than 60 mL/min ✓ 0.15 mg/kg/hr IV for CrCl > 60 mL/min ✓ 0.075 mg/kg/hr IV forCrCl 45-60 mL/min ✓ 0.05 mg/kg/hr IV for CrCl 30-44 mL/min ✓ 0.025 mg/kg/hr IV for CrCl less than 30 mL/min or renal replacement therapy	• Preferred in patients with renal insufficiency, unless hepatic insufficiency is present • Dosage adjustment for Child Pugh B or C, or T.Bili greater than 2 mg/dL ✓ 1.5 mcg/kg/min IV in normal hepatic function ✓ 0.5 mcg/kg/min IV in mod hepatic insuff (Child Pugh B, T.Bili >2 mg/dL) ✓ 0.25 mcg/kg/min IV in severe hepatic insuff (Child Pugh C)

(See Direct Thrombin Inhibitor order set for titration nomogram)

- ☑ Check aPTT at baseline, 2 hours after initiation, every 4 hours after any dosing change, then every morning after 2 consecutive aPTTs in goal.
- ☑ UCH goal aPTT for Argatroban and Bivalirudin is 50-80 seconds (Approximately 1.5-2.5 times baseline aPTT). Standard aPTT goal and dosage adjustment will be utilized unless prescriber fills out "Patient Specific aPTT goal"
  (Prescribers for neurosurgery patients and patients receiving thrombolytic therapy should always utilize patient specific aPTT ranges)

Subcutaneous alternative to argatroban or bivalirudin therapy for patients with history of HIT *(not for active HIT or HITTS)*

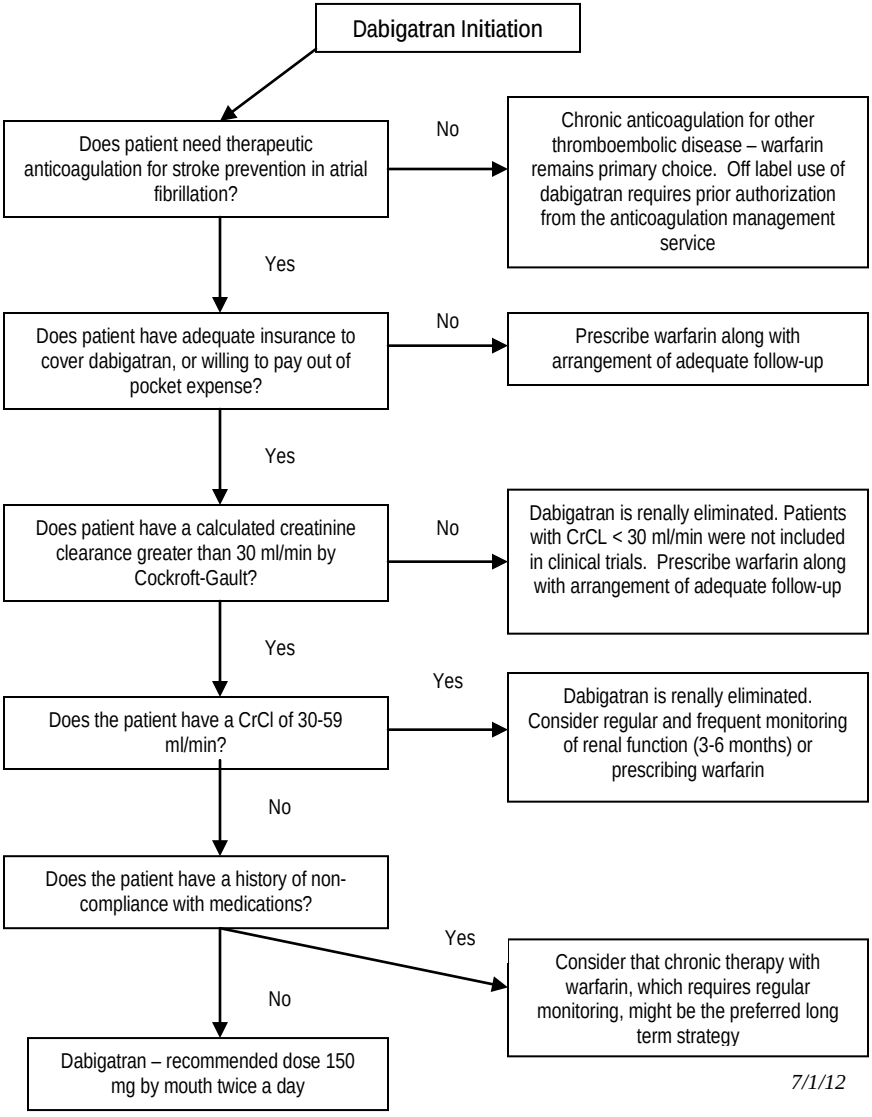
- Prophylaxis: Fondaparinux 2.5 mg subcutaneous once daily
- Treatment: Fondaparinux – Dose based upon weight

<50kg = 5mg subcutaneous daily 50 -100kg= 7.5 mg subcutaneous daily >100kg= 10 mg subcutaneous daily

- Fondaparinux is renally eliminated. Avoid use in patients with CrCl less than 30 mL/min

Dabigatran Etexilate (Pradaxa®)

- Dabigatran is an orally administered direct thrombin inhibitor. Because thrombin enables the conversion of fibrinogen into fibrin during the coagulation cascade, dabigatran inhibition prevents the development of a thrombus.
- Dabigatran is FDA approved for long term treatment of patients with non-valvular atrial fibrillation to reduce the risk of stroke and systemic embolism
- The recommended dose of dabigatran is 150 mg twice daily
- Dabigatran is renally eliminated; patients should have a CrCl >30 mL/min to receive dabigatran
- The risk of major bleeding with dabigatran anticoagulation is similar to that of warfarin
- P-gp inducers (e.g., rifampin) reduce exposure to dabigatran and should generally be avoided



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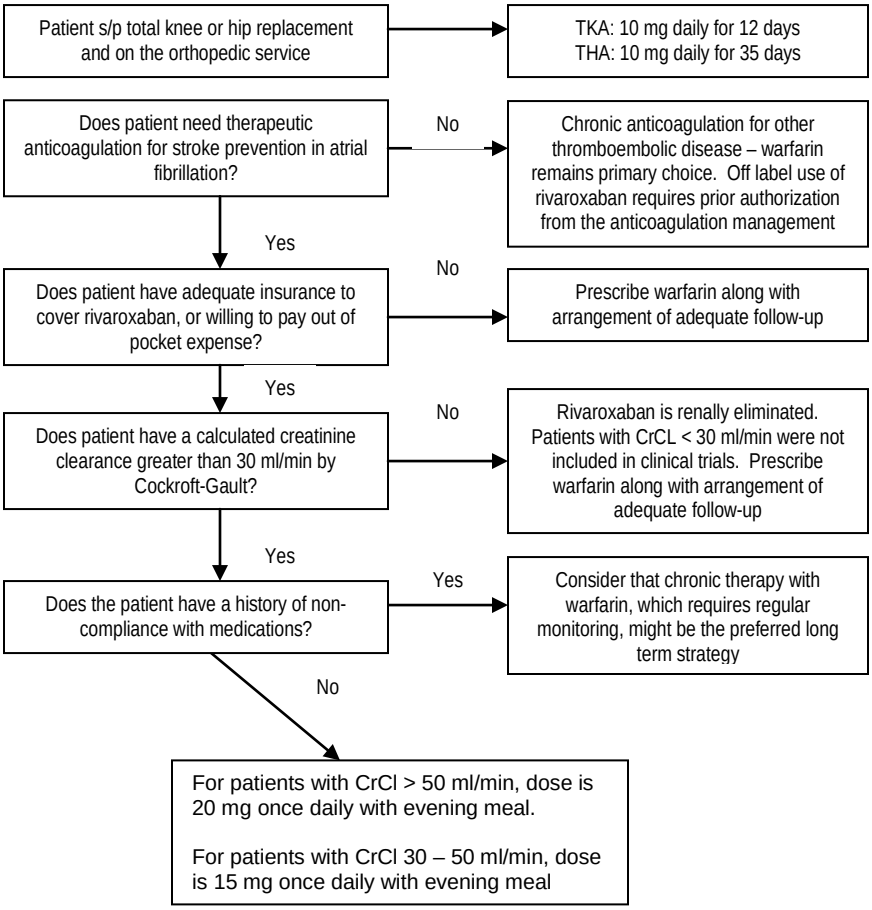
Rivaroxaban (Xarelto®)

- Rivaroxaban is an orally administered direct factor Xa inhibitor.
- Rivaroxaban is renally eliminated; patients should have a CrCl >30 mL/min to receive rivaroxaban. Avoid use in patients with moderate (Child-Pugh B) or severe (Child-Pugh C) hepatic impairment
- FDA approved for indications and dosing:
    - Prophylaxis for DVT and PE for patients with knee and hip replacement surgery. Dose is 10 mg daily, with or without food
    - Prevention of stroke in patients with nonvalvular atrial fibrillation. For patients with CrCl > 50 ml/min, dose is 20 mg once daily with evening meal. For patients with CrCl 30 – 50 ml/min, dose is 15 mg once daily with evening meal
- The risk of major bleeding with rivaroxaban anticoagulation is similar to that of warfarin
- Rivaroxaban is a substrate of CYP3A4/5, CYP2J2, and the P-gp transporter. Avoid concomitant use with strong inhibitors (e.g. itraconazole, ritonavir, conivaptan) or inducers (e.g. carbamazepine, phenytoin, rifampin, St. John's wort) of these pathways



LMWH Therapeutic Interchange Dosing Card

University of Colorado Hospital Dalteparin-Enoxaparin Dosing Chart		
VTE Treatment	Dalteparin (Fragmin®) Preferred at UCH	Enoxaparin (Lovenox®)
All patients	200 units/kg SQ q24h (or 100 units/kg q12h) + warfarin (Use 100 units/kg SQ every 12 hours for pts > 95 kg)	1 mg/kg SQ q12h or 1.5 mg/kg SQ q24h (if inpatient) + warfarin
VTE Prophylaxis	Dalteparin (Fragmin®) Preferred at UCH	Enoxaparin (Lovenox®)
Abdominal/ General Surgery Moderate Risk for VTE	2,500 units SQ q24h begin 1-2h preop, then daily for 5-10d postop	30 mg SQ q24h (begin 2h preop)
Abdominal/ General Surgery High Risk for VTE	5,000 units SQ q24h begin evening prior to surgery, then daily for 5-10d postop	40 mg SQ q24h (begin 2h preop)
Elective Hip Arthroplasty	5,000 SQ q24h	30 mg SQ q12h (begin 12-24h postop) or 40 mg SQ q24h (begin 10-12h preop)
Elective Knee Arthroplasty	2,500 units SQ 6-8h postop, then 5000 units SQ q24h	30 mg SQ q12h (begin 12-24h postop)
Hip Fracture Surgery	5,000 units SQ q24h	30 mg SQ q12h (begin 12-24h postop)
Acutely Ill Medical Patients	5,000 units SQ q24h	40 mg SQ q24h
Patients w/active cancer (Solid tumors)	5,000 units SQq24h	30 mg SQ q12h or 40 mg SQ q24h
Neurosurgery	5,000 units SQ q24h	40 mg SQ q24h
Trauma	5,000 units SQ q24h begin within 48h of admission	30 mg SQ q12h
Unstable Angina or Non-Q-Wave MI*	120 units/kg SQ q12h x 5-8 days + 75-165 mg ASA (NTE 10,000 units q12h) DO NOT SUBSTITUTE*	1 mg/kg SQ q12h* x 2-8 days + 100-325 mg ASA PREFERRED*
"Bridge Therapy" for warfarin patients hospitalized for surgery/invasive procedures	200 units/kg SQ q24h (Use 100 units/kg SQ every 12 hours for pts > 95 kg)	1 mg/kg SQ q12h

Goal therapeutic peak anti-Xa level (drawn 4-5 hours after dose)

- Twice daily administration= 0.5-1.2 units/ml
- Once daily administration= 1.0-2.0 units/ml

NTE= not to exceed (max dose)

7/1/12

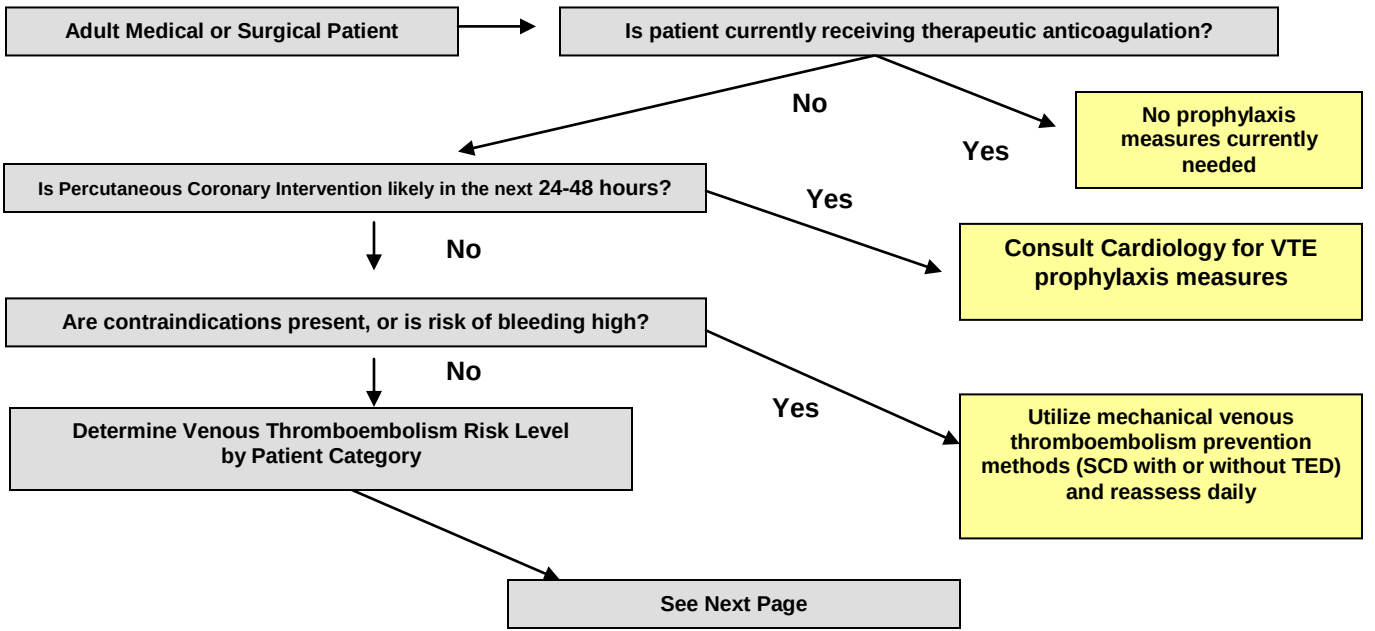
Management of anticoagulation in patients on warfarin therapy undergoing elective procedure

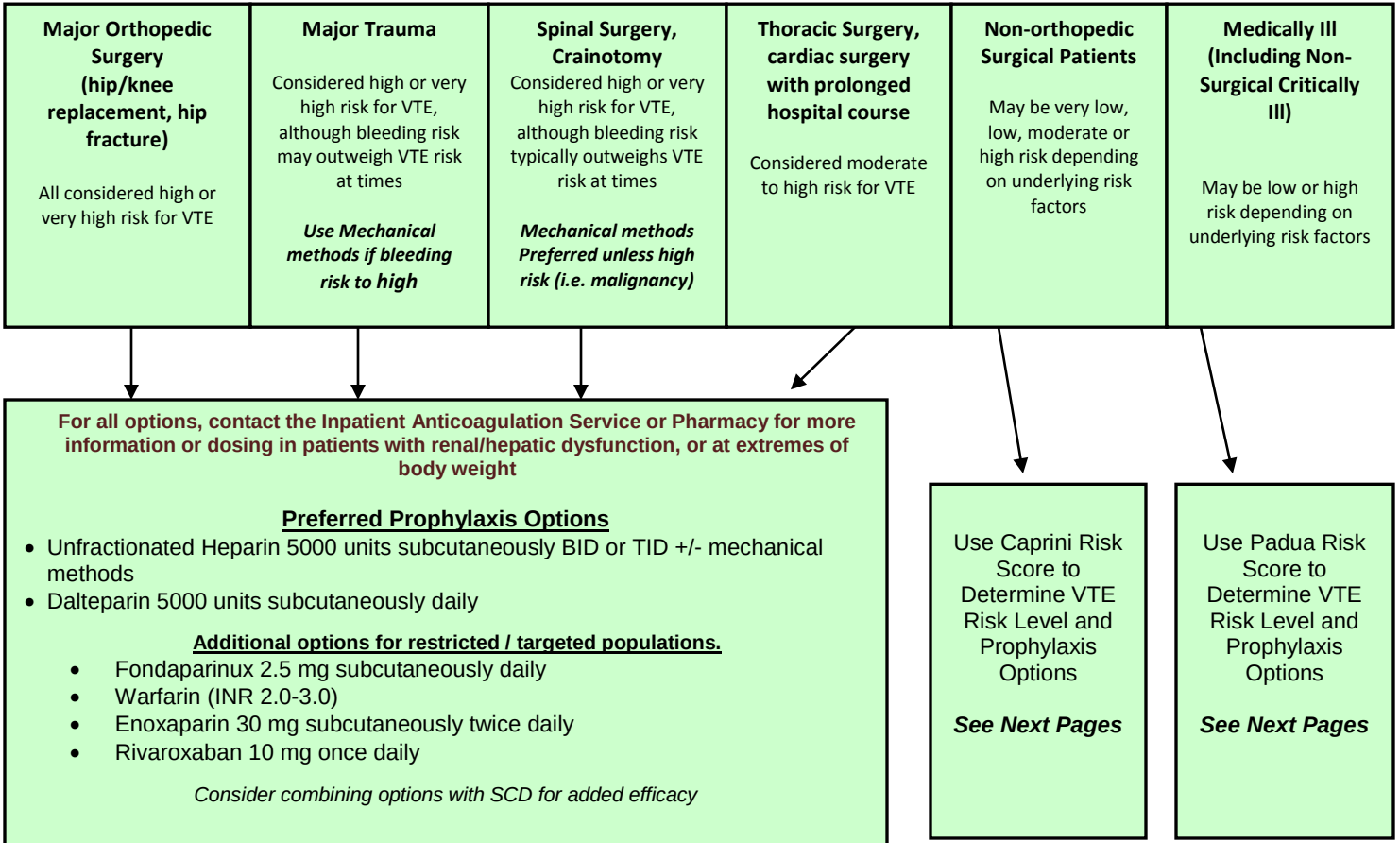
- ✓ Stop warfarin approximately 5 days prior to procedure
- ✓ If applicable, begin therapy with subcutaneous (SQ) LMWH as the INR falls (approximately 3 days pre-procedure)
- ✓ Discontinue LMWH SQ injections 24 hours before procedure. (Administer approximately ½ total daily dose for the last dose)
- ✓ Resume LMWH 24 hours and warfarin 12-24 hours post procedure when there is adequate homeostasis (based on post-procedural risk of bleeding).
- ✓ Continue both LMWH and warfarin until INR is therapeutic (approximately 5-7 days)

RISK	Examples	Dosing
HIGH	• AF with high risk of stroke (i.e., $CHADS_2$ score of 5 or 6) • AF with recent (within 3 months) stroke/TIA • Severe thrombophilic conditions (e.g., protein C , protein S or antithrombin, antiphospholipid antibodies or multiple abnormalities) • Recent VTE (within 3 months) • Mechanical valve (mitral position), older (caged-ball or tilting disc) aortic valve • Mechanical heart valve patients with recent (within 6 mo) h/o CVA/TIA	FULL DOSE LMWH: Enoxaparin 1 mg/kg/bid, or Enoxparin 1.5 mg/kg/day or dalteparin 200 nits/kg/day
MODERATE	• AF with moderate risk of stroke (i.e., $CHADS_2$ score of 3 or 4) • VTE within the past 3 to 12 months • Nonsevere thrombophilic conditions (e.g. heterozygous factor V leiden/ factor II mutation) • Recurrent VTE • Active cancer (treated within 6 mo or palliative) • Bileaflet aortic valve prosthesis and one of the following: AF, prior stroke/TIA, HTN, DM, CHF, age greater than 75	FULL DOSE LMWH or LOW DOSE LMWH: Enoxaparin 30 mg twice daily or 40 mg once daily, dalteparin 2500 or 5000 units once daily
LOW	• AF with low risk of stroke (i.e., $CHADS_2$ score of 0 to 2 and no history of stroke/TIA) • Single VTE occurred > 12 months ago and no other risk factors • Bileaflet aortic valve without AF and no other risk factors for stroke	Not suggested. If risk factors warrant bridging, use low dose LMWH

Adult Venous Thromboembolism (VTE) Prevention
Decision Support and Evidence Based Guidelines

Adapted from the ACCP Evidence-Based Clinical Practice Guidelines (9th Edition)
For more information contact the Inpatient Anticoagulation-Thrombosis Management Service – Pager 303-266-0791




Major Orthopedic Surgery (hip/knee replacement, hip fracture)
All considered high or very high risk for VTE
Major Trauma
Considered high or very high risk for VTE, although bleeding risk may outweigh VTE risk at times
Use Mechanical methods if bleeding risk to high
Spinal Surgery, Crainotomy
Considered high or very high risk for VTE, although bleeding risk typically outweighs VTE risk at times
Mechanical methods Preferred unless high risk (i.e. malignancy)
Thoracic Surgery, cardiac surgery with prolonged hospital course
Considered moderate to high risk for VTE
Non-orthopedic Surgical Patients
May be very low, low, moderate or high risk depending on underlying risk factors
Medically Ill (Including Non-Surgical Critically Ill)
May be low or high risk depending on underlying risk factors
For all options, contact the Inpatient Anticoagulation Service or Pharmacy for more information or dosing in patients with renal/hepatic dysfunction, or at extremes of body weight
Preferred Prophylaxis Options
Unfractionated Heparin 5000 units subcutaneously BID or TID +/- mechanical methods
Dalteparin 5000 units subcutaneously daily
Additional options for restricted / targeted populations.
Fondaparinux 2.5 mg subcutaneously daily
Warfarin (INR 2.0-3.0)
Enoxaparin 30 mg subcutaneously twice daily
Rivaroxaban 10 mg once daily
Consider combining options with SCD for added efficacy
Use Caprini Risk Score to Determine VTE Risk Level and Prophylaxis Options
See Next Pages
Use Padua Risk Score to Determine VTE Risk Level and Prophylaxis Options
See Next Pages

VTE Prevention in Patients Who Are Medically Ill (Including Non-Surgical Critical Care Patients)

Determine Venous Thromboembolism Risk Level by Padua Score

Risk Factor	Point Score
Active Cancer	3
Previous VTE	3
Reduced Mobility (anticipated bed rest for at least 3 days)	3
Known Thrombophilic condition	3
Recent trauma and/or surgery within last month	2
Age > 70	1
Heart and/or respiratory failure	1
Acute MI or ischemic stroke	1
Acute Infection and/or rheumatologic disorder	1
Obesity (BMI > 30)	1
Ongoing hormonal treatment	1

High Risk **Critically ill, or Padua Score = 4 points or more**	**VTE Prophylaxis Options** **For all options, contact the Inpatient Anticoagulation Service or Pharmacy for more information or dosing in patients with renal/hepatic dysfunction, or at extremes of body weight** • Unfractionated Heparin 5000 units subcutaneously every 8 or 12 hours • Dalteparin 5000 units subcutaneously daily • Mechanical Methods recommended for patients at high risk of bleeding **Additional options for restricted / targeted populations.** • Fondaparinux 2.5 mg subcutaneously daily
Low Risk **Padua Score = 3 points or less**	**No VTE prophylaxis options, either pharmacologic or mechanical, are recommended**

VTE Prevention in Non-Orthopedic Surgical Patients

Determine Venous Thromboembolism Risk Level by Caprini Risk Assessment Model

1 point	2 points	3 points	5 points
Age 41-60	Age 61-74	Age ≥ 75	Stroke (< 1 month)
Minor surgery	Arthroscopic surgery	History of VTE	Elective arthroplasty
BMI > 25 Kg/meters squared	Major open surgery (> 45 min)	Family history of VTE	Hip, pelvis or leg fracture
Swollen legs	Laproscopic surgery(> 45 min)	Factor V Leiden	Acute spinal cord injury (< 1 month)
Varicose veins	Malignancy	Prothrombin 20210A	
Pregnancy or post-partum	Confined to bed (> 72 hours)	Lupus Anticoagulant	
History of spontaneous abortion	Immobilizing plaster cast	Anti-cardiolipin Antibodies	
Oral contraceptives/hormone replacement	Central venous access	Elevated serum homocysteine	
Sepsis		Heparin-induced thrombocytopenia	
Serious lung disease including pneumonia		Other congenital or acquired thrombophilia	
Abnormal pulmonary function			
AMI			
HF			
Inflammatory Bowel Disease			

Very Low Risk Caprini Score = 0	Low Risk Caprini Score = 1-2	Moderate Risk Caprini Score = 3-4	High Risk Caprini Score ≥ 5
No specific pharmacologic or mechanical methods recommended other than early ambulation	Mechanical Methods preferred	• Unfractionated Heparin 5000 units subcutaneously every 8 or 12 hours ***or*** • Dalteparin 5000 units subcutaneously daily ***or*** • Mechanical Methods recommended for patients at high risk of bleeding	• Unfractionated Heparin 5000 units subcutaneously every 8 or 12 hours ***or*** • Dalteparin 5000 units subcutaneously daily ***plus*** • Mechanical Methods recommended for patients at high risk of bleeding