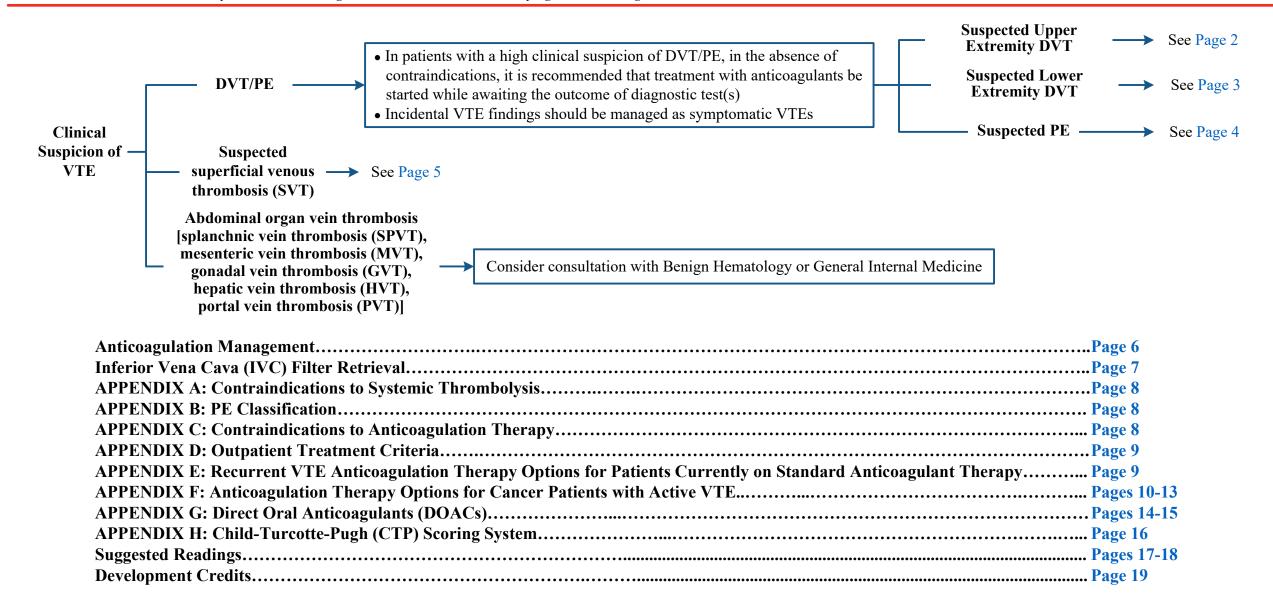
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BNP = brain natriuretic peptide DVT = deep vein thrombosis

sis ECHO = echocardiogram

PE = pulmonary embolism

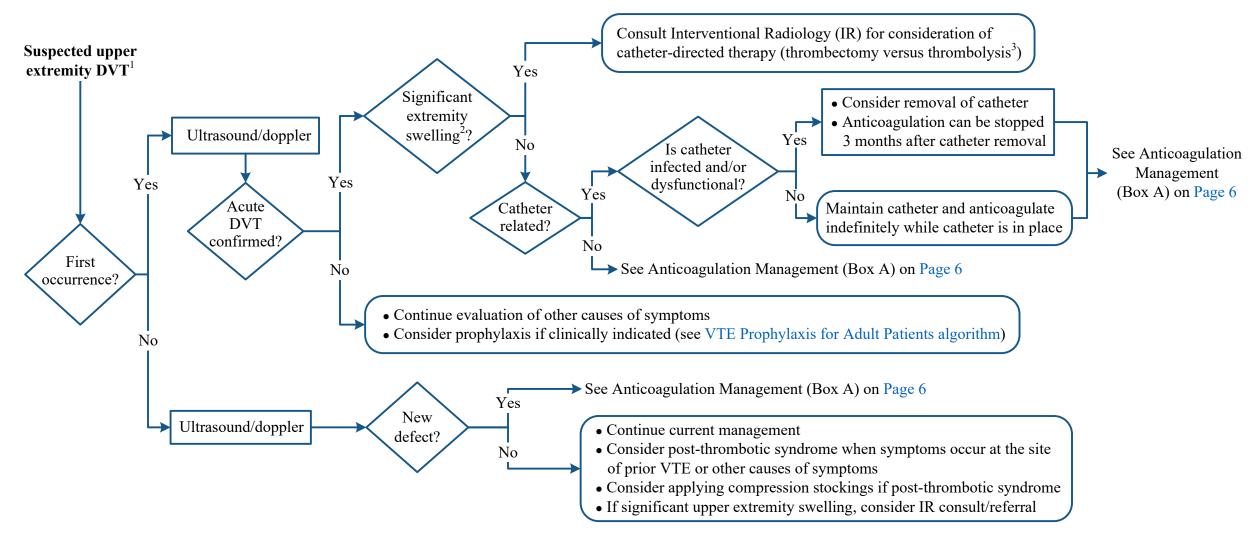
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¹ In patients with a high clinical suspicion of DVT/PE, in the absence of contraindications, it is recommended that treatment with anticoagulants be started while awaiting the outcome of diagnostic test(s) ² Significant extremity swelling as evidenced by significant impact on performance status that affects quality of life, or is associated with phlegmasia or lymphedema ³ See Appendix A: Contraindications to Systemic Thrombolysis

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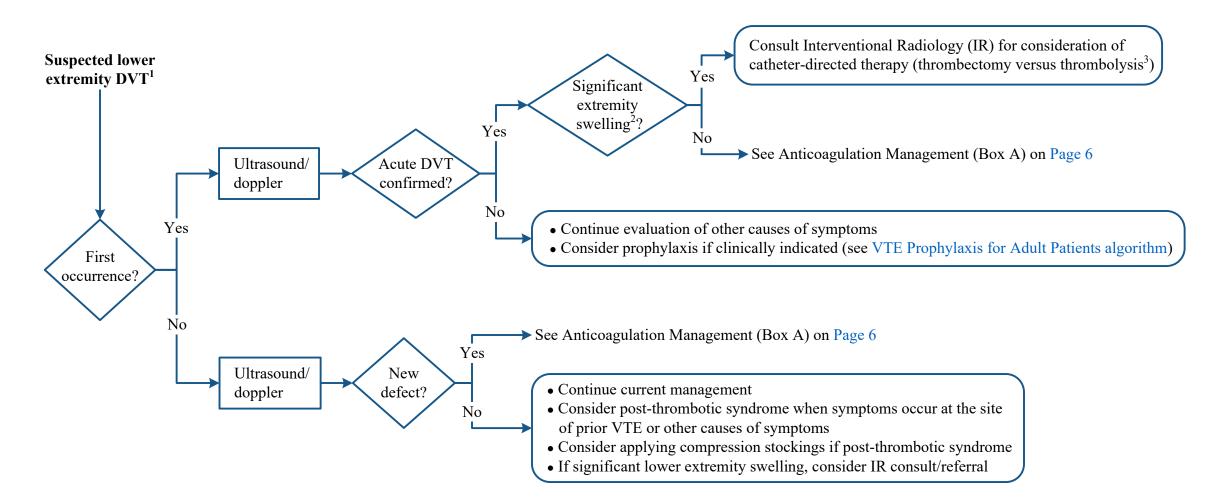
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¹ In patients with a high clinical suspicion of DVT/PE, in the absence of contraindications, it is recommended that treatment with anticoagulants be started while awaiting the outcome of diagnostic test(s)

² Significant extremity swelling: significant impact on performance status that affects quality of life, or is associated with phlegmasia or lymphedema

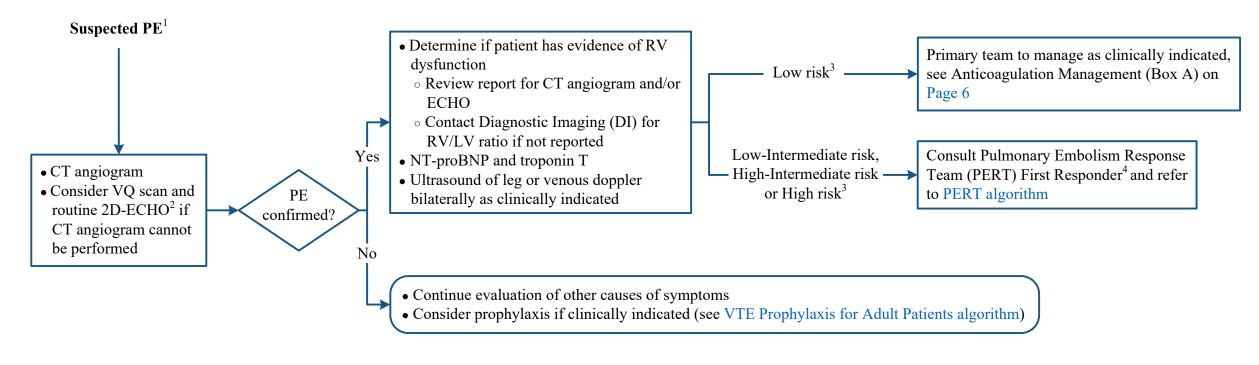
³ See Appendix A: Contraindications to Systemic Thrombolysis

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LV = left ventricular

RV = right ventricular

VQ = ventilation/perfusion

¹ In patients with a high clinical suspicion of DVT/PE, in the absence of contraindications, it is recommended that treatment with anticoagulants be started while awaiting the outcome of diagnostic test(s)

² Consider STAT 2D-ECHO only for hemodynamically unstable patients when PE is highly suspected and unable to get CT angiogram/VQ scan

³ See Appendix B: PE Classification

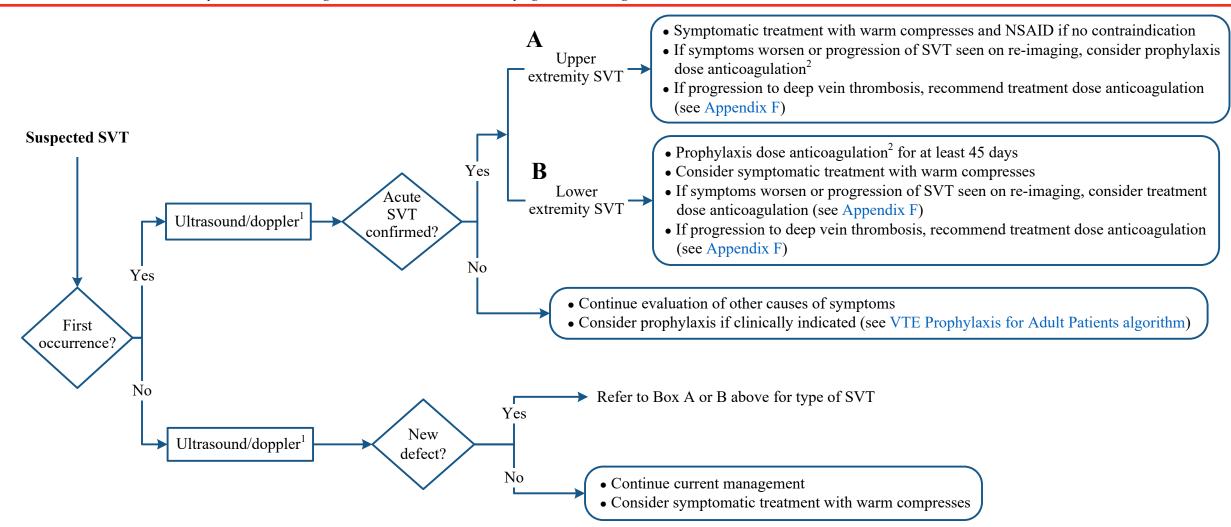
⁴ PERT First Responder: On-Call fellow/trainee and attending provider

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NSAID = non-steroidal anti-inflammatory drug

¹Recommend obtaining ultrasound/doppler for lower extremity SVT if not previously obtained to rule out concurrent DVT

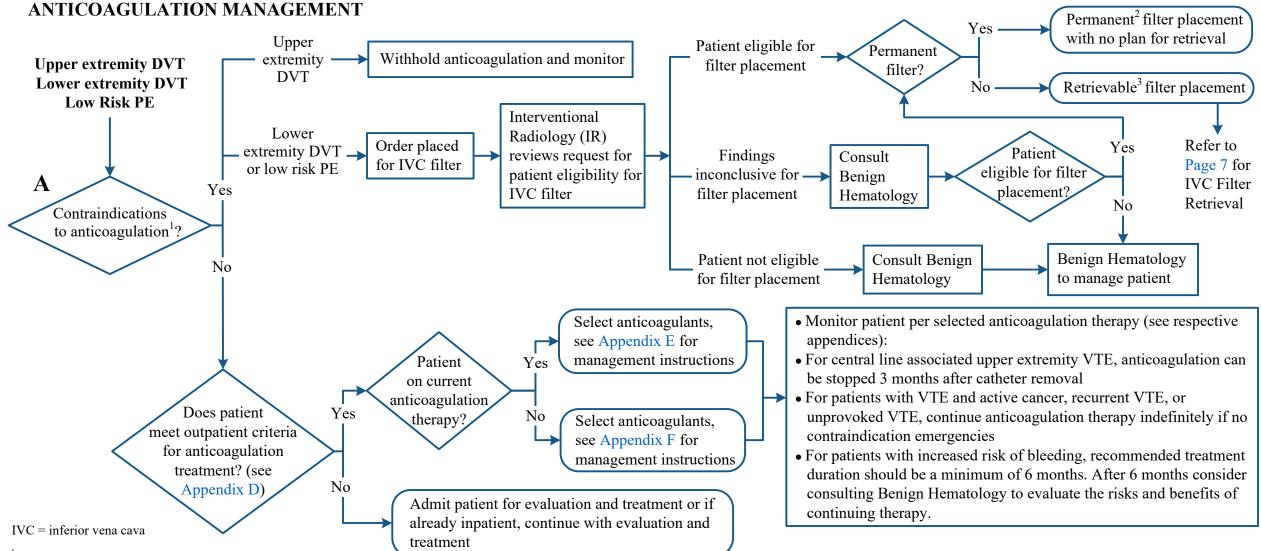
² Prophylaxis dose of anticoagulation used in SVT include: fondaparinux 2.5 mg SQ daily, rivaroxaban 10 mg PO daily, or enoxaparin 40 mg SQ daily for 45 days

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¹ See Appendix C: Contraindications to Anticoagulation Therapy

² Permanent IVC filter placement: permanent contraindication to anticoagulation with no plan to retrieve; expected survival < 6 months or persistent and/or irreversible bleeding; persistent and/or irreversible thrombocytopenia; hemorrhagic brain tumor

³Criteria to consider placement of retrievable filter for a temporary indication: anticipated surgery; temporary contraindication to anticoagulation with potential for retrieval

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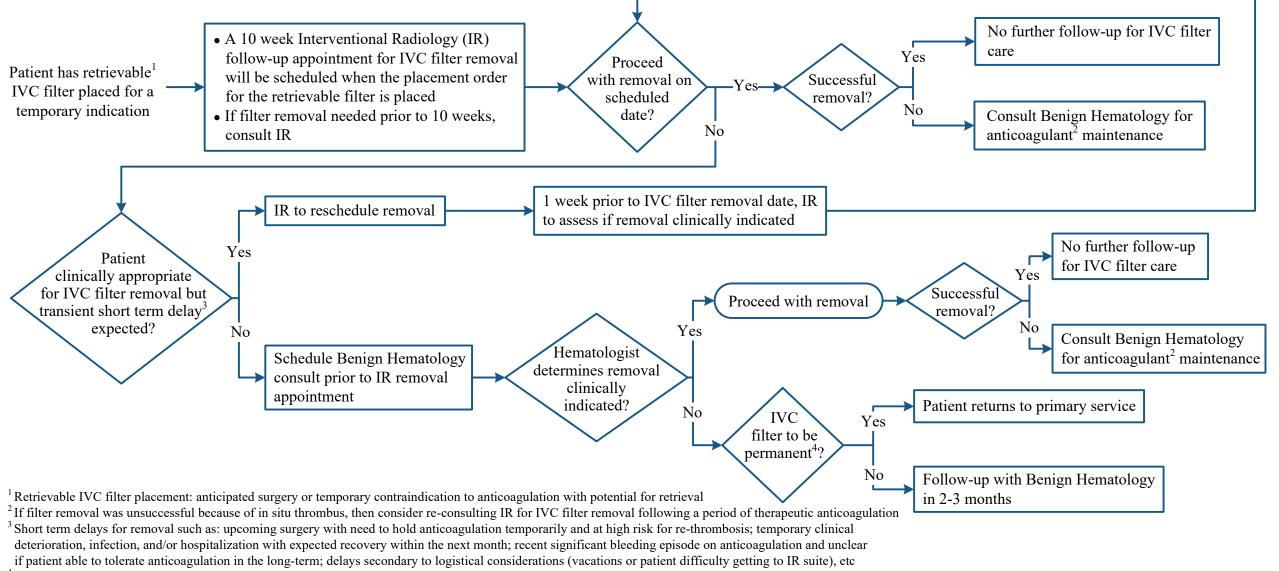
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INFERIOR VENA CAVA (IVC) FILTER RETRIEVAL



⁴Change in patient status where filter will not be removed: for example recurrent hemorrhage or patient going to hospice

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APPENDIX A: Contraindications to Systemic Thrombolysis

Absolute Contraindications	Relative Contraindications		
Active bleeding	• Age > 75 years old		
 History of hemorrhagic stroke or stroke of unknown origin 	• Pregnancy or first post-partum week		
Intracranial tumor	Non-compressible puncture sites		
• Ischemic stroke in previous 3 months (if ischemic stroke onset within 4.5 hours,	 Traumatic cardiopulmonary resuscitation 		
see Management of Acute Ischemic Stroke in Hospitalized Adult Patients algorithm)	• Recent major surgery, invasive procedure, and/or trauma (within 1 month)		
• Recent brain or spinal surgery ¹ and/or head or facial trauma	• Refractory hypertension (SBP > 180 mmHg; DBP > 100 mmHg)		
Suspected or confirmed aortic dissection	• Significant non-intracranial bleeding within 1 month		
Platelet count below 100 K/microliter	• Life expectancy ≤ 6 months		

¹Discussion with Neurosurgery for recent brain or spine surgery

SBP = systolic blood pressure DBP = diastolic blood pressure

APPENDIX B: PE Classification

Low Risk	Intermediate Risk		High Risk
Any PE:	Low-Intermediate	High-Intermediate	• Sustained hypotension (SBP < 90 mmHg for at least 15 minutes) <u>or</u>
• Without right ventricular (RV) dysfunction and	RV dysfunction or	RV dysfunction and	 Persistent bradycardia (heart rate < 40 bpm) or signs or symptoms of shock <u>or</u>
• With normal BNP/troponin		elevated BNP <u>or</u> troponin	• Need for inotropic support

APPENDIX C: Contraindications to Anticoagulation Therapy

Absolute Contraindications	Relative Contraindications
 Major active bleeding (<i>e.g.</i>, bleeding requiring ≥ 2 units of packed red blood cells (PRBC) transfusion, decrease in hemoglobin ≥ 2 g/dL, or bleeding in a critical area or organ) Platelets < 25 K/microliter¹, consult to Benign Hematology Spinal procedure and/or epidural catheter placement Severe uncontrolled malignant hypertension 	 Brain metastases conferring risk of bleeding (renal, choriocarcinoma, melanoma, thyroid cancer) Intracranial or central nervous system (CNS) bleeding within the past 4 weeks Recent high-risk surgery or bleeding event Active but non-life threatening bleeding Active GI ulceration at high risk of bleeding Platelets < 50 K/microliter, consider consult to Benign Hematology Patient on active protocol that prohibits use of anticoagulation

¹ Consider placing a retrievable IVC filter for patients with an acute PE or lower extremity DVT within 1 month, and thrombocytopenia is anticipated to last more than 7 days *Copyright 2022 The University of Texas MD Anderson Cancer Center*Approved

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APPENDIX D: Outpatient Treatment Criteria

- No co-morbidity requiring inpatient hospitalization
- No clinical conditions requiring hospitalization
- Likelihood of good compliance, ability to provide self-care and not at high-risk for falls
- Adequate home support system and geographical accessibility for follow-ups
- If pulmonary embolism, low risk and pulse oximetry \geq 95%; stable vital signs

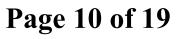
APPENDIX E: Recurrent VTE Anticoagulation Therapy Options for Patients Currently on Standard Anticoagulant Therapy

- If patient is on sub-therapeutic warfarin, adjust dose to achieve a target INR of 2-3
- If INR is therapeutic, change warfarin to low molecular weight heparin (LMWH) or a direct-acting oral anticoagulant (DOAC)
- If patient is on a LMWH, check anti-factor Xa level 4 hours post injection
- If peak anti-factor Xa level is subtherapeutic, adjust dose of the LMWH¹
- If peak factor Xa level is within the therapeutic range², consider increasing dose of LMWH¹ by 20% or switching to a DOAC
- If peak factor Xa level is therapeutic and the VTE event is a symptomatic pulmonary embolism, consider increasing the dose of LMWH by 20% or switching to a DOAC. Also consider placement of a permanent IVC filter.
- Consider General Internal Medicine or Benign Hematology consult/referral
- If patient on DOACs, consider changing to alternative class of anticoagulants

¹ See Appendix F for LMWH dose adjustments to achieve therapeutic anti-factor Xa level

² Range may vary, based on specific institutional ranges

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APPENDIX F: Anticoagulation Therapy^{1,2} Options for Cancer Patients with Active VTE

LMWH ³ Treatments	DOSE / R	OUTE / FRE	QUENCY	MONITORING ^{4,5}	DOSE ADJUSTMENTS
Dalteparin (Fragmin [®]) ⁶ – FDA approved for		est Internation subcutaneous	ly daily	 serum creatinine Therapeutic laboratory tests: Routine monitoring not required. However, antifactor Xa levels may be useful in certain high-risk patients (<i>e.g.</i>, obesity, malnutrition, renal insufficiency, and 	 <u>Platelets:</u> Consider reducing the daily dose by 2,500 units when platelets are between 50-100 K/microliter
cancer patients	Actual Body Weight (kg)	Month 1 200 IU/kg	Month 2-6 150 IU/kg		However, antifactor Xa levels may be useful in certain high-risk patients (<i>e.g.</i> , obesity, malnutrition, renal insufficiency, and platelets are < 50 K/microliter
Hold in patients with platelets < 25 K/microliter	≤ 56 57-68 69-82 83-98	10,000 IU 12,500 IU 15,000 IU 18,000 IU	7,500 IU 10,000 IU 12,500 IU 15,000 IU	 unexplained bleeding or thrombosis) Surgical inpatient: Hemoglobin/hematocrit and platelet count 24 hours after starting LMWH, then every 3 days from days 4-14 unless LMWH is stopped or patient is discharged After day 14, hemoglobin/hematocrit and platelet count at least once weekly Medical inpatient and all outpatient: New start: For medical patients, hemoglobin/hematocrit and platelet count at least once weekly. For outpatient, no other monitoring needed except platelet count at least once during the first 14 days of therapy if prior recent (within 30 days) exposure to heparin or LMWH. Maintenance therapy: Hemoglobin/hematocrit, platelet count, serum creatinine, and hepatic function tests at least once yearly If CrCl 30-60 mL/minute, serum creatinine every 3 months 	 For platelet count < 25 K/microliter, hold dalteparin <u>Renal:</u> If CrCl < 30 mL/minute: adjust dose to obtain anti-Xa level of 0.5-1.5 IUs/mL (4-6 hours after fourth dose) <u>Weight:</u> Consider obtaining anti-Xa level in patients weighing > 150 kg or < 50 kg, or BMI ≥ 40 kg/m² and adjust dose to obtain anti-Xa level of 0.5-1.5 IU/mL (4-6 hours after fourth dose)
	≥ 99 Consider monitoring anti-Xa levels and adjust dose as needed. Limited data suggests dalteparin 200 IU/kg based on actual body weight (with no d capping) in one or two divided doses ⁷ . An alternative option is enoxaparin 1 mg/kg twice daily (see below).				

¹ Prior to anticoagulation therapy, check for contraindications to anticoagulation therapy (see Appendix C) CrCl = creatinine clearance (mL/minute) LMWH = low molecular weight heparin

Continued on next page

² For bleeding complications refer to Emergency Anticoagulation Reversal Order Set

³ Patient should be observed closely for bleeding and signs and symptoms of neurological impairment if therapy is administered during or immediately following diagnostic lumbar puncture, epidural anesthesia, or spinal anesthesia ⁴ If lab results indicate heparin induced thrombocytopenia, follow management guideline per Heparin Induced Thrombocytopenia (HIT) Treatment algorithm

⁵ See the Anticoagulant Management and Required Laboratory Monitoring Policy (MD Anderson Institutional Policy #CLN0984)

⁶ See the Anticoagulant Management and Required Laboratory Monitoring Policy (MD Anderson Institutional Policy #CLN0984

⁶ For concerns regarding affordability, consider submitting a test claim 48 hours prior to discharge via Pecon (for internal use only)

⁷ Multi-dose vials not recommended for home use



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APPENDIX F: Anticoagulation Therapy^{1,2} Options for Cancer Patients with Active VTE - continued

LMWH ³ Treatments	DOSE / ROUTE / FREQUENCY	MONITORING ^{4,5}	DOSE ADJUSTMENTS
Enoxaparin (Lovenox [®]) ⁶ Hold in patients with platelets < 25 K/microliter	or 1.5 mg/kg subcutaneously daily in selected patients	 Baseline: Hemoglobin/hematocrit, platelet count, aPTT/PT, and serum creatinine Therapeutic laboratory tests: Routine monitoring not required. However, antifactor Xa levels may be useful in certain highrisk patients (<i>e.g.</i>, obesity, malnutrition, renal insufficiency, and unexplained bleeding or thrombosis) Surgical inpatient: Hemoglobin/hematocrit and platelet count 24 hours after starting LMWH, then every 3 days from days 4-14 unless LMWH is stopped or patient is discharged After day 14, hemoglobin/hematocrit, and platelet count at least once weekly Medical inpatient and all outpatient: New start: For medical patients, hemoglobin/hematocrit, and platelet count at least once during the first 14 days of therapy if prior recent (within 30 days) exposure to heparin or LMWH. Maintenance therapy: Hemoglobin/hematocrit, platelet count, serum creatinine, and hepatic function tests at least once yearly If CrCl 30-60 mL/minute, serum creatinine every 3 months 	 Platelets: Limited data suggest the following enoxaparin dose modification: For platelet count > 50 K/microliter: full-dose, 1 mg/kg twice daily; alternative dose, 1.5 mg/kg once daily For platelet count 25-50 K/microliter: half-dose, 0.5 mg/kg twice daily For platelet count < 25 K/microliter, hold all anticoagulants Renal: If CrCl < 30 mL/minute: 1 mg/kg daily Weight: Consider obtaining anti-Xa level in patients with weight < 50 kg or weight > 150 kg or BMI ≥ 40 kg/m²: For 1 mg/kg every 12 hour dosing regimen: adjust dose to obtain anti-Xa level of 0.6-1 IU/mL (4-6 hours after fourth dose) For 1.5 mg/kg every 24 hour dosing regimen: adjust dose to obtain anti-Xa level of 1-2 IU/mL (4-6 hours after fourth dose)

CrCl = creatinine clearance (mL/minute) LMWH = low molecular weight heparin

Continued on next page

¹ Prior to anticoagulation therapy, check for contraindications to anticoagulation therapy (see Appendix C)

² For bleeding complications refer to Emergency Anticoagulation Reversal Order Set

³ Patient should be observed closely for bleeding and signs and symptoms of neurological impairment if therapy is administered during or immediately following diagnostic lumbar puncture, epidural anesthesia, or spinal anesthesia

⁴ If lab results indicate heparin induced thrombocytopenia, follow management guideline per Heparin Induced Thrombocytopenia (HIT) Treatment algorithm

⁵ See the Anticoagulant Management and Required Laboratory Monitoring Policy (MD Anderson Institutional Policy #CLN0984)

⁶ For concerns regarding affordability, consider submitting a test claim 48 hours prior to discharge via Pecon (for internal use only)

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APPENDIX F: Anticoagulation Therapy^{1,2} Options for Cancer Patients with Active VTE - continued

Unfractionated Heparin (UFH)					
TREATMENT	MONITORING ^{3,4}				
 IV heparin infusion (refer to Adult Heparin Infusion Order Set for dosing) If fixed dose, unmonitored subcutaneous UFH is chosen Initial dose: 333 units/kg subcutaneously times one dose, followed by 250 units/kg subcutaneously twice daily in addition to warfarin for at least 5 days until the INR is > 2 for 24 hours 	 Baseline: Hemoglobin/hematocrit, platelet count, and aPTT/PT Therapeutic laboratory tests: aPTT to achieve specified target range per protocol for therapeutic doses Inpatient: Hemoglobin/hematocrit and platelet count 24 hours after starting heparin infusion, then every 2 days from days 4-14 unless heparin is stopped After day 14, hemoglobin/hematocrit and platelet count at least once weekly Outpatient: New start: Platelet count at least once during the first 14 days of therapy regardless of prior exposure history Maintenance therapy: Hemoglobin/hematocrit and platelet count every 3 months 				
Warfarin ⁵ (Selected Vitamin K Anta	gonist) – For long-term management				
TREATMENT	MONITORING ^{3,4}				
 Overlap warfarin (2.5-5 mg PO) with induction therapy (LMWH, Factor Xa Inhibitor, or subcutaneous UFH) beginning on Day 1 of therapy Continue induction therapy until INR ≥ 2 for two days, AND patient has received at least 4-5 days of induction therapy overlap 	 General INR goal: 2-3 Mechanical aortic valve, INR goal: 2.5 (range 2-3) Mechanical mitral valve, INR goal: 2.5-3.5 Baseline: Hemoglobin/hematocrit, platelet count, PT/INR, and hepatic function tests Therapeutic laboratory tests: INR to achieve specified target range Inpatient: Hemoglobin/hematocrit, platelet count, and INR at least once weekly Outpatient: INR every 3 months at a minimum, hemoglobin/hematocrit, platelet count, serum creatinine, and hepatic function tests at least once year 				

¹ Prior to anticoagulation therapy, check for contraindications to anticoagulation therapy (see Appendix C)

Continued on next page

² For bleeding complications refer to Emergency Anticoagulation Reversal Order Set

³ If lab results indicate heparin induced thrombocytopenia, follow management per Heparin Induced Thrombocytopenia (HIT) Treatment algorithm

⁴ See the Anticoagulant Management and Required Laboratory Monitoring Policy (MD Anderson Institutional Policy #CLN0984)

⁵ Use of warfarin in cancer patients has been shown to be less effective at preventing clot recurrence than LMWH

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APPENDIX F: Anticoagulation Therapy^{1,2} Options for Cancer Patients with Active VTE - continued

Fondaparinux (Arixtra [®]) ³ Factor Xa Inhibitor					
ACTUAL BODY WEIGHT (kg)	FONDAPARNUX Daily SC DOSE	MONITORING			
< 50 50 - 100 > 100	5 mg 7.5 mg 10 mg	 Baseline: Hemoglobin/hematocrit, platelet count, aPTT/PT, and serum creatinine Therapeutic laboratory tests: Routine monitoring not required. However, antifactor Xa levels may be useful in certain high-risk patients (<i>e.g.</i>, obesity, malnutrition, renal insufficiency, and unexplained bleeding or thrombosis) Inpatient: Hemoglobin/hematocrit, platelet count, and serum creatinine at least once weekly Outpatient: Hemoglobin/hematocrit, platelet count, serum creatinine, and hepatic function tests at least once yearly If CrCl 30-60 mL/minute, serum creatinine every 6 months If CrCl < 30 mL/minute, serum creatinine every 3 months 	 <u>Renal:</u> If CrCl is between 30-50 mL/minute: use with caution If CrCl is < 30 mL/minute: contraindicated <u>Weight:</u> For BMI ≥ 40 kg/m², no dose adjustment necessary <u>Platelets:</u> Use fondaparinux with caution in patients with platelets < 100 K/microliter 		

CrCl = creatinine clearance (mL/minute)

¹ Prior to anticoagulation therapy, check for contraindications to anticoagulation therapy (see Appendix C)

² For bleeding complications refer to Emergency Anticoagulation Reversal Order Set

³ For concerns regarding affordability, consider submitting a test claim 48 hours prior to discharge via Pecon (for internal use only)

⁴ If lab results indicate heparin induced thrombocytopenia, follow management per Heparin Induced Thrombocytopenia (HIT) Treatment algorithm

⁵ See the Anticoagulant Management and Required Laboratory Monitoring Policy (MD Anderson Institutional Policy #CLN0984)



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APPENDIX G: Direct Oral Anticoagulants (DOACs)

Note: DOACs are suggested for treatment of VTE. There is no evidence available of DOACs use in cancer patients who experience chemotherapy induced thrombocytopenia. DOACs are not recommended in patients with gastrointestinal cancer.

DOACs	Rivaroxaban (Xarelto[®])¹ Oral Factor Xa Inhibitor		Apixaban (Eliquis [®]) ¹ Oral Factor Xa Inhibitor		
VTE Dosing Instructions	$CrCl \ge 15 mL/minute$	15 mg PO twice daily with food for 3 weeks followed by 20 mg PO daily with food	No dose adjustment is recommended for CrCl, 10 mg PO twice dail		
	CrCl < 15 mL/minute or ESRD	Avoid use	No recommendations		
Use in liver disease	CTP ² class B or C: NOT recommended		ecommended Use in CTP^2 class C not recommended and there is limited experience for use in class		
Class specific contraindications	Moderate to severe mitral stenosis or mechanical heart valve				
Significant drug-drug interactions	P-glycoprotein and CYP 3A4 interactions		P-glycoprotein and CYP	P-glycoprotein and CYP 3A4 interactions	
Monitoring parameters	 Baseline: Hemoglobin/hematocrit, platelet count, aPTT/PT, serum creatinine, and hepatic function tests Therapeutic laboratory tests: Routine monitoring not required. However, antifactor Xa levels may be useful in certain high-risk patients (<i>e.g.</i>, obesity, malnutrition, renal insufficiency, and unexplained bleeding or thrombosis). Antifactor Xa levels are only avail for apixaban and rivaroxaban currently. 		red. h-risk id • Outpatient: Hemoglobin creatinine, and hepatic f • If CrCl 30-60 mL/mi	nematocrit, platelet count, and serum weekly /hematocrit, platelet count, serum function tests at least once yearly inute, serum creatinine every 6 months nute, serum creatinine every 3 months	

CrCl = creatinine clearance (mL/minute)

ESRD = end stage renal disease

¹ For concerns regarding affordability, consider submitting a test claim 48 hours prior to discharge via Pecon (for internal use only) ² See Appendix H: Child-Turcotte-Pugh (CTP) Scoring System

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APPENDIX G: Direct Oral Anticoagulants (DOACs) - continued

Note: DOACs are suggested for treatment of VTE. There is no evidence available of DOACs use in cancer patients who experience chemotherapy induced thrombocytopenia. DOACs are not recommended in patients with gastrointestinal cancer.

DOACs	Dabigatran (Pradaxa [®]) ¹ Direct Thrombin Inhibitor		Edoxaban (Savaysa [®]) ^{1,2} Oral Factor Xa Inhibitor		
VTE Dosing Instructions	CrCl > 30 mL/minute	150 mg twice daily AFTER 5 days of treatment with parenteral anticoagulant	CrCl > 50 mL/minute		 60 mg PO daily started after at least 5 days of treatment with a parenteral anticoagulant: If body weight ≤ 60 kg dose reduce to 30 mg PO daily
	$CrCl \le 30 \text{ mL/minute or HD}$	No recommendations	CrCl 15-50 mL/minute		Dose reduce to 30 mg PO daily
			CrCl < 15 mL/	minute or ESRD	Avoid use
Use in liver disease	CTP ³ class B or C: NOT recommended				
Class specific contraindications	Moderate to severe mitral stenosis or mechanical heart valve				
Significant drug-drug interactions	P-glycoprotein interactions P-glycoprotein and CYP 3A4 interactions			and CYP 3A4 interactions	
Monitoring parameters	 Baseline: Hemoglobin/hematocrit, platelet count, aPTT/PT, serum creatinine, and hepatic function tests Therapeutic laboratory tests: Routine monitoring not required. Edoxaban: Antifactor Xa levels may be useful in certain high-risk patients (<i>e.g.</i>, obesity, malnutrition, renal insufficiency, and unexplained bleeding or thrombosis) Dabigatran: Thrombin time (TT) may be useful in certain high-risk patients (<i>e.g.</i>, obesity, malnutrition, renal insufficiency, and unexplained bleeding or thrombosis) 		 creatinine at lea Outpatient: Herric creatinine, and line or If CrCl 30-60 	globin/hematocrit, platelet count, and serum st once weekly noglobin/hematocrit, platelet count, serum nepatic function tests at least once yearly 0 mL/minute, serum creatinine every 6 months mL/minute, serum creatinine every 3 months	

CrCl = creatinine clearance (mL/minute) ESRD = end stage renal disease HD = Hemodialysis

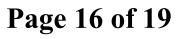
¹ For concerns regarding affordability, consider submitting a test claim 48 hours prior to discharge via Pecon (for internal use only)

²Edoxaban is currently not on the MD Anderson formulary

³ See Appendix H: Child-Turcotte-Pugh (CTP) Scoring System

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APPENDIX H: Child-Turcotte-Pugh (CTP) Scoring System

Chemical and Biochemical Parameters	Points for Increasing Abnormality				
	1	2	3		
Hepatic encephalopathy	None	Grade 1 or 2, or suppressed with medication	Grade 3 or 4, or refractory to medication		
Ascites	None	Mild to moderate (diuretic responsive)	Severe (diuretic refractory)		
Serum albumin	Greater than 3.5 g/dL	2.8-3.5 g/dL	Less than 2.8 g/dL		
Total bilirubin For primary biliary cirrhosis	Less than 2 mg/dL 1 – 4 mg/dL	2 – 3 mg/dL 4 – 10 mg/dL	Greater than 3 md/dL Greater than 10 mg/dL		
Prothrombin time prolonged or INR	Less than 4 seconds Less than 1.7	4 – 6 seconds 1.7 – 2.3	Greater than 6 seconds Greater than 2.3		

*CTP score is obtained by adding the score for each parameter.

CTP class:

Class A = 5 to 6 points

Class B = 7 to 9 points

Class C = 10 to 15 points



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Adult Venous Thromboembolism (VTE) **Treatment for Cancer Patients (DVT and PE) MDAnderson** ancer Center

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DEVELOPMENT CREDITS

This practice consensus statement is based on majority opinion of the VTE workgroup experts at the University of Texas MD Anderson Cancer Center for the patient population. These experts incuded:

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