Adult Venous Thromboembolism (VTE) Treatment for Cancer Patients (DVT and PE)

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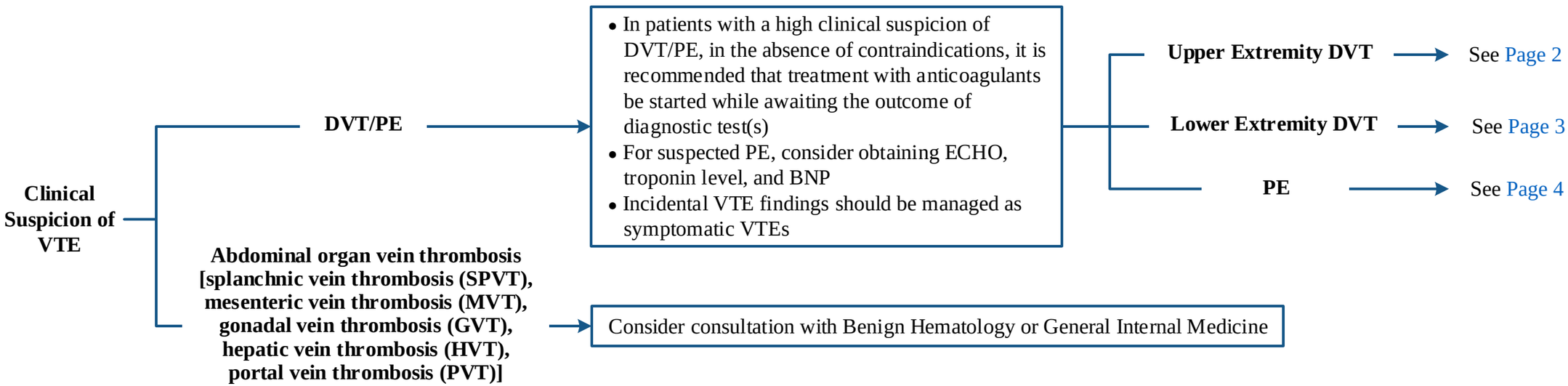

BNP = brain natriuretic peptide DVT = deep vein thrombosis ECHO = echocardiogram PE = pulmonary embolism

Department of Clinical Effectiveness V7
Approved by The Executive Committee of the Medical Staff 02/18/2020

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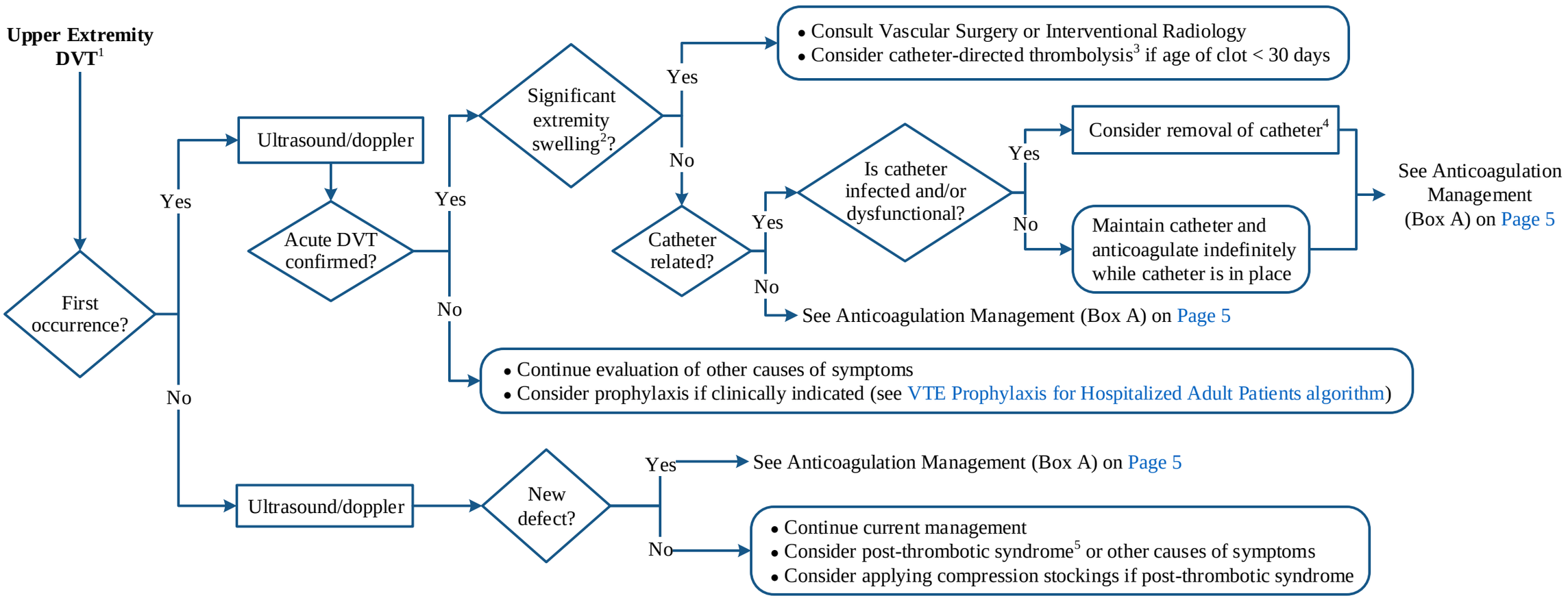

[1] In patients with a high clinical suspicion of DVT/PE, in the absence of contraindications, it is recommended that treatment with anticoagulants be started while awaiting the outcome of diagnostic test(s)
[2] Significant extremity swelling as evidenced by significant impact on performance status that affects quality of life, or is associated with phlegmasia or lymphedema
[3] See Appendix A: Contraindications to Systemic Thrombolysis
[4] Anticoagulation after catheter removal can be stopped after 3 months
[5] Consider post-thrombotic syndrome if symptoms occur in same extremity as prior VTE

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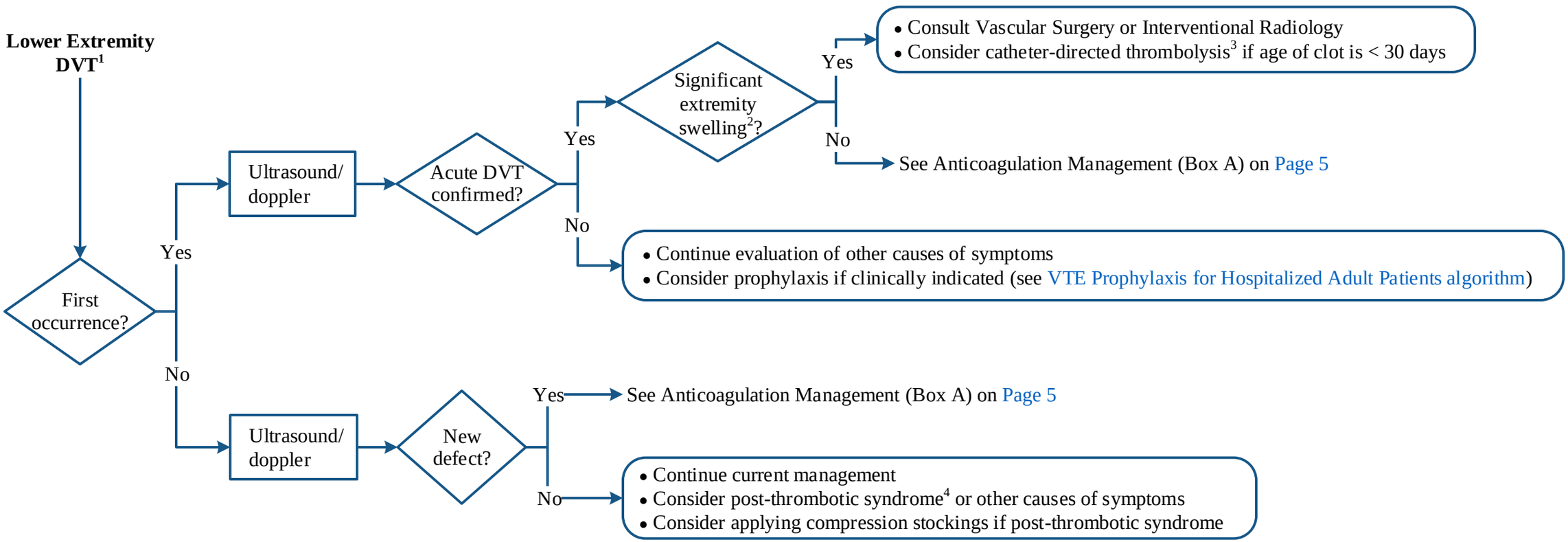

[1] In patients with a high clinical suspicion of DVT/PE, in the absence of contraindications, it is recommended that treatment with anticoagulants be started while awaiting the outcome of diagnostic test(s)
[2] Significant extremity swelling: significant impact on performance status that affects quality of life, or is associated with phlegmasia or lymphedema
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[4] Consider post-thrombotic syndrome when symptoms occur in site of prior VTE

Adult Venous Thromboembolism (VTE) Treatment for Cancer Patients (DVT and PE)

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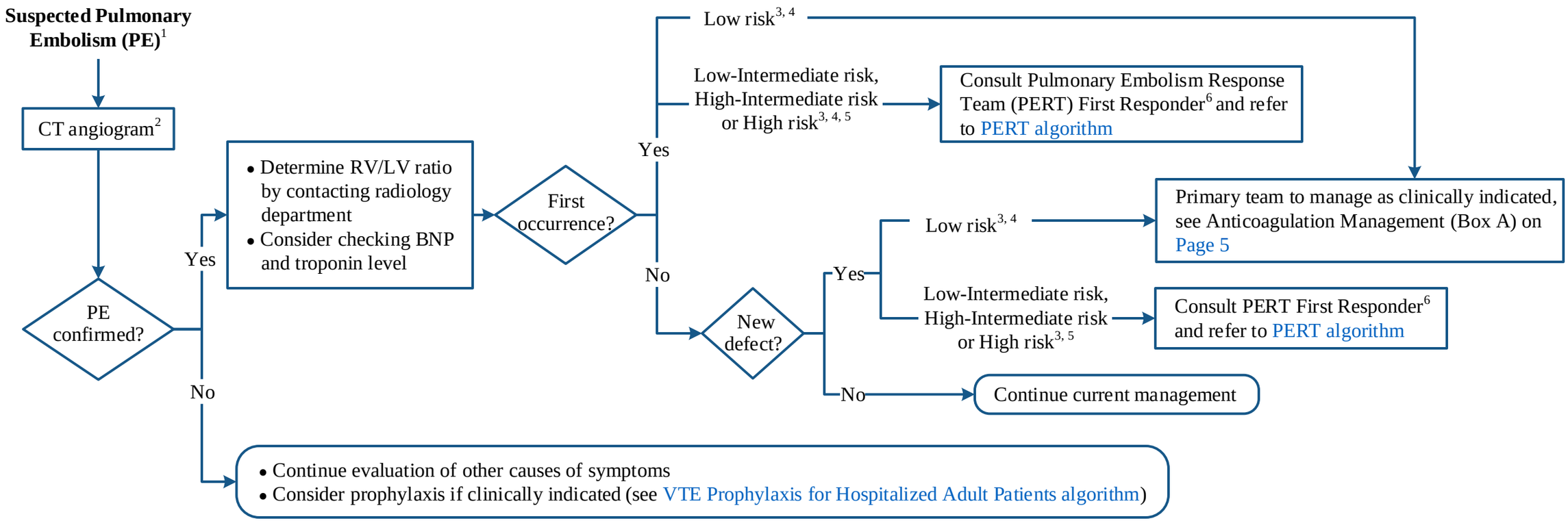
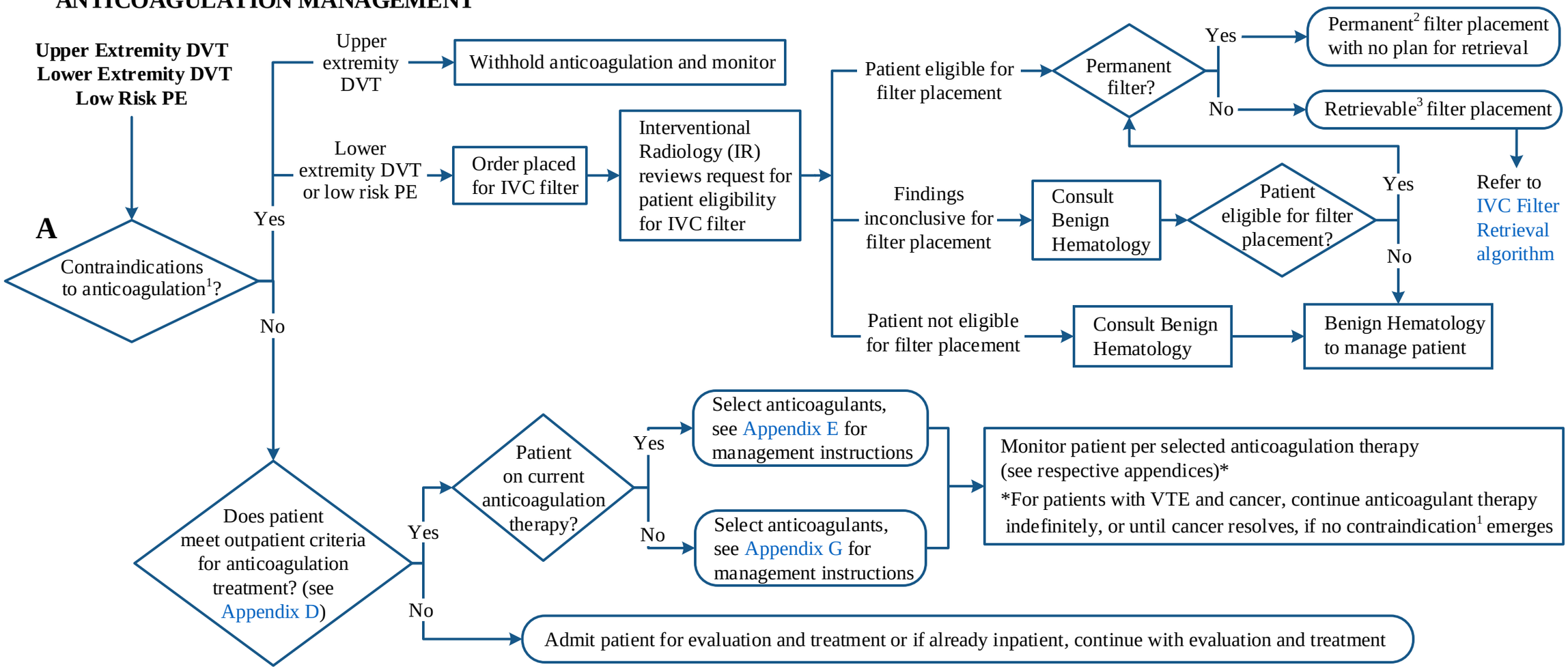


[1] In patients with a high clinical suspicion of DVT/PE, in the absence of contraindications, it is recommended that treatment with anticoagulants be started while awaiting the outcome of diagnostic test(s). For suspected PE, obtain the following: ECHO, troponin level, BNP.
[2] If CT angiogram cannot be performed, consider VQ scan. Consider STAT ECHO if clinical criterias are met, refer to Appendix B: Criteria for after hours STAT 2D-ECHO for Patients with Suspected PE.
[3] See Appendix C: PE Classification
[4] Admission criteria to Telemetry/intermediate unit: Low-Intermediate Risk patients requiring anticoagulation
[5] Admission criteria for ICU: High-Intermediate and High Risk patients in need of inotropic support with bradycardia, hypotension, or right ventricular dysfunction, RV/LV diameter ratio > 1 by 2D ECHO or CT, and elevated troponin or BNP
[6] PERT First Responder: On-Call fellow/trainee and attending provider

Adult Venous Thromboembolism (VTE) Treatment for Cancer Patients (DVT and PE)

ANTICOAGULATION MANAGEMENT



[1] See Appendix F: 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

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

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APPENDIX A: Contraindications to Systemic Thrombolysis

Absolute Contraindications:

- History of hemorrhagic stroke or stroke of unknown origin
- Intracranial tumor
- Ischemic stroke in previous 3 months (except ischemic stroke within 4.5 hours)
- History of major trauma, surgery or head injury in previous 3 weeks
- Platelet count below 100 K/microliter

Relative Contraindications:

- Pregnancy or first post-partum week
- Non-compressible puncture sites
- Traumatic resuscitation
- Refractory hypertension (systolic blood pressure (SBP) > 180 mmHg; diastolic blood pressure (DBP) > 100 mmHg)
- Advanced liver disease
- Infective endocarditis
- Recent gastrointestinal bleed (last 3 months)
- Life expectancy ≤ 6 months

APPENDIX B: Criteria for After Hours STAT 2D-ECHO for Patients with Suspected PE

Criteria
• Patient has to be seen first by a member of the PERT team in order to confirm that none of the other imaging modalities are possible (CT angiogram or VQ scan) • Patient is hemodynamically unstable (SBP < 90 mmHg or receiving vasopressors) • PE has to be highly suspected and no other etiology would explain shock (no septic, hemorrhagic or hypovolemic shock) • PERT team member is to contact and discuss directly the need of the echo with the cardiologist on-call before sonographer is contacted

APPENDIX C: PE Classification

<table>
<tr><th>Low Risk</th><th colspan="2">Intermediate Risk</th><th>High Risk</th></tr>
<tr><td rowspan="2">Any PE:
• Without right ventricular (RV) dysfunction <u>and</u>
• With normal BNP/troponin</td><td>Low-Intermediate</td><td>High-Intermediate</td><td rowspan="2">• Sustained hypotension (SBP < 90 mmHg for at least 15 minutes) <u>or</u>
• Persistent bradycardia (heart rate < 40 bpm) with signs or symptoms of shock <u>or</u>
• Need for inotropic support</td></tr>
<tr><td>RV dysfunction
<u>or</u>
elevated BNP <u>or</u> troponin</td><td>RV dysfunction
<u>and</u>
elevated BNP <u>or</u> troponin</td></tr>
</table>

APPENDIX D: Outpatient Treatment Criteria

- See Appendix F for contraindications
- 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 > 95%; stable vital signs
- Not intermediate risk (not submassive)

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)
- If patient is on a LMWH, check anti-factor Xa level 4 hours post injection
- If peak anti-factor Xa level is subtherapeutic (< 0.5 anti-factor Xa units), adjust dose of the LMWH[1] to achieve a peak anti-factor Xa of 0.5 – 1.5 units
- If peak factor Xa level is within the therapeutic range[2], consider increasing dose of LMWH[1] by 20%
- If peak factor Xa level is therapeutic and the VTE event is a symptomatic pulmonary embolism, place a permanent IVC filter
- Consider General Internal Medicine or Benign Hematology consult
- If patient on direct oral anticoagulants (DOAC), consider changing to alternative class of anticoagulants

[1] See recommendations for specific agents on Pages 9-10

[2] Range may vary, based on specific institutional ranges

APPENDIX F: Contraindications to Anticoagulation Therapy

Absolute Contraindications:

- Cerebral hemorrhage, hemorrhage in the eye or vital organs or a drop in hemoglobin of 2 grams/dL in 24 hours
- Neurosurgery, ocular surgery or intracranial bleeding within past 10 days
- Platelets < 25 K/microliter, consult to benign hematology

Relative Contraindications:

- Brain metastases conferring risk of bleeding (renal, choriocarcinoma, melanoma, thyroid cancer)
- Spinal procedure and/or epidural placement
- Major trauma or head trauma
- Major abdominal surgery within 48 hours
- Severe hypertension (SBP > 200 mmHg, DBP > 120 mmHg)
- Endocarditis/pericarditis
- Gastrointestinal, genitourinary bleeding within past 14 days
- Preexisting coagulopathy
- Platelets < 50 K/microliter, consider consult to benign hematology
- Hypersensitivity to heparin, low molecular weight heparin (LMWH) or heparin induced thrombocytopenia
- Patient on active protocol that prohibits use of anticoagulation
- Bleeding diathesis

Adult Venous Thromboembolism (VTE) Treatment for Cancer Patients (DVT and PE)

APPENDIX G: Anticoagulation Therapy Options for Cancer Patients with Active VTE (does not include prophylactic dosing)

<table>
<tr><th>LMWH[1] Treatments</th><th>DOSE / ROUTE / FREQUENCY</th><th>MONITORING[2]</th><th>DOSE ADJUSTMENTS</th></tr>
<tr><td rowspan="3">Dalteparin (Fragmin®)*

*FDA approved for cancer patients

• Hold in patients with platelets < 25 K/microliter</td><td colspan="3">Round to nearest International Units (IU) dose, given subcutaneously daily</td><td rowspan="2">• Baseline CBC with platelets, aPTT, PT and serum creatinine
• For surgical patients, platelets every 3 days between days 4 and 14 after beginning LMWH then, as clinically indicated</td><td rowspan="2"><u>Renal:</u>
• If creatinine clearance < 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>
• Obtain anti-Xa level in patients weighing > 150 kg or < 50 kg, or BMI ≥ 40 kg/m^2 and adjust dose to obtain anti-Xa level of 1.5 IU/mL (4-6 hours after fourth dose)
<u>Platelets:</u>
• Consider reducing the daily dose by 2,500 units when platelets are between 50-100 K/microliter and use with caution in cancer patients when platelets are < 50 K/microliter
• For platelet count < 25 K/microliter, hold dalteparin</td></tr>
<tr><td>Actual Body Weight (kg)</td><td>Month 1
200 IU/kg</td><td>Month 2-6
150 IU/kg</td></tr>
<tr><td>≤ 56
57-68
69-82
83-98</td><td>10,000 IU
12,500 IU
15,000 IU
18,000 IU</td><td>7,500 IU
10,000 IU
12,500 IU
15,000 IU</td></tr>
<tr><td>≥ 99</td><td colspan="3">Consider monitoring anti-Xa levels and adjust dose as needed. Limited data suggests dalteparin 200 IU/kg based on actual body weight (with no dose capping) in one or two divided doses[3]. An alternative option is enoxaparin 1 mg/kg twice daily (see below).</td></tr>
<tr><td>Enoxaparin (Lovenox®)

• Hold in patients with platelets < 25 K/microliter</td><td colspan="3">1 mg/kg subcutaneously every 12 hours <u>or</u> 1.5 mg/kg subcutaneously daily in selected patients

• Limited data suggest once per day dosing is inferior in cancer patients and may increase risk of bleeding
• Limited data suggest dose of 0.75-0.85 mg/kg every 12 hours in obese patients (BMI ≥ 40 kg/m^2)</td><td>• Baseline CBC with platelets, aPTT, PT and serum creatinine
• For surgical patients, platelets every 3 days between days 4 and 14 after beginning LMWH then, as clinically indicated</td><td><u>Renal:</u>
• If creatinine clearance < 30 mL/minute: 1 mg/kg daily
<u>Weight:</u>
• Obtain anti-Xa level in patients with weight < 50 kg or weight > 150 kg or BMI ≥ 40 kg/m^2:
◦ 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)
<u>Platelets:</u>
• 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</td></tr>
</table>

[1] **Note**:
- Low-molecular-weight heparin = LMWH (preferred agents)
- If LMWHs are not accessible, consider switching to warfarin after 5 days of LMWH therapy. Heparin and warfarin therapy should overlap 5 days during the acute management of venous thrombosis
- Patients who tolerate anticoagulation should be continued on it indefinitely or until active cancer resolves
- 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

Continued on next page

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

[3] Multi-dose vials not recommended for home use

APPENDIX G: Anticoagulation Therapy Options for Cancer Patients with Active VTE (does not include prophylactic dosing) - continued

Unfractionated Heparin (UFH)

DOSE / ROUTE / FREQUENCY	MONITORING
• **If fixed dose, unmonitored subcutaneous UFH is chosen** • Initial dose: 333 units/kg subcutaneously for one dose, followed by 250 units/kg subcutaneously twice daily in addition to warfarin for at least 5 days until the INR is > 2	Baseline labs for heparin should be CBC with platelets, aPTT/PT, serum creatinine

Warfarin[1] (Selected Vitamin K Antagonis) – For Long-term Management

DOSE / ROUTE / FREQUENCY	MONITORING
• Overlap warfarin (5 mg PO) with induction therapy (LMWH, Factor Xa Inhibitor, or UFH-SC) 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	• INR Goal: 2-3 • Baseline CBC with platelet count, aPTT/PT, liver function tests • Follow-up for PT/INR regularly

Fondaparinux (Arixtra®) (Factor Xa Inhibitor)

ACTUAL BODY WEIGHT (kg)	FONDAPARNUX Daily SC DOSE	MONITORING	
< 50 50 – 100 > 100	5 mg 7.5 mg 10 mg	Requires baseline laboratory tests: CBC with platelets, aPTT/PT, serum creatinine	Renal: • If creatinine clearance is between 30-50 mL/minute: use with caution • If creatinine clearance is < 30 mL/minute: contraindicated Weight: • For BMI ≥ 40 kg/m^2, no dose adjustment necessary Platelets: • Use fondaparinux with caution in patients with platelets < 100 K/microliter

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

Adult Venous Thromboembolism (VTE) Treatment for Cancer Patients (DVT and PE)

APPENDIX H: Direct Oral Anticoagulants (DOACs)

Notes: DOACs are suggested for treatment of VTE in selected patients who have compelling indications to avoid LMWH. A multidisciplinary consultation is strongly recommended with Benign Hematology, Cardiology, and/or General Internal Medicine. Each case needs to be individually assessed prior to use of DOACs. There is no evidence available with DOACs in cancer patients who experience chemotherapy induced thrombocytopenia. See note below for reasons to avoid the use of DOACs.

Reasons to avoid use of DOACs in the cancer population

- Gastrointestinal and genitourinary cancers have shown increased risk of major bleeds with DOACs. DOACs should also be used with caution in cancers with high risk for mucosal bleeding.
- Lack of standardized testing for monitoring
- Complicated drug-drug interactions with chemotherapy agents. Assessing for drug-drug interaction and to transition patient to and from DOACs: Lexicomp®, Micromedex® or Clinical Pharmacology available at http://insidemdanderson.org (for internal use only).

<table>
<tr><th>DOACs</th><th colspan="2">Rivaroxaban (Xarelto®) Oral Factor Xa Inhibitor</th><th colspan="2">Apixaban (Eliquis®) Oral Factor Xa Inhibitor</th></tr>
<tr><td rowspan="4">VTE Dosing Instructions</td><td>CrCl ≥ 15 mL/minute</td><td>15 mg PO twice daily with food for 3 weeks followed by 20 mg PO daily with food</td><td>No dose adjustment is recommended for CrCl, even when CrCl < 15 mL/minute
Note: Patients with a serum creatinine > 2.5 mg/dL or CrCl < 25 mL/minute (as determined by Cockcroft-Gault equation) were excluded from clinical trials</td><td>10 mg PO twice daily for 1 week followed by 5 mg PO twice daily</td></tr>
<tr><td>CrCl < 15 mL/minute or ESRD</td><td>Avoid use</td><td>Strong dual CYP 3A4 <u>and</u> concomitant P-glycoprotein inhibitor[1]</td><td>Decrease dose by 50% [if patient already on 2.5 mg twice daily, then avoid]</td></tr>
<tr><td>Strong dual CYP 3A4 <u>and</u> concomitant P-glycoprotein inhibitor[1]</td><td rowspan="2">Avoid use</td><td rowspan="2">Strong dual CYP 3A4 <u>and</u> concomitant P-glycoprotein inducer[2]</td><td rowspan="2">Avoid use</td></tr>
<tr><td>Strong dual CYP 3A4 <u>and</u> concomitant P-glycoprotein inducer[2]</td></tr>
<tr><td>Use in liver disease</td><td colspan="4">CTP[3] class B or C: NOT recommended</td></tr>
<tr><td>Significant drug-drug interactions</td><td colspan="4">P-glycoprotein and CYP 3A4 interactions</td></tr>
<tr><td>Contraindications</td><td colspan="4">Active bleed, spinal puncture, neuroaxial anesthesia</td></tr>
<tr><td>Monitoring parameters</td><td colspan="4">• Routine monitoring of coagulation tests not required
• Baseline CBC with differential, serum creatinine, renal function test, hepatic function tests (then periodically)</td></tr>
</table>

[1] Strong dual CYP3A4 and P-glycoprotein inhibitors (*i.e.*, ketoconazole, itraconazole, ritonavir)
[2] Strong dual CYP3A4 and P-glycoprotein inducers (*i.e.*, carbamazepine, phenytoin, rifampin, St. John's Wort)
[3] See Appendix I: Child-Turcotte-Pugh (CTP) Scoring System

CrCl = creatinine clearance (mL/minute)
ESRD = end stage renal disease
CTP = Child-Turcotte-Pugh score

Continued on next page

Adult Venous Thromboembolism (VTE) Treatment for Cancer Patients (DVT and PE)

APPENDIX H: Direct Oral Anticoagulants (DOACs) - continued

Notes: DOACs are suggested for treatment of VTE in selected patients who have compelling indications to avoid LMWH. A multidisciplinary consultation is strongly recommended with Benign Hematology, Cardiology, and/or General Internal Medicine. Each case needs to be individually assessed prior to use of DOACs. There is no evidence available with DOACs in cancer patients who experience chemotherapy induced thrombocytopenia. See note below for reasons to avoid the use of DOACs.

Reasons to avoid use of DOACs in the cancer population

- Gastrointestinal and genitourinary cancers have shown increased risk of major bleeds with DOACs. DOACs should also be used with caution in cancers with high risk for mucosal bleeding.
- Lack of standardized testing for monitoring
- Complicated drug-drug interactions with chemotherapy agents. Assessing for drug-drug interaction and to transition patient to and from DOACs: Lexicomp®, Micromedex® or Clinical Pharmacology available at http://insidemdanderson.org (for internal use only).

DOACs	**Dabigatran (Pradaxa®)** Direct Thrombin Inhibitor		**Edoxaban[1] (Savaysa®)** Oral Factor Xa Inhibitor	
VTE Dosing Instructions	CrCl > 30 mL/minute	150 mg twice daily AFTER 5 days of treatment with parenteral anticoagulant	CrCl ≥ 51 mL/minute	60 mg PO daily started after at least 5 days of treatment with a parenteral anticoagulant: • If body weight ≤ 60 kg **or** on P-glycoprotein inhibitor[2] dose reduce to 30 mg PO daily
	CrCl < 50 mL/minute **and** any concomitant administration of P-glycoprotein inhibitor[2]	Avoid use	CrCl 15-50 mL/minute	Dose reduce to 30 mg PO daily
	CrCl ≤ 30 mL/minute or HD	No recommendations	CrCl < 15 mL/minute or ESRD	Avoid use
	Any concomitant administration of P-glycoprotein inducer[3]	Avoid use	Any concomitant administration of P-glycoprotein inducer[3]	Avoid use
Use in liver disease	CTP[4] class B or C: NOT recommended			
Significant drug-drug interactions	P-glycoprotein interactions			
Contraindications	Active bleed, spinal puncture, neuroaxial anesthesia			
Monitoring parameters	• Routine monitoring of coagulation tests not required • Baseline CBC with differential, renal function test, hepatic function tests (then periodically)			

[1] Edoxaban is currently not on the MD Anderson formulary

[2] P-glycoprotein inhibitors (*i.e.*, amiodarone, azithromycin, erithromycin, clarithromycin, dronedarone, oral ketoconazole, quinidine, verapamil)

[3] P-glycoprotein inducers (*i.e.*, rifampin)

[4] See Appendix I: Child-Turcotte-Pugh (CTP) Scoring System

CrCl = creatinine clearance (mL/minute) CTP = Child-Turcotte-Pugh score
ESRD = end stage renal disease HD = Hemodialysis

APPENDIX I: 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

SUGGESTED READINGS

Bauersachs, R., Berkowitz, S. D., Brenner, B., Buller, H. R., Decousus, H., Gallus, A. S., . . . Schellong, S. (2010). Oral rivaroxaban for symptomatic venous thromboembolism. *The New England Journal of Medicine*, *363*(26), 2499–2510. https://doi.org/10.1056/NEJMoa1007903

Büller, H. R., Prins, M. H., Lensin, A. W. A., Decousus, H., Jacobson, B. F., Minar, E., . . . Segers, A. (2012). Oral rivaroxaban for the treatment of symptomatic pulmonary embolism. *The New England Journal of Medicine*, *366*(14), 1287–1297. https://doi.org/10.1056/NEJMoa1113572

Cohen, A., Spiro, T., Büller, H., Haskell, L., Hu, D., Hull, R., . . . Tapson, V. (2013). Rivaroxaban for thromboprophylaxis in acutely Ill medical patients. *The New England Journal of Medicine*, *368*(6), 513–523. https://doi.org/10.1056/NEJMoa1111096

Jaff, M., Mcmurtry, M., Archer, S., Cushman, M., Goldenberg, N., Goldhaber, S., . . . Zierler, B. (2011). Management of massive and submassive pulmonary embolism, iliofemoral deep vein thrombosis, and chronic thromboembolic pulmonary hypertension. *Circulation*, *123*(16), 1788–1830. https://doi.org/10.1161/CIR.0b013e318214914f

Key, N., Khorana, A., Kuderer, N., Bohlke, K., Lee, A., Arcelus, J., . . . Falanga, A. (2019). Venous thromboembolism prophylaxis and treatment in patients with cancer: ASCO Clinical Practice Guideline update. *Journal of Clinical Oncology*. Advanced online publication. https://doi.org/10.1200/JCO.19.01461

Khorana, A., Streiff, M., Farge, D., Mandala, M., Debourdeau, P., Cajfinger, F., . . . Lyman, G. (2009). Venous thromboembolism prophylaxis and treatment in cancer: A consensus statement of major guidelines panels and call to action. *Journal Of Clinical Oncology*, *27*(29), 4919–4926. https://doi.org/10.1200/JCO.2009.22.3214

Lalama, J., Feeney, M., Vandiver, J., Beavers, K., Walter, L., & McClintic, J. (2015). Assessing an enoxaparin dosing protocol in morbidly obese patients. *Journal of Thrombosis and Thrombolysis*, *39*(4), 516–521. https://doi.org/10.1007/s11239-014-1117-y

Lee, A. (2009). Anticoagulation in the treatment of established venous thromboembolism in patients with cancer. *Journal of Clinical Oncology*, *27*(29), 4895–4901. https://doi.org/10.1200/JCO.2009.22.3958

Lee, A. (2012). Treatment of established thrombotic events in patients with cancer. *Thrombosis Research*, *129*, S146–S153. https://doi:10.1016/S0049-3848(12)70035-X

Lee, A. (2014). Prevention and treatment of venous thromboembolism in patients with cancer. *Hematology*, *2014*(1), 312–317. https://doi.org/10.1182/asheducation-2014.1.312

Lee, A., Levine, M., Baker, R., Bowden, C., Kakkar, A., Prins, M., . . . Gent, M. (2003). Low-molecular-weight heparin versus a coumarin for the prevention of recurrent venous thromboembolism in patients with cancer. *The New England Journal of Medicine*, *349*(2), 146–153. https://doi.org/10.1056/NEJMoa025313

Lee, Y., Vega, J., Duong, H., & Ballew, A. (2015). Monitoring Enoxaparin with Antifactor Xa Levels in Obese Patients. *Pharmacotherapy*, *35*(11), 1007–1015. https://doi.org/10.1002/phar.1658

Levine, M., Gu, C., Liebman, H., Escalante, C., Solymoss, S., Deitchman, D., . . . Julian, J. (2012). A randomized phase II trial of apixaban for the prevention of thromboembolism in patients with metastatic cancer. *Journal of Thrombosis and Haemostasis*, *10*(5), 807–814. https://doi.org/10.1111/j.1538-7836.2012.04693.x

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SUGGESTED READINGS - continued

Merli, G., Spiro, T., Olsson, C., Abildgaard, U., Davidson, B., Eldor, A., . . . Zawilska, K. (2001). Subcutaneous enoxaparin once or twice daily compared with intravenous unfractionated heparin for treatment venous thromboembolic disease. *Annals of Internal Medicine, 134*(3), 191–202. https://doi.org/10.7326/0003-4819-134-3-200102060-00009

National Comprehensive Cancer Network. (2019). *Cancer-Associated Venous Thromboembolic Disease* (NCCN Guideline Version 1.2019). Retrieved from https://www.nccn.org/professionals/physician_gls/pdf/vte.pdf.

Raskob, G., Van Es, N., Verhamme, P., Carrier, M., Di Nisio, M., Garcia, D., . . . Buller, H. (2018). Edoxaban for the treatment of cancer-associated venous thromboembolism. *New England Journal of Medicine, 378*, 615-624. https://doi.org/10.1056/NEJMoa1711948

Sebaaly, J., & Covert, K. (2018). Enoxaparin dosing at extremes of weight: Literature review and dosing recommendations. *Annals of Pharmacotherapy*, *52*(9), 898–909. https://doi.org/10.1177/1060028018768449

Schulman, S., Kearon, C., Kakkar, A., Mismetti, P., Schellong, S., Eriksson, H., . . . Goldhaber, S. (2009). Dabigatran versus warfarin in the treatment of acute venous thromboembolism. *The New England Journal of Medicine*, *361*(24), 2342–2352. https://doi.org/10.1056/NEJMoa0906598

Schulman, S., Kearon, C., Kakkar, A., Schellong, S., Eriksson, H., Baanstra, D., . . . Goldhaber, S. (2013). Extended use of dabigatran, warfarin, or placebo in venous thromboembolism. *The New England Journal of Medicine*, *368*(8), 709–718. https://doi.org/10.1056/NEJMoa1113697

Streiff, M. (2009). Diagnosis and initial treatment of venous thromboembolism in patients with cancer. *Journal of Clinical Oncology*, *27*(29), 4889–4894. https://doi.org/10.1200/JCO.2009.23.5788

van Oosterom, N., Winckel, K., & Barras, M. (2019). Evaluation of weight based enoxaparin dosing on anti-Xa concentrations in patients with obesity. *Journal of Thrombosis and Thrombolysis*. Advanced online publication. https://doi.org/10.1007/s11239-019-01847-4

Young, A., Marshall, A., Thirlwall, J., Chapman, O., Lokare, A., Hill, C., . . . Levine, M. (2018). Comparison of an oral factor Xa inhibitor with low molecular weight heparin in patients with cancer with venous thromboembolism: Results of a randomized trial (SELECT-D). *Journal of Clinical Oncology, 36*(20), 2017–2023. https://doi.org/10.1200/JCO.2018.78.8034

DEVELOPMENT CREDITS

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