In patients with a high clinical suspicion of deep vein thrombosis (DVT)/pulmonary embolism (PE), in the absence of contraindications, it is recommended that treatment with anticoagulants be started while awaiting the outcome of diagnostic tests(s).

For suspected PE, consider obtaining ECHO, Troponin level, and BNP.
Upper Extremity DVT

First occurrence?

Yes

Ultrasound/doppler

Acute DVT confirmed?

Yes

Significant extremity swelling?

Yes

Consult Vascular Surgery or Interventional Radiology

Consider catheter-directed thrombolysis if age of clot less than 30 days

No

Ultrasound/doppler

New defect?

Yes

See box A, Page 5

No

Consult Vascular Surgery or Interventional Radiology

Consider catheter-directed thrombolysis if age of clot less than 30 days

Is catheter infected and/or dysfunctional?

Yes

Consider removal of catheter

Maintain catheter and anticoagulate indefinitely while catheter is in place

No

See box A, Page 5

Lottery

Yes

Consult Vascular Surgery or Interventional Radiology

Consider catheter-directed thrombolysis if age of clot less than 30 days

No

Consult Vascular Surgery or Interventional Radiology

Consider catheter-directed thrombolysis if age of clot less than 30 days

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 Anticoagulation after catheter removal can be stopped after 3 months.

4 Consider post-thrombotic syndrome if symptoms occur in same extremity as prior VTE.

Approved by The Executive Committee of the Medical Staff 06/27/2017
Adult Venous Thromboembolism (VTE)
Treatment for Cancer Patients (DVT and PE)

This practice algorithm has been specifically developed for MD Anderson using a multidisciplinary approach and taking into consideration circumstances particular to MD Anderson, including the following: MD Anderson’s specific patient population; MD Anderson’s services and structure; and MD Anderson’s clinical information. Moreover, this algorithm is not intended to replace the independent medical or professional judgment of physicians or other health care providers. This algorithm should not be used to treat pregnant or lactating women.

Lower Extremity DVT

First occurrence?

Yes

- Ultrasound/doppler
- Acute DVT confirmed?

Yes

- Significant extremity swelling?\(^1\)

Yes

- Consult Vascular Surgery or Interventional Radiology
- Consider catheter-directed thrombolysis if age of clot is less than 30 days

No

- See box A, Page 5

No

- Continue evaluation of other causes of symptoms
- Consider prophylaxis if clinically indicated (See VTE Prophylaxis for Hospitalized Adult Patients Algorithm)

No

- See box A, Page 5

No

- Ultrasound/doppler
- New defect?

Yes

- See box A, Page 5

No

- Continue current management
- Consider post-thrombotic syndrome\(^2\) or other causes of symptoms
- Consider applying compression stockings if post-thrombotic syndrome

---

\(^1\) 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

\(^3\) Consider post-thrombotic syndrome when symptoms occur in site of prior VTE
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.

If CT angiogram cannot be performed, consider VQ scan. Consider STAT ECHO if clinical criteria are met, refer to Appendix E: Criteria for after hours STAT 2D-ECHO.

Refer to Appendix F for PE Classification.

Admission criteria to Telemetry/intermediate unit: Low-Intermediate Risk patients requiring anticoagulation

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 greater than 1 by 2D ECHO or CT, and elevated troponin or BNP.

Vascular group members include faculty from IR and 2 vascular surgeons.
Adult Venous Thromboembolism (VTE) Treatment for Cancer Patients (DVT and PE)

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Department of Clinical Effectiveness V6
Approved by The Executive Committee of the Medical Staff 06/27/2017

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**Upper Extremity DVT**

**Lower Extremity DVT**

**Low Risk PE**

A

Contraindications to anticoagulation?

- **Yes**
  - Withhold anticoagulation and monitor

- **No**
  - **Temporary IVC Filter**
  - **Permanent IVC Filter**

Patient on current anticoagulation therapy?

- **Yes**
  - Select anticoagulants, see Appendix D for management instructions

- **No**
  - Select anticoagulants, see Appendix G for management instructions

Does patient meet outpatient criteria for anticoagulation treatment? (see Appendix C)

- **Yes**
  - Monitor patient per selected anticoagulation therapy (see respective appendices)*
  - For patients with VTE and cancer, continue anticoagulant therapy indefinitely, or until cancer resolves, if no contraindication emerges

- **No**
  - Admit patient for evaluation and treatment or if already inpatient, continue with evaluation and treatment

---

1. See Appendix A for Contraindications to Anticoagulation
2. Criteria to consider for placement of a retrievable filter
   - If temporary/limited time (less than or equal to 2-3 months) of contraindication to anticoagulants place a retrievable IVC filter
   - Greater than 6 months survival expected
   - Performance Status less than or equal to 1

---

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

This practice algorithm has been specifically developed for MD Anderson using a multidisciplinary approach and taking into consideration circumstances particular to MD Anderson, including the following: MD Anderson’s specific patient population; MD Anderson’s services and structure; and MD Anderson’s clinical information. Moreover, this algorithm is not intended to replace the independent medical or professional judgment of physicians or other health care providers. This algorithm should not be used to treat pregnant or lactating women.

### APPENDIX A: Contraindications to Anticoagulation Therapy

<table>
<thead>
<tr>
<th>Absolute Contraindications:</th>
<th>Relative Contraindications:</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Cerebral hemorrhage, hemorrhage in the eye or vital organs or a drop in hemoglobin of 2 grams/dL in 24 hours</td>
<td>- Brain metastases conferring risk of bleeding (renal, choriocarcinoma, melanoma, thyroid cancer)</td>
</tr>
<tr>
<td>- Neurosurgery, ocular surgery or intracranial bleeding within past 10 days</td>
<td>- Spinal procedure and/or epidural placement</td>
</tr>
<tr>
<td>- Platelets less than 25 K/microliter, consult to benign hematology</td>
<td>- Major trauma or head trauma</td>
</tr>
<tr>
<td></td>
<td>- Major abdominal surgery within 48 hours</td>
</tr>
<tr>
<td></td>
<td>- Severe hypertension (systolic blood pressure greater than 200 mmHg, diastolic blood pressure greater than 120 mmHg)</td>
</tr>
<tr>
<td></td>
<td>- Endocarditis/pericarditis</td>
</tr>
<tr>
<td></td>
<td>- GI, GU bleeding within past 14 days</td>
</tr>
<tr>
<td></td>
<td>- Preexisting coagulopathy</td>
</tr>
<tr>
<td></td>
<td>- Platelets less than 50 K/microliter, consider consult to benign hematology</td>
</tr>
<tr>
<td></td>
<td>- Hypersensitivity to heparin, low molecular weight heparin (LMWH) or heparin induced thrombocytopenia</td>
</tr>
<tr>
<td></td>
<td>- Patient on active protocol that prohibits use of anticoagulation</td>
</tr>
<tr>
<td></td>
<td>- Bleeding diathesis</td>
</tr>
</tbody>
</table>

### APPENDIX B: Contraindications to Systemic Thrombolysis

<table>
<thead>
<tr>
<th>Absolute Contraindications:</th>
<th>Relative Contraindications:</th>
</tr>
</thead>
<tbody>
<tr>
<td>- History of hemorrhagic stroke or stroke of unknown origin</td>
<td>- Pregnancy or first post-partum week</td>
</tr>
<tr>
<td>- Intracranial tumor</td>
<td>- Non-compressible puncture sites</td>
</tr>
<tr>
<td>- Ischemic stroke in previous 3 months (except ischemic stroke within 4.5 hours)</td>
<td>- Traumatic resuscitation</td>
</tr>
<tr>
<td>- History of major trauma, surgery or head injury in previous 3 weeks</td>
<td>- Refractory hypertension (systolic blood pressure greater than 180 mmHg; diastolic blood pressure greater than 100 mmHg)</td>
</tr>
<tr>
<td>- Platelet count below 100 K/microliter</td>
<td>- Advanced liver disease</td>
</tr>
<tr>
<td></td>
<td>- Infective endocarditis</td>
</tr>
<tr>
<td></td>
<td>- Recent GI bleed (last 3 months)</td>
</tr>
<tr>
<td></td>
<td>- Life expectancy less than or equal to 6 months</td>
</tr>
</tbody>
</table>
APPENDIX C:  Outpatient Treatment Criteria

1. See Appendix A for contraindications
2. No co-morbidity requiring inpatient hospitalization
3. No clinical conditions requiring hospitalization
4. Likelihood of good compliance, ability to provide self-care and not at high-risk for falls
5. Adequate home support system and geographical accessibility for follow-ups
6. If pulmonary embolism, low risk and pulse oximetry greater than 95%; stable vital signs
7. Not intermediate risk (not submassive)

APPENDIX D:  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 LMWH.
- If patient is on a LMWH, check anti-factor Xa level 4 hours post injection.
- If peak anti-factor Xa level is subtherapeutic (less than 0.5 anti-factor Xa units), adjust dose of the LMWH to achieve a peak anti-factor Xa of 0.5 – 1.5 units\(^1\).
- If peak factor Xa level is within the therapeutic range\(^2\), consider increasing dose of LMWH 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.

\(^1\) See recommendations for specific agents on Page 8.
\(^2\) Range may vary, based on specific institutional ranges.
APPENDIX E: Criteria for After Hours STAT 2D-ECHO for Patients with Suspected PE

<table>
<thead>
<tr>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. 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)</td>
</tr>
<tr>
<td>b. Patient is hemodynamically unstable (systolic blood pressure less than 90 mmHg or receiving vasopressors)</td>
</tr>
<tr>
<td>c. PE has to be highly suspected and no other etiology would explain shock (no septic, hemorrhagic or hypovolemic shock)</td>
</tr>
<tr>
<td>d. PERT team member is to contact and discuss directly the need of the echo with the cardiologist on-call before sonographer is contacted.</td>
</tr>
</tbody>
</table>

APPENDIX F: PE Classification

<table>
<thead>
<tr>
<th>Low Risk</th>
<th>Intermediate Risk</th>
<th>High Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any PE:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Without RV dysfunction <em><strong>and</strong></em></td>
<td>Low-Intermediate</td>
<td>• Sustained hypotension (systolic blood pressure less than 90 mmHg for at least 15 minutes) <em><strong>or</strong></em></td>
</tr>
<tr>
<td>• With normal BNP/troponin</td>
<td>High-Intermediate</td>
<td>• Persistent bradycardia (heart rate less than 40 bpm) with signs or symptoms of shock <em><strong>or</strong></em></td>
</tr>
<tr>
<td>RV dysfunction <em><strong>or</strong></em> elevated BNP <em><strong>or</strong></em> troponin</td>
<td>RV dysfunction <em><strong>and</strong></em> elevated BNP <em><strong>or</strong></em> troponin</td>
<td>• Need for inotropic support</td>
</tr>
</tbody>
</table>
APPENDIX G: Anticoagulation Therapy Options for Cancer Patients

## LMWH1 Regimens for Treatment of Cancer Associated Thrombosis

<table>
<thead>
<tr>
<th>DRUG</th>
<th>DOSE / ROUTE / FREQUENCY</th>
<th>MONITORING2</th>
<th>DOSE ADJUSTMENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dalteparin (Fragmin®)</strong>*</td>
<td><strong>Round to nearest International Units (IU) dose, given subcutaneously daily</strong></td>
<td></td>
<td>• Consider reducing the daily dose by 50% when platelets are between 20 K/microliter – 50 K/microliter and to 5,000 IU when platelets are less than 20 K/microliter</td>
</tr>
<tr>
<td><em>Preferred choice, FDA approved for cancer patients</em></td>
<td>Actual Body Weight (kg)</td>
<td>Month 1 200 IU/kg</td>
<td>Month 2-6 150 IU/kg</td>
</tr>
<tr>
<td></td>
<td>Less than or equal to 56</td>
<td>10,000 IU</td>
<td>7,500 IU</td>
</tr>
<tr>
<td></td>
<td>57-68</td>
<td>12,500 IU</td>
<td>10,000 IU</td>
</tr>
<tr>
<td></td>
<td>69-82</td>
<td>15,000 IU</td>
<td>12,500 IU</td>
</tr>
<tr>
<td></td>
<td>83-98</td>
<td>18,000 IU</td>
<td>15,000 IU</td>
</tr>
<tr>
<td>Greater than or equal to 99</td>
<td>Limited data suggests dalteparin 200 IU/kg based on actual body weight (with no dose capping) in one or two divided doses. An alternative option is enoxaparin 1 mg/kg twice daily. Consider monitoring anti-Xa levels and adjust dose as needed.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Enoxaparin (Lovenox®)</strong></td>
<td>1 mg/kg subcutaneously every 12 hours or 1.5 mg/kg* subcutaneously daily in selected patients</td>
<td>Same as above</td>
<td>• If creatinine clearance less than 30 mL/minute: 1 mg/kg daily</td>
</tr>
<tr>
<td><em>Use enoxaparin with caution in patients with platelets less than 100 K/microliter</em></td>
<td><em>Limited data suggest once per day dosing is inferior in cancer patients</em></td>
<td></td>
<td>• Obtain anti-Xa level in patients with weight greater than 150 kg or less than 50 kg</td>
</tr>
</tbody>
</table>

1 Note: • Low-Molecular Weight Heparins (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

2 If lab results indicate Heparin Induced Thrombocytopenia (HIT) Treatment Algorithm

*Appendix G continued on next page*
## APPENDIX G – continued: Anticoagulation Therapy Options for Cancer Patients

### Unfractionated Heparin (UFH)

<table>
<thead>
<tr>
<th>TREATMENT</th>
<th>MONITORING</th>
</tr>
</thead>
</table>
| • 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 greater than 2 for 24 hours. | Baseline labs for heparin should be CBC with platelets, aPTT/PT, serum creatinine |

### Warfarin¹ (Selected Vitamin K Antagonists) – For Long-term Management

<table>
<thead>
<tr>
<th>TREATMENT</th>
<th>MONITORING</th>
</tr>
</thead>
</table>
| • Overlap warfarin (2.5 – 5 mg PO) with induction therapy (LMWH, Factor Xa Inhibitor, or UFH-SC) beginning on Day 1 of therapy  
  • Continue induction therapy until INR greater than or equal to 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 within 3-5 days, then at least every month if not more frequently |

### Fondaparinux (Arixtra®) (Factor Xa Inhibitor)

<table>
<thead>
<tr>
<th>ACTUAL BODY WEIGHT (kg)</th>
<th>FONDAPARNUX Daily SC DOSE</th>
<th>MONITORING</th>
</tr>
</thead>
</table>
| Less than 50  
50 – 100  
Greater than 100 | 5 mg  
7.5 mg  
10 mg | Requires baseline laboratory tests: CBC with platelets, aPTT/PT, serum creatinine |

<table>
<thead>
<tr>
<th>MONITORING</th>
<th></th>
</tr>
</thead>
</table>
| • If creatinine clearance is between 30 - 50 mL/minute: use with caution  
  • If creatinine clearance is less than 30 mL/minute: contraindicated  
  • Use fondaparinux with caution in patients with platelets less than 100 K/microliter | |

¹ Use of warfarin in cancer patients has been shown to be less effective at preventing clot recurrence than LMWH.
APPENDIX H: Direct Oral Anticoagulants (DOAC) (ATTENTION: Expert panels DO NOT RECOMMEND use of these drugs in patients with cancer. 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.

<table>
<thead>
<tr>
<th>Direct Oral Anticoagulants (DOAC)</th>
<th>Rivaroxaban (Xarelto®) Oral Factor Xa Inhibitor</th>
<th>Dabigatran (Pradaxa®) Direct Thrombin Inhibitor</th>
</tr>
</thead>
<tbody>
<tr>
<td>VTE Dosing Instructions</td>
<td>15 mg PO twice daily with food for 3 weeks followed by 20 mg PO daily with food</td>
<td>150 mg twice daily AFTER 5-10 days of treatment with parenteral anticoagulant</td>
</tr>
<tr>
<td>CrCl greater than or equal to 30 mL/minute</td>
<td>CrCl greater than 30 mL/minute</td>
<td>Avoid use</td>
</tr>
<tr>
<td>CrCl less than 30 mL/minute or ESRD</td>
<td>Avoid use</td>
<td>CrCl less than 30 mL/minute or HD</td>
</tr>
<tr>
<td>Use in liver disease</td>
<td>CTP class B or C: NOT recommended</td>
<td>CTP class B or C: NOT recommended</td>
</tr>
<tr>
<td>Contraindications</td>
<td>Active bleed, spinal puncture, neuroaxial anesthesia</td>
<td></td>
</tr>
<tr>
<td>Significant drug-drug interactions</td>
<td>P-glycoprotein and CYP 3A4 interactions</td>
<td></td>
</tr>
<tr>
<td>Monitoring parameters</td>
<td>Routine monitoring of coagulation tests not required</td>
<td>No recommendations</td>
</tr>
<tr>
<td></td>
<td>Baseline CBC with differential, serum creatinine, renal function test, hepatic function tests</td>
<td></td>
</tr>
</tbody>
</table>

Pgp-I = P-glycoprotein inhibitor; CrCl = creatinine clearance (mL/minute); ESRD = end stage renal disease; HD = Hemodialysis; CTP = Child-Turcotte-Pugh score

Note:

Reasons to avoid use of Direct Oral Anticoagulants (DOAC) in the cancer population:

- Limited number of patients with cancer studied in DOAC clinical trials
- Lack of standardized testing for monitoring
- Assessing for drug-drug interaction: Lexicomp® or Micromedex®, available at http://insidemdanderson.org (for internal use only)
- Limited availability of reversal agents available
- Complicated drug-drug interactions with chemotherapy agents

Appendix H continued on next page
APPENDIX H continued: Direct Oral Anticoagulants (DOAC) (ATTENTION: Expert panels DO NOT RECOMMEND use of these drugs in patients with cancer. 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.

<table>
<thead>
<tr>
<th>Direct Oral Anticoagulants (DOAC)</th>
<th>Apixaban (Eliquis®) Oral Factor Xa Inhibitor</th>
<th>Edoxaban¹ (Savaysa®) Oral Factor Xa Inhibitor</th>
</tr>
</thead>
<tbody>
<tr>
<td>VTE Dosing Instructions</td>
<td>No dose adjustment is recommended</td>
<td>CrCl greater than 51 mL/minute</td>
</tr>
<tr>
<td>Strong dual CYP3A4 and concomitant Pgp-I,² ketoconazole, itraconazole, ritonavir, clarithromycin</td>
<td>10 mg PO twice daily for 1 week followed by 5 mg PO twice daily</td>
<td>60 mg PO daily started after at least 5-10 days of treatment with a parenteral anticoagulant ¹If body weight less than or equal to 60 kg or on P-gp I² dose reduce to 30 mg PO daily</td>
</tr>
<tr>
<td>CrCl 15-50 mL/minute</td>
<td>Dose reduce to 30mg PO daily</td>
<td></td>
</tr>
</tbody>
</table>

### Use in liver disease
- CTP class B or C: NOT recommended
- CTP class B or C: NOT recommended

### Contraindications
- Active bleed, spinal puncture, neuroaxial anesthesia

### Significant drug-drug interactions
- P-glycoprotein and CYP 3A4 interactions

### Monitoring parameters
- Routine monitoring of coagulation tests not required
- Baseline CBC with differential, renal function test, hepatic function tests

**Note:**

- Reasons to avoid use of Direct Oral Anticoagulants (DOAC) in the cancer population:
  - Limited number of patients with cancer studied in DOAC clinical trials
  - Lack of standardized testing for monitoring
  - Assessing for drug-drug interaction: Lexicomp® or Micromedex®, available at http://inside.mdanderson.org (for internal use only)

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¹Edoxaban is currently not on the MD Anderson formulary.

²P-gp-I (verapamil and quinidine or short-term concomitant azithromycin, clarithromycin, erythromycin, oral itraconazole or oral ketoconazole)

Pgp-I = P-glycoprotein inhibitor; CrCl = creatinine clearance (mL/minute); Scr = Serum creatinine; ESRD = end stage renal disease; CTP = Child-Turcotte-Pugh score

---

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*Department of Clinical Effectiveness V6
Approved by The Executive Committee of the Medical Staff 06/27/2017*
SUGGESTED READINGS


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

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DEVELOPMENT CREDITS

This practice consensus algorithm is based on majority expert opinion of the VTE workgroup consisting of Faculty at the University of Texas MD Anderson Cancer Center. It was developed using a multidisciplinary approach that included input from the faculty and staff. The core team included:

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