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.

Clinical Suspicion of 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 consider obtaining ECHO, Troponin level, and BNP

APPENDIX A: Contraindications to Anticoagulation Therapy………………...Page 6
APPENDIX B: Contraindications to Thrombolysis…………………………...Page 6
APPENDIX C: Outpatient Treatment Criteria………………………………Page 7
APPENDIX D: Recurrent VTE Anticoagulation Therapy Options ………...Page 7
for patients currently on standard anticoagulant therapy
APPENDIX E: Anticoagulation Therapy Options for the Cancer Patients….Page 8-9
APPENDIX F: New Oral Anticoagulants ………………………………………....Page 10-12
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Upper Extremity DVT

First occurrence?

Yes

No

Ultrasound/Doppler

Acute DVT confirmed?

Yes

No

Significant extremity swelling?

Yes

No

Catheter related?

Yes

No

Is catheter functional and not infected?

Yes

No

Maintain catheter and anticoagulate indefinitely while catheter is in place

No new defect

See Box A Page 5

Consult Vascular Surgery or Interventional Radiology

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

See Box A Page 5

Consider removal of catheter

Continue current management

Consider post-thrombotic syndrome or other causes of symptoms

Consider applying sleeve compression if post-thrombotic syndrome

Continue evaluation of other causes of symptoms

Consider prophylaxis if clinically indicated (See VTE Prophylaxis Algorithm)

Yes

No

New defect

Yes

No

Ultrasound/Doppler

Continued evaluation of other causes of symptoms

Consider prophylaxis if clinically indicated (See VTE Prophylaxis Algorithm)

Yes

No

Consult Vascular Surgery or Interventional Radiology

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

Maintain catheter and anticoagulate indefinitely while catheter is in place

Consider removal of catheter

Continue current management

Consider post-thrombotic syndrome or other causes of symptoms

Consider applying sleeve compression if post-thrombotic syndrome

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
Lower Extremity DVT

First occurrence?

Yes

Utrasound/Doppler

No new defect

See Box A Page 5

New defect

Ultrasound/Doppler

No

Significant extremity swelling?

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 new defect

Continue evaluation of other causes of symptoms

Consider prophylaxis if clinically indicated (See VTE Prophylaxis Algorithm)

Yes

Acute DVT confirmed?

Yes

Consider post-thrombotic syndrome or other causes of symptoms

Consider applying compression stockings if post-thrombotic syndrome

No

Continue current management

Consider post-thrombotic syndrome 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
Adult Venous Thromboembolism (VTE) Treatment for Cancer Patients (DVT and PE)

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Pulmonary Embolism (PE)

First occurrence of PE?

CT angiogram?

PE confirmed?

Massive?

Contraindications to anticoagulation?

No

Yes

Consult Vascular Surgery

Systolic blood pressure greater than 90 mmHg?

No

Yes

Treat with systemic thrombolytics?

No

Yes

Consult Vascular Surgery

Follow-up

No new defect

Continue current management

Submassive?

See Page 5

No

Yes

Contraindications to thrombolytics?

No

Yes

Treat with anticoagulant

No new defect

See Box A on Page 5

CT angiogram?

New defect

Continue evaluation of other causes of symptoms

Consider prophylaxis if clinically indicated (See VTE Prophylaxis Algorithm)

Yes

No

Contraindications to anticoagulation?

No

Yes

Consult Vascular Surgery

4 See Appendix A for Contraindications to Anticoagulation

5 See Appendix B for Contraindications to Thrombolytics

6 See Appendix F for Alteplase treatment and monitoring

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 done, consider VQ scan

3 Submassive pulmonary embolism (PE): Any PE that is not massive (see below).

Massive pulmonary embolism (PE):

- Sustained hypotension (systolic blood pressure less than 90 mmHg for at least 15 minutes) or
- Persistent bradycardia (Heart Rate less than 40 bpm with signs or symptoms of shock
- Need for inotropic support

4 See Appendix A for Contraindications to Anticoagulation

5 See Appendix B for Contraindications to Thrombolytics

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Treatment for all VTE

A

Contraindications to anticoagulation?

Yes

No

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

Yes

No

Patient on current anticoagulation therapy?

Yes

No

Upper extremity DVT

Withhold anticoagulation and monitor

Temporary contraindication to anticoagulant?

Yes

Retrievable IVC Filter

No

Permanent IVC Filter

Lower extremity DVT or PE

Monitor patient per selected anticoagulation therapy (see respective appendices)*

*For patients with VTE and cancer, continue anticoagulant therapy indefinitely, or until cancer resolves, or if no contraindication emerges

Treatment for all VTE

Upper extremity DVT

Withhold anticoagulation and monitor

Temporary contraindication to anticoagulant?

Yes

Retrievable IVC Filter

No

Permanent IVC Filter

Lower extremity DVT or PE

Monitor patient per selected anticoagulation therapy (see respective appendices)*

*For patients with VTE and cancer, continue anticoagulant therapy indefinitely, or until cancer resolves, or if no contraindication emerges

Contraindications to Anticoagulation

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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Department of Clinical Effectiveness V5
Approved by The Executive Committee of the Medical Staff 06/30/2015
APPENDIX A: Contraindications to Anticoagulation Therapy:

### Absolute Contraindications:
- Cerebral hemorrhage, hemorrhage in the eye or vital organs or a drop in hemoglobin of 2 gm/dL in 24 hours
- Neurosurgery, ocular surgery or intracranial bleeding within past 10 days

### 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 (Systolic BP greater than 200 mmHg, Diastolic BP greater than 120 mmHg)
- Endocarditis/pericarditis
- GI, GU bleeding within past 14 days
- Preexisting coagulopathy
- Thrombocytopenia less than 50,000/ul
- Hypersensitivity to heparin, low molecular weight heparin (LMWH) or heparin induced thrombocytopenia
- Patient on active protocol that prohibits use of anticoagulation
- Bleeding diathesis

APPENDIX B: Contraindications to Systemic Thrombolysis:

### Absolute
- History of hemorrhagic stroke or stroke of unknown origin
- Intracranial tumor
- Ischemic stroke in previous 3 months
- History of major trauma, surgery or head injury in previous 3 weeks
- Platelet count below 100,000/mm³

### Relative
- Pregnancy or first post-partum week
- Non-compressible puncture sites
- Traumatic resuscitation
- Refractory hypertension (systolic pressure greater than 180 mmHg; diastolic blood pressure greater than 100)
- Advanced liver disease
- Infective endocarditis
- Recent GI bleed (last 3 months)
- Life expectancy less than or equal to 6 months
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, pulse oximetry greater than 95%; stable vital signs

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
- If peak factor Xa level is within the therapeutic range, 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: Anticoagulation Therapy Options for the Cancer Patients

#### LMWH Regimens for Treatment of Cancer Associated Thrombosis

<table>
<thead>
<tr>
<th>DRUG</th>
<th>DOSE / ROUTE / FREQUENCY</th>
<th>MONITORING</th>
<th>DOSE ADJUSTMENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dalteparin (Fragmin®)</td>
<td>Round to nearest International Units (IU) dose, given subcutaneously daily</td>
<td>Baseline CBC with platelets, aPTT, PT and serum creatinine</td>
<td>Consider reducing the daily dose by 50% when platelets are between 20,000/mm³ - 50,000/mm³ and to 5,000 international units when platelets are less than 20,000/mm³</td>
</tr>
<tr>
<td>*Preferred choice, FDA approved for cancer patients</td>
<td>Actual Body Weight (kg)</td>
<td>Month 1</td>
<td>Month 2-6</td>
</tr>
<tr>
<td></td>
<td>200 IU/kg</td>
<td>150 IU/Kg</td>
<td>For surgical patients, platelets every 3 days between days 4 and 14 after beginning LMWH then as clinically indicated</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></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></td>
<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>
</tr>
<tr>
<td>Enoxaparin (Lovenox®)</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: Use 50% of total daily dose</td>
</tr>
<tr>
<td>*Use enoxaparin with caution in patients with platelets less than 100,000/mm³</td>
<td>▪️ Limited data suggest once per day dosing is inferior in cancer patients</td>
<td></td>
<td>Obtain anti-Xa in patients with weight greater than 150 kg or less than 50 kg</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>a. For 1 mg/kg every 12 hour dosing regimen: adjust dose to obtain anti-Xa level of 0.6 - 1.0 InternationalUnits/mL (4-6 hours after fourth dose)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>b. For 1.5 mg/kg every 24 hour dosing regimen: adjust dose to obtain anti-Xa level of 1.0 - 1.5 International Units/mL (4-6 hours after fourth dose)</td>
</tr>
</tbody>
</table>

**NOTES:**
- 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.
- If lab results indicates Heparin Induced Thrombocytopenia, follow management guideline per Heparin Induced Thrombocytopenia (HIT) Algorithm.

---

**Appendix E Continued on Next Page**
APPENDIX E – continued:  Anticoagulation Therapy Options for the Cancer Patients

### Unfractionated Heparin (UFH)

<table>
<thead>
<tr>
<th>TREATMENT</th>
<th>MONITORING</th>
</tr>
</thead>
<tbody>
<tr>
<td>• If fixed dose, unmonitored subcutaneous UFH is chosen.</td>
<td>Baseline labs for heparin should be CBC with platelets, aPTT/PT, serum creatinine</td>
</tr>
<tr>
<td>• 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 greater than 2.0 for 24 hours.</td>
<td></td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>TREATMENT</th>
<th>MONITORING</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Overlap warfarin (2.5 – 5 mg PO) with induction therapy (LMWH, Factor Xa Inhibitor, or UFH-SC) beginning on Day 1 of therapy</td>
<td>• INR Goal: 2-3</td>
</tr>
<tr>
<td>• Continue LMWH/Factor Xa Inhibitor subcutaneously until INR greater than or equal to 2 for two days, AND patient has received at least 4-5 days of induction therapy overlap</td>
<td>• Baseline CBC with platelet count, aPTT/PT, liver function tests</td>
</tr>
<tr>
<td></td>
<td>• Follow-up for PT/INR within 3-5 days, then at least every month if not more frequently</td>
</tr>
</tbody>
</table>

#### Fondaparinux (Arixtra®) (Factor Xa Inhibitor) – Fondaparinux Dose Subcutaneously Daily

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

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)

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**APPENDIX F**: New Oral Anticoagulants (NOAC) (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 NOACs.

<table>
<thead>
<tr>
<th>DABIGATRAN DOSE</th>
<th>MONITORING</th>
<th>COMMENTS</th>
</tr>
</thead>
</table>
| After at least 5 days of induction therapy (LMWH, Factor Xa Inhibitor, or UFH-SC), begin dabigatran 150 mg PO twice daily after last dose of Dalteparin, or 12 hours after Enoxaparin, or 4 hours after UFH infusion is stopped | • Routine monitoring of coagulation tests not required  
• Baseline CBC with differential, renal function tests, hepatic function tests, Anti-Factor Xa if clinically indicated and available | • If creatinine clearance less than 30 mL/minute – avoid use  
• Mild hepatic impairment – no adjustment  
• Moderate to severe hepatic impairment (Child Pugh class B or C) and patients with any hepatic disease associated with coagulopathy – avoid use  
• Please be aware of drug interactions |

<table>
<thead>
<tr>
<th>RIVAROXABAN (Xarelto®) DOSE</th>
<th>MONITORING</th>
<th>COMMENTS</th>
</tr>
</thead>
</table>
| 15 mg PO twice daily with food for 3 weeks followed by 20 mg PO with food daily | • Routine monitoring of coagulation tests not required  
• Baseline CBC with differential, renal function tests, hepatic function tests, Anti-Factor Xa if clinically indicated and available | • If creatinine clearance less than 30 mL/minute – avoid use  
• Mild hepatic impairment – no adjustment  
• Moderate to severe hepatic impairment (Child Pugh class B or C) and patients with any hepatic disease associated with coagulopathy – avoid use  
• Please be aware of drug interactions |

**Note:**

**Reasons to avoid use of New Oral Anticoagulants (NOAC) in the cancer population:**

- Limited number of patients with cancer studied in NOAC clinical trials
- Lack of standardized testing for monitoring
- No reversal agents available
- Complicated drug-drug interactions with chemotherapy agents

---

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APPENDIX F: New Oral Anticoagulants (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 NOACs.

Reasons to avoid use of New Oral Anticoagulants (NOAC) in the cancer population:
- Limited number of patients with cancer studied in NOAC clinical trials
- Lack of standardized testing for monitoring
- No reversal agents available
- Complicated drug-drug interactions with chemotherapy agents

### APIXABAN1 (Factor Xa Inhibitor)

<table>
<thead>
<tr>
<th>APIXABAN1 DOSE</th>
<th>MONITORING</th>
<th>COMMENTS</th>
</tr>
</thead>
</table>
| 10 mg PO twice daily for 1 week followed by 5 mg PO twice daily | - Routine monitoring of coagulation tests not required  
- Baseline CBC with differential, renal function tests, hepatic function tests, Anti-Factor Xa if clinically indicated and available | - If creatinine clearance less than 15 mL/minute – avoid use  
- Mild hepatic impairment – no adjustment  
- Moderate to severe hepatic impairment (Child Pugh class B or C) and patients with any hepatic disease associated with coagulopathy – avoid use  
- Please be aware of drug interactions |

### EDOXABAN1 (Factor Xa Inhibitor)

<table>
<thead>
<tr>
<th>EDOXABAN1 DOSE</th>
<th>MONITORING</th>
<th>COMMENTS</th>
</tr>
</thead>
</table>
| 60 mg PO Daily started after at least 5 days of treatment with a parenteral anticoagulant  
- If body weight less than or equal to 60 kg dose reduce to 30 mg PO daily | - Routine monitoring of coagulation tests not required  
- Baseline CBC with differential, renal function tests, hepatic function tests, Anti-Factor Xa if clinically indicated and available | - If creatinine clearance less than 15 mL/minute – avoid use  
- If creatinine clearance between 15-50mL/minute – dose reduce to 30mg PO Daily  
- Hepatic Impairment Mild – no adjustment required  
- Hepatic Impairment Moderate-Severe – avoid use  
- If patient is on a concomitant P-glycoprotein inhibitors (quinidine, verapamil, azithromycin, clarithromycin, erythromycin, itraconazole, and ketoconazole) – dose reduce to 30mg PO daily |

1 Apixaban and Edoxaban are currently not on the MD Anderson formulary.
APPENDIX G: Thrombolytics

<table>
<thead>
<tr>
<th>ALTEPLASE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>TREATMENT</strong></td>
</tr>
</tbody>
</table>
| Alteplase 100 mg IV over 2 hours | C1: Critical Care, Emergency Department, Operating Room  
C2: Monitored Intermediate Care  
C3: Acute Care Unit | • Utilization of a portable cardiac monitor with a physician/designee at bedside  
• Neurologic exam to rule out intracranial bleeding  
• Vital signs per routine, based on level of care  
• HOLD ANTICOAGULATION while receiving alteplase treatment |
SUGGESTED READINGS


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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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