Adult Venous Thromboembolism (VTE)

Treatment for Cancer Patients (DVT and PE)

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).

Incidental VTE findings should be managed as symptomatic VTEs.

Suspected Upper Extremity DVT

Suspected Lower Extremity DVT

Suspected PE

Clinical Suspicion of VTE

DVT/PE

Suspected superficial venous thrombosis (SVT)

Abdominal organ vein thrombosis [splanchnic vein thrombosis (SPVT), mesenteric vein thrombosis (MVT), gonadal vein thrombosis (GVT), hepatic vein thrombosis (HVT), portal vein thrombosis (PVT)]

Consider consultation with Benign Hematology or General Internal Medicine

Anticoagulation Management

Inferior Vena Cava (IVC) Filter Retrieval

APPENDIX A: Contraindications to Systemic Thrombolysis

APPENDIX B: PE Classification

APPENDIX C: Contraindications to Anticoagulation Therapy

APPENDIX D: Outpatient Treatment Criteria

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

APPENDIX F: Anticoagulation Therapy Options for Cancer Patients with Active VTE

APPENDIX G: Direct Oral Anticoagulants (DOACs)

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

Suggested Readings

Development Credits

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

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Suspected upper extremity DVT

First occurrence?

Yes

Ultrasound/doppler

No

Ultrasound/doppler

Acute DVT confirmed?

Yes

Ultrasound/doppler

No

New defect?

Yes

Consult Interventional Radiology (IR) for consideration of catheter-directed therapy (thrombectomy versus thrombolysis)

No

See Anticoagulation Management (Box A) on Page 6

Significant extremity swelling?

Yes

Catheter related?

Yes

Maintain catheter and anticoagulate indefinitely while catheter is in place

No

See Anticoagulation Management (Box A) on Page 6

No

Is catheter infected and/or dysfunctional?

Yes

Consider removal of catheter

Anticoagulation can be stopped 3 months after catheter removal

No

See Anticoagulation Management (Box A) on Page 6

Yes

• Continue evaluation of other causes of symptoms

• Consider prophylaxis if clinically indicated (see VTE Prophylaxis for Adult Patients algorithm)

No

See Anticoagulation Management (Box A) on Page 6

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)

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

See Appendix A: Contraindications to Systemic Thrombolysis

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

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---

**Suspected lower extremity DVT**

- **First occurrence?**
  - Yes
    - Ultrasound/doppler
    - Acute DVT confirmed?
      - Yes
        - Continue current management
        - Consider post-thrombotic syndrome when symptoms occur at the site of prior VTE or other causes of symptoms
        - Consider applying compression stockings if post-thrombotic syndrome
        - If significant lower extremity swelling, consider IR consult/referral
      - No
        - See Anticoagulation Management (Box A) on Page 6
  - No
    - Ultrasound/doppler
    - New defect?
      - Yes
        - See Anticoagulation Management (Box A) on Page 6
      - No
        - Continue evaluation of other causes of symptoms
        - Consider prophylaxis if clinically indicated (see VTE Prophylaxis for Adult Patients algorithm)

---

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

Disclaimer: This algorithm has been developed for MD Anderson using a multidisciplinary approach considering circumstances particular to MD Anderson’s specific patient population, services and structure, and clinical information. This is not intended to replace the independent medical or professional judgment of physicians or other health care providers in the context of individual clinical circumstances to determine a patient’s care. This algorithm should not be used to treat pregnant or lactating women.

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)

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

2. Consult Pulmonary Embolism Response Team (PERT) First Responder and refer to PERT algorithm

3. Determine if patient has evidence of RV dysfunction
   - Review report for CT angiogram and/or ECHO
   - Contact Diagnostic Imaging (DI) for RV/LV ratio if not reported

4. Continue evaluation of other causes of symptoms
   - Consider prophylaxis if clinically indicated (see VTE Prophylaxis for Adult Patients algorithm)

Low risk
Low-Intermediate risk, High-Intermediate risk or High risk
Primary team to manage as clinically indicated, see Anticoagulation Management (Box A) on Page 6

Suspected PE

CT angiogram
Consider VQ scan and routine 2D-ECHO if CT angiogram cannot be performed

PE confirmed?

Yes

No

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
Suspected SVT

- Continue evaluation of other causes of symptoms
- Consider prophylaxis if clinically indicated (see VTE Prophylaxis for Adult Patients algorithm)

First occurrence?

- Ultrasound/doppler

Yes

Acute SVT confirmed?

- Ultrasound/doppler

Yes

Upper extremity SVT

- Symptomatic treatment with warm compresses and NSAID if no contraindication
- If symptoms worsen or progression of SVT seen on re-imaging, consider prophylaxis dose anticoagulation²
- If progression to deep vein thrombosis, recommend treatment dose anticoagulation (see Appendix F)

No

Lower extremity SVT

- Prophylaxis dose anticoagulation² for at least 45 days
- Consider symptomatic treatment with warm compresses
- If symptoms worsen or progression of SVT seen on re-imaging, consider treatment dose anticoagulation (see Appendix F)
- If progression to deep vein thrombosis, recommend treatment dose anticoagulation (see Appendix F)

- Refer to Box A or B above for type of SVT

New defect?

- Ultrasound/doppler

Yes

- Continue evaluation of other causes of symptoms
- Consider symptomatic treatment with warm compresses

No

- Continue current management
- Consider symptomatic treatment with warm compresses

---

NSAID = non-steroidal anti-inflammatory drug

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

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ANTICOAGULATION MANAGEMENT

Upper extremity DVT
Lower extremity DVT
Low Risk PE

A

Contraindications to anticoagulation? 1

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

Withhold anticoagulation and monitor

Order placed for IVC filter

Interventional Radiology (IR) reviews request for patient eligibility for IVC filter

Consult Benign Hematology

Patient eligible for filter placement?

Permanent filter?

Retrievable filter placement? 3

Consult Benign Hematology

Benign Hematology to manage patient

Admit patient for evaluation and treatment or if already inpatient, continue with evaluation and treatment

Patient on current anticoagulation therapy?

Select anticoagulants, see Appendix E for management instructions

Select anticoagulants, see Appendix F for management instructions

Findings inconclusive for filter placement

Patient not eligible for filter placement

Consult Benign Hematology

Consult Benign Hematology

Permanent filter placement with no plan for retrieval

Retrievable filter placement

Refer to Page 7 for IVC Filter Retrieval

A

IVC = inferior vena cava

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

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

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

- For central line associated upper extremity VTE, anticoagulation can be stopped 3 months after catheter removal

- For patients with VTE and active cancer, recurrent VTE, or unprovoked VTE, continue anticoagulation therapy indefinitely if no contraindication emergencies

- For patients with increased risk of bleeding, recommended treatment duration should be a minimum of 6 months. After 6 months consider consulting Benign Hematology to evaluate the risks and benefits of continuing therapy.

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INFERIOR VENA CAVA (IVC) FILTER RETRIEVAL

- A 10 week Interventional Radiology (IR) follow-up appointment for IVC filter removal will be scheduled when the placement order for the retrievable filter is placed
- If filter removal needed prior to 10 weeks, consult IR

Patient has retrievable IVC filter placed for a temporary indication

Patient clinically appropriate for IVC filter removal but transient short term delay expected?

IR to reschedule removal

1 week prior to IVC filter removal date, IR to assess if removal clinically indicated

Yes

No

Yes

No

Yes

No

Yes

No

Yes

No

Successful removal?

Successful removal?

No further follow-up for IVC filter care

Consult Benign Hematology for anticoagulant maintenance

Consult Benign Hematology for anticoagulant maintenance

Patient returns to primary service

Follow-up with Benign Hematology in 2-3 months

Schedule Benign Hematology consult prior to IR removal appointment

Hematologist determines removal clinically indicated?

Yes

No

IVC filter to be permanent?

Yes

No

Consult Benign Hematology for anticoagulant maintenance

No further follow-up for IVC filter care

---

1 Retrievable IVC filter placement: anticipated surgery or temporary contraindication to anticoagulation with potential for retrieval
2 If filter removal was unsuccessful because of in situ thrombus, then consider re-consulting IR for IVC filter removal following a period of therapeutic anticoagulation
3 Short term delays for removal such as: upcoming surgery with need to hold anticoagulation temporarily and at high risk for re-thrombosis; temporary clinical deterioration, infection, and/or hospitalization with expected recovery within the next month; recent significant bleeding episode on anticoagulation and unclear if patient able to tolerate anticoagulation in the long-term; delays secondary to logistical considerations (vacations or patient difficulty getting to IR suite), etc
4 Change in patient status where filter will not be removed: for example recurrent hemorrhage or patient going to hospice
Adult Venous Thromboembolism (VTE)
Treatment for Cancer Patients (DVT and PE)

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APPENDIX A: Contraindications to Systemic Thrombolysis

<table>
<thead>
<tr>
<th>Absolute Contraindications</th>
<th>Relative Contraindications</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Active bleeding</td>
<td>• Age &gt; 75 years old</td>
</tr>
<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 (if ischemic stroke onset within 4.5 hours, see Management of Acute Ischemic Stroke in Hospitalized Adult Patients algorithm)</td>
<td>• Traumatic cardiopulmonary resuscitation</td>
</tr>
<tr>
<td>• Recent brain or spinal surgery(^1) and/or head or facial trauma</td>
<td>• Recent major surgery, invasive procedure, and/or trauma (within 1 month)</td>
</tr>
<tr>
<td>• Suspected or confirmed aortic dissection</td>
<td>• Refractory hypertension (SBP &gt; 180 mmHg; DBP &gt; 100 mmHg)</td>
</tr>
<tr>
<td>• Platelet count below 100 K/microliter</td>
<td>• Significant non-intracranial bleeding within 1 month</td>
</tr>
</tbody>
</table>

\(^1\) Discussion with Neurosurgery for recent brain or spine surgery

APPENDIX B: 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 right ventricular (RV) dysfunction (\text{and})</td>
<td>Low-Intermediate</td>
<td>High-Intermediate</td>
</tr>
<tr>
<td>• With normal BNP/troponin</td>
<td>RV dysfunction (\text{or}) elevated BNP (\text{or}) troponin</td>
<td>RV dysfunction (\text{and}) elevated BNP (\text{or}) troponin</td>
</tr>
<tr>
<td></td>
<td>(\text{or}) elevated BNP (\text{or}) troponin</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(\text{or}) elevated BNP (\text{or}) troponin</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Sustained hypotension (SBP &lt; 90 mmHg for at least 15 minutes) (\text{or})</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Persistent bradycardia (heart rate &lt; 40 bpm) or signs or symptoms of shock (\text{or})</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Need for inotropic support</td>
</tr>
</tbody>
</table>
| SBP = systolic blood pressure \(\text{and}\) DBP = diastolic blood pressure

APPENDIX C: Contraindications to Anticoagulation Therapy

<table>
<thead>
<tr>
<th>Absolute Contraindications</th>
<th>Relative Contraindications</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Major active bleeding (e.g., 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)</td>
<td>• Brain metastases conferring risk of bleeding (renal, choriocarcinoma, melanoma, thyroid cancer)</td>
</tr>
<tr>
<td>• Platelets &lt; 25 K/microliter(^1), consult to Benign Hematology</td>
<td>• Intracranial or central nervous system (CNS) bleeding within the past 4 weeks</td>
</tr>
<tr>
<td>• Spinal procedure and/or epidural catheter placement</td>
<td>• Recent high-risk surgery or bleeding event</td>
</tr>
<tr>
<td>• Severe uncontrolled malignant hypertension</td>
<td>• Active but non-life threatening bleeding</td>
</tr>
<tr>
<td></td>
<td>• Active GI ulceration at high risk of bleeding</td>
</tr>
<tr>
<td></td>
<td>• Platelets &lt; 50 K/microliter, consider consult to Benign Hematology</td>
</tr>
<tr>
<td></td>
<td>• Patient on active protocol that prohibits use of anticoagulation</td>
</tr>
</tbody>
</table>

\(^1\) 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

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Approved by The Executive Committee of the Medical Staff 05/17/2022
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 ≥ 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
APPENDIX F: Anticoagulation Therapy\textsuperscript{1,2} Options for Cancer Patients with Active VTE

<table>
<thead>
<tr>
<th>LMWH\textsuperscript{3} Treatments</th>
<th>DOSE / ROUTE / FREQUENCY</th>
<th>MONITORING\textsuperscript{4,5}</th>
<th>DOSE ADJUSTMENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dalteparin (Fragmin\textsuperscript{6}) – FDA approved for cancer patients</td>
<td>Round to nearest International Units (IU) dose, given subcutaneously daily</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Actual Body Weight (kg)</td>
<td>Month 1</td>
<td>Month 2-6</td>
<td>Month 2-6</td>
</tr>
<tr>
<td>≤ 56</td>
<td>10,000 IU</td>
<td>7,500 IU</td>
<td>150 IU/kg</td>
</tr>
<tr>
<td>57-68</td>
<td>12,500 IU</td>
<td>10,000 IU</td>
<td>12,500 IU</td>
</tr>
<tr>
<td>69-82</td>
<td>15,000 IU</td>
<td>12,500 IU</td>
<td>15,000 IU</td>
</tr>
<tr>
<td>83-98</td>
<td>18,000 IU</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 99</td>
<td>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. An alternative option is enoxaparin 1 mg/kg twice daily (see below).</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\textsuperscript{1} Prior to anticoagulation therapy, check for contraindications to anticoagulation therapy (see Appendix C)  
\textsuperscript{2} For bleeding complications refer to Emergency Anticoagulation Reversal Order Set  
\textsuperscript{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  
\textsuperscript{4} If lab results indicate heparin induced thrombocytopenia, follow management guideline per Heparin Induced Thrombocytopenia (HIT) Treatment algorithm  
\textsuperscript{5} See the Anticoagulant Management and Required Laboratory Monitoring Policy (MD Anderson Institutional Policy #CLN0984)  
\textsuperscript{6} For concerns regarding affordability, consider submitting a test claim 48 hours prior to discharge via Pecon (for internal use only)  
\textsuperscript{7} Multi-dose vials not recommended for home use

\[ \text{CrCl} = \text{creatinine clearance (mL/minute)} \quad \text{LMWH} = \text{low molecular weight heparin} \]

\[ \text{Continued on next page} \]
APPENDIX F: Anticoagulation Therapy\textsuperscript{1,2} Options for Cancer Patients with Active VTE - continued

<table>
<thead>
<tr>
<th>LMWH\textsuperscript{3} Treatments</th>
<th>DOSE / ROUTE / FREQUENCY</th>
<th>MONITORING\textsuperscript{4,5}</th>
<th>DOSE ADJUSTMENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enoxaparin (Lovenox)\textsuperscript{6}</td>
<td>1 mg/kg subcutaneously every 12 hours or 1.5 mg/kg subcutaneously daily in selected patients</td>
<td>• Baseline: Hemoglobin/hematocrit, platelet count, aPTT/PT, and serum creatinine&lt;br&gt;• Therapeutic laboratory tests: Routine monitoring not required. However, anti-factor Xa levels may be useful in certain high-risk patients (e.g., obesity, malnutrition, renal insufficiency, and unexplained bleeding or thrombosis)&lt;br&gt;• Surgical inpatient:&lt;br&gt;  ○ 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&lt;br&gt;  ○ After day 14, hemoglobin/hematocrit, and platelet count at least once weekly&lt;br&gt;• Medical inpatient and all outpatient:&lt;br&gt;  ○ 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.&lt;br&gt;  ○ Maintenance therapy: Hemoglobin/hematocrit, platelet count, serum creatinine, and hepatic function tests at least once yearly&lt;br&gt;  - If CrCl 30-60 mL/minute, serum creatinine every 6 months&lt;br&gt;  - If CrCl &lt; 30 mL/minute, serum creatinine every 3 months&lt;br&gt;</td>
<td>Platelets:&lt;br&gt;• Limited data suggest the following enoxaparin dose modification:&lt;br&gt;  ○ For platelet count &gt; 50 K/microliter: full-dose, 1 mg/kg twice daily; alternative dose, 1.5 mg/kg once daily&lt;br&gt;  ○ For platelet count 25-50 K/microliter: half-dose, 0.5 mg/kg twice daily&lt;br&gt;  ○ For platelet count &lt; 25 K/microliter, hold all anticoagulants&lt;br&gt;Renal:&lt;br&gt;• If CrCl &lt; 30 mL/minute: 1 mg/kg daily&lt;br&gt;Weight:&lt;br&gt;• Consider obtaining anti-Xa level in patients with weight &lt; 50 kg or weight &gt; 150 kg or BMI ≥ 40 kg/m\textsuperscript{2};&lt;br&gt;  ○ 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)&lt;br&gt;  ○ 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)</td>
</tr>
</tbody>
</table>

Hold in patients with platelets < 25 K/microliter  

\textsuperscript{1} Prior to anticoagulation therapy, check for contraindications to anticoagulation therapy (see Appendix C)  
\textsuperscript{2} For bleeding complications refer to Emergency Anticoagulation Reversal Order Set  
\textsuperscript{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  
\textsuperscript{4} If lab results indicate heparin induced thrombocytopenia, follow management guideline per Heparin Induced Thrombocytopenia (HIT) Treatment algorithm  
\textsuperscript{5} See the Anticoagulant Management and Required Laboratory Monitoring Policy (MD Anderson Institutional Policy #CLN0984)  
\textsuperscript{6} For concerns regarding affordability, consider submitting a test claim 48 hours prior to discharge via Pecon (for internal use only)  

\textsuperscript{CrCl} = creatinine clearance (mL/minute)  
\textsuperscript{LMWH} = low molecular weight heparin

Continued on next page
### APPENDIX F: Anticoagulation Therapy Options for Cancer Patients with Active VTE - continued

<table>
<thead>
<tr>
<th>TREATMENT</th>
<th>MONITORING&lt;sup&gt;3,4&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Warfarin&lt;sup&gt;5&lt;/sup&gt; (Selected Vitamin K Antagonist) – For long-term management</td>
<td></td>
</tr>
<tr>
<td><strong>TREATMENT</strong></td>
<td><strong>MONITORING</strong>&lt;sup&gt;3,4&lt;/sup&gt;</td>
</tr>
<tr>
<td>● Overlap warfarin (2.5-5 mg PO) with induction therapy (LMWH, Factor Xa Inhibitor, or subcutaneous UFH) beginning on Day 1 of therapy</td>
<td>● General INR goal: 2-3</td>
</tr>
<tr>
<td>● Continue induction therapy until INR ≥ 2 for two days, AND patient has received at least 4-5 days of induction therapy overlap</td>
<td>● Mechanical aortic valve, INR goal: 2.5 (range 2-3)</td>
</tr>
<tr>
<td></td>
<td>● Mechanical mitral valve, INR goal: 2.5-3.5</td>
</tr>
<tr>
<td></td>
<td>● Baseline: Hemoglobin/hematocrit, platelet count, PT/INR, and hepatic function tests</td>
</tr>
<tr>
<td></td>
<td>● Therapeutic laboratory tests: INR to achieve specified target range</td>
</tr>
<tr>
<td></td>
<td>● Inpatient: Hemoglobin/hematocrit and platelet count at least once weekly</td>
</tr>
<tr>
<td></td>
<td>● Outpatient: INR every 3 months at a minimum, Hemoglobin/hematocrit, platelet count, serum creatinine, and hepatic function tests at least once year</td>
</tr>
</tbody>
</table>

---

<sup>1</sup> Prior to anticoagulation therapy, check for contraindications to anticoagulation therapy (see Appendix C)

<sup>2</sup> For bleeding complications refer to Emergency Anticoagulation Reversal Order Set

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

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

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

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

Disclaimer: This algorithm has been developed for MD Anderson using a multidisciplinary approach considering circumstances particular to MD Anderson’s specific patient population, services and structure, and clinical information. This is not intended to replace the independent medical or professional judgment of physicians or other health care providers in the context of individual clinical circumstances to determine a patient’s care. This algorithm should not be used to treat pregnant or lactating women.
### Fondaparinux (Arixtra®) |

#### Factor Xa Inhibitor

<table>
<thead>
<tr>
<th>ACTUAL BODY WEIGHT (kg)</th>
<th>FONDAPARINUX DAILY SC DOSE</th>
<th>MONITORING</th>
</tr>
</thead>
</table>
| < 50                   | 5 mg                       | Baseline: Hemoglobin/hematocrit, platelet count, aPTT/PT, and serum creatinine  
| 50 – 100               | 7.5 mg                     | Therapeutic laboratory tests: Routine monitoring not required. However, antifactor Xa levels may be useful in certain high-risk patients (e.g., obesity, malnutrition, renal insufficiency, and unexplained bleeding or thrombosis)  
| > 100                  | 10 mg                      | 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  

### Monitoring

- Renal:  
  - If CrCl is between 30-50 mL/minute: use with caution  
  - If CrCl is < 30 mL/minute: contraindicated  
- Weight:  
  - For BMI ≥ 40 kg/m², no dose adjustment necessary  
- Platelets:  
  - Use fondaparinux with caution in patients with platelets < 100 K/microliter

**CrCl** = creatinine clearance (mL/minute)

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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)
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.

<table>
<thead>
<tr>
<th>DOACs</th>
<th>Rivaroxaban (Xarelto®)¹ Oral Factor Xa Inhibitor</th>
<th>Apixaban (Eliquis®)¹ Oral Factor Xa Inhibitor</th>
</tr>
</thead>
<tbody>
<tr>
<td>VTE Dosing Instructions</td>
<td>CrCl ≥ 15 mL/minute</td>
<td>CrCl &lt; 15 mL/minute or ESRD</td>
</tr>
<tr>
<td></td>
<td>15 mg PO twice daily with food for 3 weeks followed by 20 mg PO daily with food</td>
<td>Avoid use</td>
</tr>
<tr>
<td></td>
<td>No dose adjustment is recommended for CrCl, even when CrCl &lt; 15 mL/minute</td>
<td>10 mg PO twice daily for 1 week followed by 5 mg PO twice daily</td>
</tr>
<tr>
<td>Use in liver disease</td>
<td>CTP² class B or C: NOT recommended</td>
<td>Use in CTP² class C not recommended and there is limited experience for use in class B</td>
</tr>
<tr>
<td>Class specific contraindications</td>
<td>Moderate to severe mitral stenosis or mechanical heart valve</td>
<td></td>
</tr>
<tr>
<td>Significant drug-drug interactions</td>
<td>P-glycoprotein and CYP 3A4 interactions</td>
<td>P-glycoprotein and CYP 3A4 interactions</td>
</tr>
</tbody>
</table>
| 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 (e.g., obesity, malnutrition, renal insufficiency, and unexplained bleeding or thrombosis). Antifactor Xa levels are only available for apixaban and rivaroxaban currently. | • 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 |

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

Continued on next page
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.

<table>
<thead>
<tr>
<th>DOACs</th>
<th>Dabigatran (Pradaxa&lt;sup&gt;®&lt;/sup&gt;)&lt;sup&gt;1&lt;/sup&gt;</th>
<th>Direct Thrombin Inhibitor</th>
<th>Edoxaban (Savaysa&lt;sup&gt;®&lt;/sup&gt;)&lt;sup&gt;1,2&lt;/sup&gt;</th>
<th>Oral Factor Xa Inhibitor</th>
</tr>
</thead>
</table>
| **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 ≤ 30 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**

<table>
<thead>
<tr>
<th>CTP&lt;sup&gt;3&lt;/sup&gt; class B or C: NOT recommended</th>
</tr>
</thead>
</table>

**Class specific contraindications**

- Moderate to severe mitral stenosis or mechanical heart valve

**Significant drug-drug interactions**

- P-glycoprotein 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 (e.g., obesity, malnutrition, renal insufficiency, and unexplained bleeding or thrombosis)
  - Dabigatran: Thrombin time (TT) may be useful in certain high-risk patients (e.g., obesity, malnutrition, renal insufficiency, and unexplained bleeding or thrombosis)

- P-glycoprotein and CYP 3A4 interactions

- 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

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

<sup>1</sup> For concerns regarding affordability, consider submitting a test claim 48 hours prior to discharge via Pecon (for internal use only)  
<sup>2</sup> Edoxaban is currently not on the MD Anderson formulary  
<sup>3</sup> See Appendix H: Child-Turcotte-Pugh (CTP) Scoring System
**APPENDIX H: Child-Turcotte-Pugh (CTP) Scoring System**

<table>
<thead>
<tr>
<th>Chemical and Biochemical Parameters</th>
<th>Points for Increasing Abnormality</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Hepatic encephalopathy</td>
<td>None</td>
</tr>
<tr>
<td>Ascites</td>
<td>None</td>
</tr>
<tr>
<td>Serum albumin</td>
<td>Greater than 3.5 g/dL</td>
</tr>
<tr>
<td>Total bilirubin</td>
<td>Less than 2 mg/dL</td>
</tr>
<tr>
<td></td>
<td>1 – 4 mg/dL</td>
</tr>
<tr>
<td></td>
<td>Greater than 3 mg/dL</td>
</tr>
<tr>
<td>Prothrombin time prolonged or INR</td>
<td>Less than 4 seconds</td>
</tr>
<tr>
<td></td>
<td>Less than 1.7</td>
</tr>
</tbody>
</table>

*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


Continued on next page
SUGGESTED READINGS - continued


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

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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 included:

Core Development Team Leads

- Michael Kroll, MD (Benign Hematology)
- Katy M. Toale, PharmD (Pharmacy Quality-Regulatory)
- Ali Zalpour, PharmD (Pharmacy Clinical Programs)

Workgroup Members

- Sheree Cheung, PA-C (Interventional Radiology)
- Jean-Bernard Durand, MD (Cardiology)
- Carmen Escalante, MD (General Internal Medicine)
- Wendy Garcia, BS*
- Josiah Halm, MD (Hospital Medicine)
- Steven Y. Huang, MD (Interventional Radiology)
- Deborah McCue, PharmD (Pharmacy Clinical Programs)
- Zeyad Metwalli, MD (Interventional Radiology)
- Joseph L. Nates, MD (Critical Care Medicine)
- Amy Pai, PharmD*
- Cristhiam M. Rojas Hernandez, MD (Benign Hematology)
- SWamique Yusuf, MD (Cardiology)

* Clinical Effectiveness Development Team