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Inpatient Anticoagulation Committee

Committee Approvals/Dates:
Inpatient Anticoagulation Committee – November 2014
Pharmacy and Therapeutics Committee – March 2015

Release Date:
Initial December 26, 2012
Update: June 18, 2015

Next Review Date:
March 2017
Executive Summary

Guideline Overview
Recommendations for outpatient treatment and management of venous thromboembolism in adult patients in the emergency department or ambulatory setting.

Target Population (optional)
Adult patients diagnosed with pulmonary embolism or deep vein thrombosis in the ED or outpatient setting.

Key Practice Recommendations
This will be added after content reviewed/approved

Companion Documents
Tables
Algorithms
ED – VTE Outpatient Care Discharge Order set 4781

Pertinent UWHC Policies & Procedures
None identified

Patient Resources:
Deep vein thrombosis (DVT) and Pulmonary Embolism (PE) Treatment and Prevention HFFY #7522
Heparin (Unfractionated and Low Molecular Weight Heparin) HFFY #6915
Warfarin (Coumadin®, Jantoven®) HFFY #6900
Scope

Disease/Condition(s):
- Pulmonary embolism (PE)
- Deep vein thrombosis (DVT)

Clinical Specialty:
- Emergency Department (ED)

Intended Users:
- Emergency Department Clinicians

CPG objective(s):
To assist clinicians by providing a framework for the evaluation and outpatient treatment of adult VTE patients

Target Population:
Adult patients diagnosed with PE or DVT in the ED or ambulatory setting.

Interventions and Practices Considered:
This guideline contains strategies and recommendation designed to assist clinicians in delivering and supporting effective outpatient treatment for VTE. It focuses on the initial presentation of the patient to determine the appropriate care setting and therapy option, as well, as recommendations for communicating anticoagulation management plans across the care setting. This guideline does not address maintenance monitoring of treatment options or the length of therapy of anticoagulation.

Major Outcomes Considered:
Number of patients with PE and/or DVT admitted versus treated as outpatients
Number of readmissions or complications in the outpatient treatment population

Guideline Metrics:
Metrics will include appropriate selection for outpatient treatment, appropriate selection of treatment agent, assessment of follow up, recurrent VTE, bleeding events, urgency care/ED visits, and/or readmissions.
Methodology

Methods Used to Collect/Select the Evidence:
(1) completing a comprehensive literature search of electronic databases; (2) conducting an in-depth review of relevant abstracts and articles; (3) conducting thoughtful discussion and interpretation of findings; (4) ranking strength of evidence underlying the current recommendations that are made.

Methods Used to Assess the Quality and Strength of the Evidence:
Comprehensive review of literature from 1998 to 2014

Rating Scheme for the Strength of the Evidence:
Rating Scheme for the Strength of the Evidence: A modified Grading of Recommendations Assessment, Development and Evaluation (GRADE) developed by the American Heart Association and American College of Cardiology (Appendix A) has been used to assess the Quality and Strength of the Evidence in this Clinical Practice Guideline.

Cost Analysis:
Table 1. Cost Analysis – reflect cash pricing

<table>
<thead>
<tr>
<th>Medication</th>
<th>Price per dose ($)</th>
<th>Price per month ($)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apixaban 10 mg</td>
<td>3.47</td>
<td>48.58 (7 days)</td>
</tr>
<tr>
<td>Apixaban 5 mg</td>
<td>3.47</td>
<td>208.2</td>
</tr>
<tr>
<td>Dabigatran 150 mg</td>
<td>4.17</td>
<td>250.2</td>
</tr>
<tr>
<td>Enoxaparin 80 mg</td>
<td>68.2</td>
<td>955.29 (7 days)</td>
</tr>
<tr>
<td>Rivaroxaban 15 mg*</td>
<td>8.09</td>
<td>339.78 (21 days)</td>
</tr>
<tr>
<td>Rivaroxaban 20 mg*</td>
<td>8.09</td>
<td>242.7</td>
</tr>
<tr>
<td>Warfarin 5 mg</td>
<td>0.64</td>
<td>19.2</td>
</tr>
</tbody>
</table>

*this is available in a starter pack for $487.05

Definitions:
Pulmonary Embolism: embolism of a pulmonary artery or one of its branches that is produced by foreign matter and most often a blood clot originating in a vein of the leg or pelvis and that is marked by labored breathing, chest pain, fainting, rapid heart rate, cyanosis, shock, and sometimes death.

Introduction
Outpatient management of acute DVT has not been associated with increased mortality, recurrent VTE or increases in major bleeding events and generally has been accepted as a standard of care. Outpatient management of PE, while not as well documented, has started gaining favor in the medical community. Two randomized trials and several observational studies have suggested that management of acute PE, in low risk patients, in the ambulatory setting did not increase mortality, recurrent VTE or major bleeding events. The American

**Recommendations**

**Pulmonary Embolism (PE) Management – Appendix B**

1. **Eligibility Criteria for Outpatient PE management: (Class Ila, Level B)**
   1.1 ≥ 18 years of age  
   1.2 Diagnosis of acute pulmonary embolism  
   1.3 Able and willing to comply with home care  
   1.4 Able to obtain necessary medications  

2. If patient meets the eligibility criteria, calculate the Pulmonary Embolism Severity Index (PESI) score (Class Ila, Level B):

   **Table 2. Pulmonary Embolism Severity Index Scoring Tool**

<table>
<thead>
<tr>
<th>Calculate the PESI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age + 1 per year</td>
</tr>
<tr>
<td>Male + 10</td>
</tr>
<tr>
<td>Recent history of malignancy* + 30</td>
</tr>
<tr>
<td>Any history of Heart Failure + 10</td>
</tr>
<tr>
<td>Any history of Chronic Lung Disease + 10</td>
</tr>
<tr>
<td>Triage HR &gt; 110 + 20</td>
</tr>
<tr>
<td>Triage SBP &lt; 100 + 30</td>
</tr>
<tr>
<td>Triage Temp &lt; 36C + 20</td>
</tr>
<tr>
<td>Triage RR &gt; 29 + 20</td>
</tr>
<tr>
<td>Triage Oxygen sat &lt; 90% + 20</td>
</tr>
<tr>
<td>Altered Mental Status + 60</td>
</tr>
</tbody>
</table>

   *Any diagnosis of cancer other than basal-cell or squamous-cell carcinoma of the skin, within the prior 6 months, any treatment for cancer in the previous 6 months, or recurrent or metastatic cancer*

2.1 If PESI score is ≥ 86, hospitalize the patient (Class Ila, Level B)  
2.2 If PESI score is ≤ 85, continue to the exclusion criteria (Class Ila, Level B)  

3. **Additional exclusion criteria (Class Iib, Level C)**
   3.1 Intracardiac or central vein thrombus  
   3.2 Central PE (main pulmonary artery)  
   3.3 Requires admission for reasons other than acute PE/DVT
3.4 Not appropriate for long term anticoagulation (unreliable, or unable to comply with follow up)
3.5 Any stroke in the last 6 weeks
3.6 Brain, spinal, or ophth surgery (excludes cataract) in the last 6 weeks
3.7 Non-cutaneous surgery in the last 2 weeks
3.8 GI bleed in the last 2 weeks
3.9 Active major bleeding
3.10 Therapeutic anticoagulation at the time of diagnosis (e.g. INR ≥ 2)
3.11 Thrombocytopenia (Plt< 75,000 K/uL)
3.12 Bleeding disorder (e.g. Von Willebrand Disease)
3.13 Creatinine clearance < 30 mL/min
3.14 Hypoxia (< 90% at any time in the ED)
3.15 Hypotension (SBP < 100mmHg at any time in the ED)
3.16 Evidence of RV strain on echocardiogram or computerized tomography (CT) (if obtained)
3.17 Treated with thrombolytics in the ED
3.18 Pregnant (verified by negative pregnancy test in women of childbearing age)
3.29 > 150 kg

4. If no to all exclusion criteria, then the patient may be discharged on anticoagulant therapy with proper home care instructions (Class Ila, Level B).

Deep Vein Thrombosis (DVT) Management – Appendix C

5. Eligibility Criteria for Outpatient DVT management: (Class Ila, Level B)
   5.1 ≥ 18 years of age
   5.2 Diagnosis of DVT
   5.3 Able and willing to comply with home care
   5.4 Able to obtain necessary medications

6. Exclusion Criteria (Class Iib, Level C)
   6.1 Requires admission for reasons other than acute DVT
   6.2 Diagnosis of PE (see #1)
   6.3 Impending gangrene due to venous thrombosis
   6.4 Not appropriate for long term anticoagulation (unreliable, or unable to comply with follow up)
   6.5 Any stroke in the last 6 weeks
   6.6 Brain, spinal, or ophth surgery (excludes cataract) in the last 6 weeks
   6.7 Non-cutaneous surgery in the last 2 weeks
   6.8 GI bleed in the last 2 weeks
   6.9 Active major bleeding
   6.10 Therapeutic anticoagulation at the time of diagnosis (e.g. INR ≥ 2)
   6.11 Thrombocytopenia (< 75,000 Plt K/uL)
   6.12 Bleeding disorder (e.g. Von Willebrand Disease)
   6.13 Creatinine clearance < 30 mL/min
   6.14 Treated with thrombolytics in the ED
   6.15 Pregnant (verified by negative pregnancy test in women of childbearing age)
   6.16 > 150 kg

7. If no to all exclusion criteria, then the patient may be discharged on anticoagulant therapy with proper home care instructions (Class Ila, Level B)
Treatment of PE and DVT – Appendix D

Prior to selecting an anticoagulation regimen, the benefits and risks of therapy options should be discussed with the patient, being sure to incorporate their priorities in the decision making process.3

Traditionally, dose-adjusted vitamin K antagonist, such as warfarin, combined with a low molecular weight heparin, was the preferred treatment option for VTE. However, the development of targeted anticoagulants have been shown to produce more predictable anticoagulation, do not require monitoring of anticoagulation status, have similar efficacy in treatment of VTE with improved safety profiles when compared to warfarin.3,12-14

Each direct oral anticoagulant (DOAC) has published data compared to traditional treatment (warfarin and low molecular weight heparin). To date there is no published data with direct comparisons between the DOACs.12-14

Prior to discharge from the ED the patient’s outpatient medication list should be reviewed for medications that may contribute to either a hypercoagulable state or that may cause an increased risk of bleeding in the setting of therapeutic anticoagulation. These medications should not preclude starting therapeutic anticoagulation but instead should be reviewed for discontinuation prior to ED discharge.

8. The ED physician may choose to discontinue a medication that has the potential to increase or decrease the risk of bleeding or thrombosis (ex. oral contraception, hormone replacement therapy, NSAIDs) (Class IIb, Level C)

8.1 The ED physician should discuss with the patient the risks vs benefit of discontinuing the identified medication and provide alternative therapy options (ex. alternative birth control methods) or instruct the patient to call the prescriber to review alternative options.

8.2 If a medication is stopped the prescribing provider will be notified of the change through either electronic medical record notification or through patient notification.

Warfarin and Low Molecular Weight Heparin

9. Warfarin

9.1 Dose: 5 mg by mouth daily until next INR check (Class Ila, Level C)

9.2 Consider starting at 2.5 mg if risk factors for warfarin sensitivity exist15 (Class IIb, Level C)

9.2.1 Baseline INR > 1.5
9.2.2 Age > 65 years
9.2.3 Actual body weight (ABW) < 45 kg
9.2.4 Significant drug interactions
9.2.5 Current antiplatelet therapy
9.2.6 Chronic diarrhea
9.2.7 Alcohol abuse history
9.2.8 Decompensated heart failure
9.2.9 Malnourished or NPO > 3 days

9.3 INR must be resulted prior to initiating warfarin therapy15,16 (Class I, Level A)

9.4 Follow up INR within 3-4 days of discharge from ED (Class IIb, Level C)
9.5 Telephone contact must be made with the patient’s primary care provider (PCP) or on-call provider if after hours to communicate outpatient management *(Class IIb, Level C)*

9.5.1 If the patient does not have a PCP, then contact the ED case manager or social worker by either direct communication or via inbasket message to pool: CC ED SW AND CC ED CM to help arrange for PCP and follow up

9.5.2 Case management and social work coverage 7 days per week from 0700-0230

9.6 A follow up care plan including monitoring of INR must be in place prior to discharge from the ED.

9.6.1 If outpatient INR monitoring cannot be established by time of ED discharge then consider parenteral anticoagulant or an alternative oral anticoagulant

9.7 Education on compliance, dietary advice, follow up monitoring and drug interactions and adverse drug reactions must be provided to the patient and/or caregiver prior to ED discharge *(Class IIb, Level C)*

10. Enoxaparin

10.1 Preferred treatment option for patients with active cancer

10.2 Dose: 1 mg/kg ABW subcutaneously every 12 hours until INR in therapeutic range

10.2.1 1.5 mg/kg ABW subcutaneously every 24 hours may be considered if patient preferred *(Class IIb, Level C)*

10.2.2 1 mg/kg ABW subcutaneously every 24 hours if CrCl < 30 mL/min

10.3 Dose must be administered prior to ED discharge *(Class IIb, Level C)*

10.4 Patient’s ability to acquire medication must be assessed prior to ED discharge *(Class IIb, Level C)*

10.5 Education on proper injection technique and management plan must be provided prior to ED discharge *(Class IIb, Level C)*

Direct Oral Anticoagulants (listed alphabetically)

Patient’s ability to acquire medication must be assessed prior to ED discharge

11. Apixaban

11.1 Dose: 10 mg by mouth BID for 7 days then 5 mg by mouth BID

11.2 Avoid use with: *(Class IIb, Level C)*

11.2.1 CrCl < 25 mL/min

11.2.2 Platelet < 100 K/uL

11.2.3 Aspirin in doses > 162 mg per day

11.3 Use caution with: *(Class IIb, Level C)*

11.3.1 Dual or triple antiplatelet therapy

11.3.2 Strong CYP3A4 inhibitors (azole antifungals, clarithromycin, HIV protease inhibitors)

11.3.3 Strong CYP3A4 inducers (e.g. carbamazepine, nafcillin, phenobarbital, phenytoin, rifampin)

11.3.4 P-gp inhibitors (e.g. amiodarone, clarithromycin, cyclosporine, ketoconazole, quinidine, verapamil)

11.3.5 P-gp inducers (e.g. carbamazepine, dexamethasone, phenytoin, rifampin)
Table 4. Apixaban versus warfarin for VTE Treatment

<table>
<thead>
<tr>
<th></th>
<th>Apixaban</th>
<th>Traditional Therapy</th>
<th>Relative Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Efficacy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First recurrent VTE</td>
<td>59 (2.3)*</td>
<td>71 (2.7)</td>
<td>0.84 (0.6-1.18)</td>
</tr>
<tr>
<td>VTE related death</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Safety</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Major bleeding</td>
<td>15 (0.6)*</td>
<td>49 (1.8)</td>
<td>0.31 (0.71-0.55)</td>
</tr>
<tr>
<td>Clinically relevant non-major bleeding</td>
<td>103 (3.8)</td>
<td>215 (8.0)</td>
<td>0.48 (0.38-0.6)</td>
</tr>
</tbody>
</table>

12. Dabigatran

12.1 Dose: 150 mg by mouth BID
12.1.1 It is recommended to initiate therapy with 5-10 days of parenteral anticoagulation (ex. LMWH) prior to initiating dabigatran

12.2 Avoid use with: (Class IIb, Level C)
12.2.1 CrCl < 30 mL/min
12.2.2 ALT twice the upper limit of normal

12.3 Use caution with: (Class IIb, Level C)
12.3.1 Dual antiplatelet therapy
12.3.2 P-gp inhibitors (e.g. amiodarone, clarithromycin, cyclosporine, dronedarone, ketoconazole, quinidine, verapamil)
12.3.3 P-gp inducers (e.g. carbamazepine, dexamethasone, phenytoin, rifampin)

Table 5. Dabigatran versus warfarin for VTE Treatment

<table>
<thead>
<tr>
<th></th>
<th>Dabigatran</th>
<th>Traditional Therapy</th>
<th>Relative Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Efficacy</td>
<td>N=1274</td>
<td>N=1265</td>
<td></td>
</tr>
<tr>
<td>First recurrent VTE</td>
<td>30 (2.4)</td>
<td>27 (2.1)</td>
<td>1.10 (0.65-1.84)</td>
</tr>
<tr>
<td>VTE related death</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Safety</td>
<td>N=1276</td>
<td>N=1289</td>
<td></td>
</tr>
<tr>
<td>Major bleeding</td>
<td>20 (1.6)</td>
<td>24 (1.9)</td>
<td>0.82 (0.45-1.48)</td>
</tr>
<tr>
<td>Major or clinically relevant non-major bleeding</td>
<td>71 (5.6)</td>
<td>111 (8.8)</td>
<td>0.63 (0.47-0.84)</td>
</tr>
</tbody>
</table>

13. Rivaroxaban

13.1 Dose: 15 mg by mouth BID for 21 days, followed by 20 mg by mouth daily

13.2 Avoid use in: (Class IIb, Level C)
13.2.1 CrCl < 30 mL/min
13.2.2 ALT 3x the upper limit of normal or Child-Pugh B or C
13.2.3 Significant liver disease (acute or chronic hepatitis, cirrhosis)

13.3 Use caution with: (Class IIb, Level C)
13.3.1 Dual antiplatelet therapy
13.3.2 Strong CYP3A4 inhibitors (azole antifungals, clarithromycin, HIV protease inhibitors)
13.3.3 Strong CYP3A4 inducers (e.g. carbamazepine, nafcillin, phenobarbital, phenytoin, rifampin)
13.3.4 P-gp inhibitors (e.g. amiodarone, clarithromycin, cyclosporine, dronedarone, ketoconazole, quinidine, verapamil)
13.3.5 P-gp inducers (e.g. carbamazepine, dexamethasone, phenytoin, rifampin)

Table 6. Rivaroxaban versus warfarin for VTE Treatment\textsuperscript{16,17}

<table>
<thead>
<tr>
<th></th>
<th>Rivaroxaban</th>
<th>Traditional Therapy</th>
<th>Relative Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Efficacy</td>
<td>N=1731</td>
<td>N=1718</td>
<td></td>
</tr>
<tr>
<td>First recurrent VTE</td>
<td>36 (2.1)</td>
<td>51 (3.0)</td>
<td>0.68 (0.44-1.04)</td>
</tr>
<tr>
<td>VTE related death</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Safety</td>
<td>N=1718</td>
<td>N=1711</td>
<td></td>
</tr>
<tr>
<td>Major bleeding</td>
<td>14 (0.8)</td>
<td>20 (1.2)</td>
<td>0.65 (0.33-1.3)</td>
</tr>
<tr>
<td>Clinically relevant non-major bleeding</td>
<td>126 (7.3)</td>
<td>119 (7.0)</td>
<td></td>
</tr>
</tbody>
</table>

14. Transition to Outpatient Management

14.1 Upon starting a new anticoagulant telephone contact must be made with the patient’s primary care provider (PCP) (\textit{Class Ib, Level C})

14.1.1 The ED Case Manager will contact the PCP during normal clinic business hours

14.1.2 If new diagnosis of VTE occurs when PCP clinic is closed, the ED case manager will contact the PCP the following clinic day

14.2 Upon stopping an outpatient medication that can either increase bleeding or thrombotic risk the prescribing provider will be notified of the change through either electronic medical record notification or through patient notification. (\textit{Class Ib, Level C})

14.3 Patient follow up with a PCP should occur within 3-4 days of discharge from the ED (\textit{Class Ib, Level C})

14.4 If a patient is discharged on warfarin a follow up care plan for monitoring the INR must be in place prior to discharge from the ED. (\textit{Class Ib, Level C})

14.4.1 If outpatient INR monitoring cannot be established by the time of ED discharge, than an alternative anticoagulant that does not require monitoring or dose adjustments should be selected.

14.4.2 If warfarin is the preferred agent the ED physician will assume responsibility for INR management until outpatient management is established.

14.5 The ED pharmacist will contact the patient by telephone within 3-4 days of ED discharge to ensure acquisition of medication and follow-up with PCP and monitoring (if applicable) has occurred.
Companion/Collateral documents (algorithm, tables, and forms):

**Appendix A**

<table>
<thead>
<tr>
<th>LEVEL</th>
<th>Estimate of Certainty/Precision of Treatment Effect</th>
<th>Size of Treatment Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Multiple populations evaluated*</td>
<td>Class I: Benefit &gt;&gt; Risk; Procedure/Treatment SHOULD be performed/administered</td>
</tr>
<tr>
<td></td>
<td>Data derived from multiple randomized clinical trials or meta-analyses</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Recommendation that procedure or treatment is useful/effective</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Sufficient evidence from multiple randomized trials or meta-analyses</td>
<td></td>
</tr>
</tbody>
</table>

| B     | Limited populations evaluated* | Class IIA: Benefit >> Risk; Additional studies with focused objectives needed; IT IS REASONABLE to perform procedure/administer treatment |
|       | Data derived from a single randomized trial or nonrandomized studies |
|       | - Recommendation in favor of treatment or procedure being useful/effective |
|       | - Some conflicting evidence from multiple randomized trials or meta-analyses |

| C     | Very limited populations evaluated* | Class IIB: Benefit ≥ Risk; Additional studies with broad objectives needed; additional registry data would be helpful; Procedure/Treatment MAY BE CONSIDERED |
|       | Only expert opinion, case studies, or standard of care |
|       | - Recommendation’s usefulness/effectiveness well established |
|       | - Greater conflicting evidence from multiple randomized trials or meta-analyses |

| III    | Procedure/Treatment should NOT be performed/administered since it is NOT helpful and MAY BE HARMFUL |
|        | Recommendation that procedure or treatment is not useful/effective and may be harmful |
|        | Sufficient evidence from multiple randomized trials or meta-analyses |

Suggested phrases for writing recommendations:
- Should
- Is indicated
- Is reasonable
- Is unlikely/effective/beneficial
- May/might be considered
- Not indicated
- Not useful/effective/beneficial
- May/might be harmful

* denotes additional weight on evidence from meta-analyses or summary of multiple trials.
Appendix B: VTE Management in Emergency Department – Adults CPG
Assessment of Outpatient PE Management – Algorithm

Consider outpatient management of PE if:
- Diagnosis of acute PE
- Age > 18
- Able and willing to comply with home care
- Able to obtain necessary medications

Calculate PESI Score

<table>
<thead>
<tr>
<th>Age</th>
<th>+ 1 per year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>+ 10</td>
</tr>
<tr>
<td>Any history of malignancy*</td>
<td>+ 30</td>
</tr>
<tr>
<td>Any history of heart failure</td>
<td>+ 10</td>
</tr>
<tr>
<td>Any history of chronic lung disease</td>
<td>+ 10</td>
</tr>
<tr>
<td>Triage HR &gt; 110</td>
<td>+ 20</td>
</tr>
<tr>
<td>Triage SBP &lt; 100</td>
<td>+ 30</td>
</tr>
<tr>
<td>Triage temp &lt; 36C</td>
<td>+ 20</td>
</tr>
<tr>
<td>Triage oxygen sat &lt; 90%</td>
<td>+ 20</td>
</tr>
<tr>
<td>Altered mental status</td>
<td>+ 60</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td>If &gt; 86: hospitalize&lt;br&gt; If &lt; 85: see exclusion criteria</td>
</tr>
</tbody>
</table>

*any dx of cancer other than basal-cell or squamous-cell skin cancer, within the prior 6 months, any treatment for cancer in the previous 6 months, or recurrent or metastastic cancer

<table>
<thead>
<tr>
<th>Exclusion Criteria</th>
<th>No</th>
<th>Yes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intracardiac or central vein thrombosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Central PE (main pulmonary artery)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Requires admission for reason other than DVT/PE</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not appropriate for long term anticoagulation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any stroke in the last 6 weeks</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brain, spinal, or ophthy surgery in the last 6 weeks</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-cutaneous surgery in the last 2 weeks</td>
<td></td>
<td></td>
</tr>
<tr>
<td>GI bleed in the last 2 weeks</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Active major bleeding</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Therapeutic anticoagulation at time of diagnosis (e.g. INR ≥ 2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thrombocytopenia (&lt;75,000 K/uL)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bleeding disorder (e.g. Von Willebrand Disease)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Creatinine clearance &lt; 30 mL/min</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypoxia (&lt;90% at any time in the ED)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypotension (SBP &lt;100 mmHg at any time in the ED)</td>
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<tr>
<td>Evidence of RV strain on echo or CT</td>
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</tr>
<tr>
<td>Treated with thrombolytics in the ED</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pregnant</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight &gt; 150 kg</td>
<td></td>
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</tr>
</tbody>
</table>

If yes to any of the exclusion criteria, then hospitalize<br> If no to all exclusion criteria, then may discharge on anticoagulant therapy
### Consider outpatient management of DVT if:
- Diagnosis of DVT
- Age ≥ 18
- Able and willing to comply with home care
- Able to obtain necessary medications

### Exclusion Criteria

<table>
<thead>
<tr>
<th>Exclusion Criteria</th>
<th>No</th>
<th>Yes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Requires admission for reason other than DVT</td>
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<td></td>
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<tr>
<td>Diagnosis of PE</td>
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<tr>
<td>Impending gangrene due to venous thrombosis</td>
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</tr>
<tr>
<td>Not appropriate for long term anticoagulation</td>
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<tr>
<td>Any stroke in the last 6 weeks</td>
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<tr>
<td>Brain, spinal, or ophthalmic surgery in the last 6 weeks</td>
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<tr>
<td>Non-cutaneous surgery in the last 2 weeks</td>
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<tr>
<td>GI bleed in the last 2 weeks</td>
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<tr>
<td>Active major bleeding</td>
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</tr>
<tr>
<td>Therapeutic anticoagulation at time of diagnosis (e.g., INR ≥ 2)</td>
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<td></td>
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<tr>
<td>Thrombocytopenia (&lt;75,000 K/uL)</td>
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<tr>
<td>Bleeding disorder (e.g., Von Willebrand Disease)</td>
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<tr>
<td>Creatinine clearance &lt; 30 mL/min</td>
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<td></td>
</tr>
<tr>
<td>Treated with thrombolytics in the ED</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pregnant</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight &gt; 150 kg</td>
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</tr>
</tbody>
</table>

If yes to any of the exclusion criteria, then hospitalize
If no to all exclusion criteria, then may discharge on anticoagulant therapy
Appendix D: VTE Management in Emergency Department – Adults CPG - Outpatient Treatment of VTE – Algorithm

Eligible for Outpatient Treatment:
Choose anticoagulation therapy based on patient preference and risk factors

Warfarin with identified follow up
- Give first doses in ED prior to D/C:
  - Warfarin 2.5 mg Take as Directed per INR AND
  - Enoxaparin 1 mg/kg SQ every 12 hrs x 10 days
- Outpatient treatment:
  - Warfarin 2.5 mg Take as Directed per INR AND
  - Enoxaparin 1 mg/kg SQ every 12 hrs x 10 days (enoxaparin once daily is not recommended)

Warfarin without identified follow up or Dabigatran
- Give first doses in ED prior to D/C:
  - Enoxaparin 1 mg/kg SQ x 1
- Outpatient treatment warfarin –
  - Enoxaparin 1 mg/kg SQ every 12 hrs x 10 days
- Outpatient treatment dabigatran –
  - Enoxaparin 1 mg/kg SQ every 12 hrs x 7 days AND
  - Dabigatran 150 mg orally BID to be started after enoxaparin

Apixaban or Rivaroxaban
- Give first dose in ED prior to D/C:
  - Apixaban 10 mg orally x 1
  - Rivaroxaban 15 mg orally x 1
- Outpatient treatment: (choose one)
  - Apixaban 10 mg orally BID x 7 days then 5 mg BID
  - Rivaroxaban 15 mg orally BID x 21 days then 20 mg daily

Follow Up:
- Direct contact with patient’s PCP or on call provider if after hours to communicate outpatient management
- If no PCP contact ED case manager or social worker to assist; if not available may send inbasket message to CC ED SW AND CC ED CM
- Warfarin only: Schedule a follow up INR 2-3 days after ED discharge (an INR should not be checked on the weekend)

Provide patient education on the following prior to D/C:
- Pulmonary embolism disease state
- Injection technique (if needed)
- Anticoagulation medication
- Follow up/outpatient management plan

Pharmacist will contact patient 2-3 days after ED discharge to ensure follow up with PCP has occurred
## References

- Dabigatran (Pradaxa)
- Rivaroxaban (Xarelto)
- Apixaban (Eliquis)

### Drug Classification

- Selective thrombin inhibitor
- Selective direct Xa inhibitor
- Selective direct Xa inhibitor

### Dose for VTE Treatment

<table>
<thead>
<tr>
<th>Drug</th>
<th>150 mg BID after 5-10 days of parenteral AC</th>
<th>15 mg BID for 21 days, then 20 mg DAILY</th>
<th>10 mg BID for 7 days, followed by 5 mg BID</th>
</tr>
</thead>
<tbody>
<tr>
<td>CrCl &lt; 30: dosing recs not provided</td>
<td>CrCl &lt; 30: dosing recs not provided</td>
<td>CrCl &lt; 25: dosing recs not provided</td>
<td></td>
</tr>
</tbody>
</table>

### Half-life

- Dabigatran: 12-17 hrs
- Rivaroxaban: 5-12 hrs
- Apixaban: 8-15 hrs

### Time to max effect

- Dabigatran: 2 hrs
- Rivaroxaban: 2-4 hrs
- Apixaban: 3 hrs

### Elimination

- Dabigatran: 80% renal, 20% biliary
- Rivaroxaban: 66% renal, 33% biliary
- Apixaban: 27% renal, 73% biliary and direct intestinal excretion

### Monitoring

- No lab testing available for anticoagulation status

### Missed Dose

- **Dabigatran**:
  - Take missed dose ASAP, but if next dose is < 6 hrs away, skip the missed dose
  - Do not take 2 doses at the same time

- **Rivaroxaban**:
  - If taking 15 mg BID: Take ASAP to ensure 30 mg daily
  - For daily dose: Take missed dose immediately

- **Apixaban**:
  - Take missed dose ASAP on same day
  - The dose should not be doubled to make up for a missed dose

### Drug Interactions

- **Dabigatran**:
  - P-gp inhibitors may ↑ serum concentration (i.e. amiodarone, cyclosporine, ketoconazole, quinidine, verapamil)
  - P-gp inducers may ↓ serum concentration (i.e. carbamazepine, dexamethasone, phenytoin, rifampin)

- **Rivaroxaban**:
  - P-gp & strong CYP3A4 inhibitors may ↑ serum concentration (i.e. amiodarone, cyclosporine, quinidine, verapamil, azole antifungals, HIV protease inhibitors)
  - P-gp & strong CYP3A4 inducers may ↓ serum concentration (i.e. carbamazepine, dexamethasone, phenytoin, rifampin, nafcillin)

- **Apixaban**:
  - P-gp & strong CYP3A4 inhibitors may ↑ serum concentration (i.e. amiodarone, cyclosporine, quinidine, verapamil, azole antifungals, HIV protease inhibitors)
  - P-gp & strong CYP3A4 inducers may ↓ serum concentration (i.e. carbamazepine, dexamethasone, phenytoin, phenobarbital, rifampin, nafcillin)

### Advantages

- Fixed dose
- No bridging
- No INR monitoring required
- No dietary interactions & fewer drug interactions

### Disadvantages

- Cost
- Lack of antidote
- Missed dose may place pt at increased risk of thromboembolic event
- Renal monitoring

### Lab Frequency follow-up

**Yearly:** Hgb, renal and liver function

3-6 month: Renal function if CrCl 30-60 ml/min, if on dabigatran and > 75 years or fragile or if co-morbidity or condition that may impact renal or hepatic function
Companion/Collateral documents (as applies to CPG content)

UW Health Implementation

Potential Benefits:
By treating VTE in the outpatient setting it can avoid admissions, increase patient satisfaction and result in cost savings.

Potential Harms:
Recurrent pulmonary embolism, patient non-adherence, possible higher readmission rate

Implementation Plan
This guideline will be in the guideline tracker on UConnect and on the external anticoagulation website. Links to this guideline will be created in appropriate Health Link tools.

Implementation Tools
ED Physician Responsibilities
- Diagnosis of venous thromboembolism
- Evaluation of eligibility criteria
- Review of eligibility with pharmacist
- Completion of Outpatient venous thromboembolism order set with dosing recommendations from pharmacist
- Identification of responsible party as contact for the following business day
- Ensure patient has PCP follow up plan established
- Order any lab test (ex. INR) as needed

ED Nurse Responsibilities
- Administer first anticoagulant(s) dose
- Provide preliminary injection teaching if applicable
- Supply patient with patient information sheets
- Reinforce instructions to return the next business day to PCP

ED Pharmacist Responsibilities
- Ensure appropriate baseline labs are drawn
- Review potential for drug interactions with home medications
- Review discharge prescriptions for anticoagulant(s)
- Review patient insurance coverage
- Patient medication teaching for anticoagulant(s)

Disclaimer
CPGs are described to assist clinicians by providing a framework for the evaluation and treatment of patients. This Clinical Practice Guideline outlines the preferred approach for most patients. It is not intended to replace a clinician’s judgment or to establish a protocol for all patients. It is understood that some patients will not fit the clinical condition contemplated by a guideline and that a guideline will rarely establish the only appropriate approach to a problem.
References
15. Pradaxa [prescribing information]. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc.; 12/2014