Anticoagulation in Venous Thromboembolism

For additional info about anticoagulation in VTE, visit www.anticoagulationtoolkit.org

### Determining Need for Anticoag.

<table>
<thead>
<tr>
<th>Type/Location</th>
<th>Risk factors*</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute isolated distal DVT of leg without severe symptoms or risk factors for extension*</td>
<td>Risk factors for extension: positive D-dimer, thrombosis is extensive, thrombosis is close to proximal veins, no reversible provoking risk factor, active cancer, h/o VTE, or inpatient status</td>
<td>• No anticoagulation</td>
</tr>
<tr>
<td>Subsegmental PE without proximal DVT or risk factors for recurrence*</td>
<td>Risk factors for VTE recurrence: hospitalized/immobile patients, active cancer, no reversible provoking risk factor</td>
<td>• No anticoagulation</td>
</tr>
</tbody>
</table>

### Guidelines support home initial treatment for some types of VTE as long as certain criteria are met.

<table>
<thead>
<tr>
<th>Type/Location</th>
<th>Clinical criteria for initial treatment in home</th>
<th>Home environment criteria for initial treatment in home</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low-risk PE</td>
<td>Clinically stable with good cardiopulmonary reserve, including age ≥80, no hx of CA or chronic cardiopulmonary disease, HR &lt;110, SBP ≤100 mm Hg, and O2 ≥90%</td>
<td>• Well-maintained living conditions</td>
</tr>
<tr>
<td></td>
<td>No contra. such as recent bleeding, severe liver/kidney disease, or thrombocytopenia</td>
<td>• Strong support network</td>
</tr>
</tbody>
</table>

### Anticoagulation in VTE

<table>
<thead>
<tr>
<th>Anticoagulant</th>
<th>DOACs (dabigatran, rivaroxaban, apixaban, and edoxaban) are recommended over warfarin for DVT of the leg or PE in pts without CA. However, DOACs are contraindicated in pts with severe renal insufficiency (CrCl &lt;30 mL/min), mechanical heart valves, mod/sev hepatic dysfunction, and pregnancy.</th>
<th>Pros/Care</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apixaban (Eliquis®)</td>
<td>• Dose for initially isolated DVT/XI: 10 mg BID X 7 days then 5 mg BID • Reduce dose by 50% if co-administered with strong dual inhibitors of cytochrome CYP3A4 and P-gp (eg. ketoconazole and clarithromycin) • Avoid use with strong dual inhibitors of CYP3A4 and P-gp (eg. rifampin) • Not recommended in patients with prosthetic heart valves</td>
<td>Only DOAC to have less GI bleeding than warfarin in clinical trials</td>
</tr>
<tr>
<td>Daiabigatan (Pradaxa®)</td>
<td>• Dose for initially isolated DVT/XI: 150 mg BID (if CrCl &gt;30 mL/min)* after 5-10 days of parenteral tx • Avoid use with P-gp inhibitors (eg. rifampin) • Avoid use with P-gp inhibitors if CrCl &lt;30 mL/min* • Not recommended in patients with prosthetic heart valves</td>
<td>Reversal agent is available</td>
</tr>
<tr>
<td>Edoxaban (Savaysa®)</td>
<td>• Dose for originally isolated DVT/XI: 60 mg daily after 5-10 days of parenteral tx • Avoid use with combined P-gp and strong CYP3A4 inhibitors or inducers (eg. ketoconazole and ritonavir) • Not recommended in patients with prosthetic heart valves</td>
<td>Once daily dosing</td>
</tr>
<tr>
<td>Rivaroxaban (Xarelto®)</td>
<td>• Dose for initially isolated DVT/XI: 15 mg BID daily then 20 mg daily • Avoid use with combined P-gp and strong CYP3A4 inhibitors or inducers (eg. ketoconazole and ritonavir) • Not recommended in patients with prosthetic heart valves</td>
<td>Should be taken with food</td>
</tr>
<tr>
<td>Warfarin (Coumadin®)</td>
<td>• Initial dose: 5mg is a typical starting dose, but a lower dose may be considered in certain patients (eg. elderly, malnourished, liver disease) • Subsequent dosing based on INR with target range 2-3. • Parenteral tx should be given for at least 5 days and until INR is in range • Avoid in pregnancy</td>
<td>Can be used in patients with severe renal disease (CrCl &lt;30)</td>
</tr>
<tr>
<td>LMWH</td>
<td>• Dose for initially isolated DVT/XI: 1 mg/kg SC 12h (if CrCl&gt;30), 1mg/kg SQ daily (if CrCl&lt;30) • Dose for extended duration: 1 mg/kg SC daily (first month), 150 IU/kg SC daily (month 2)</td>
<td>Drug of choice in pregnancy</td>
</tr>
</tbody>
</table>

* Use Cockcroft-Gault with actual weight to calculate CrCl

### Choice of Anticoagulant

For DVT of leg or PE provoked by surgery or transient/reversible risk factor, 3 months is the recommended length of treatment. For an unprovoked DVT of leg or PE, treat for 3 months and then evaluate the risk/benefit ratio for extended treatment. (see table below)

<table>
<thead>
<tr>
<th>Type/Location</th>
<th>Initial dose: 5mg is a typical starting dose, but a lower dose may be considered in certain patients (eg. elderly, malnourished, liver disease) • Subsequent dosing based on INR with target range 2-3.</th>
<th>Baseline: INR and CBC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low-risk PE</td>
<td>• Avoid use with combined P-gp and strong CYP3A4 inhibitors or inducers (eg. ketoconazole and ritonavir) • Not recommended in patients with prosthetic heart valves</td>
<td>INR 3 days after initiation and approx. 7 days after any dose changes. INRs can gradually be spaced out to monthly if stable</td>
</tr>
<tr>
<td></td>
<td>• Should be taken with food • Twice daily dosing initially • Once daily maintenance dosing</td>
<td>RR can be gradually spaced out to monthly if stable</td>
</tr>
<tr>
<td></td>
<td>• Avoid use with rifampin</td>
<td>• Renal function, liver function, and CBC before initiation and at least yearly</td>
</tr>
<tr>
<td></td>
<td>• Avoid use with strong P-gp inhibitors if CrCl &lt;30 mL/min*</td>
<td>• Renal function, liver function, and CBC before initiation and at least yearly</td>
</tr>
</tbody>
</table>

### Patient Education

- **Follow-up:** at each flu, assess for compliance, sx of bleeding or thromb., interacting meds, and reinforce ed.
- **DOACs:** annually assess CBC, liver, and renal function (more often if renal insufficiency) •warfarin: INRs 3-5 days after re-starting or any changes that can effect INR (ex. med, diet change, or illness) and approx. 7 days after any dose changes. INRs can gradually be spaced out to monthly, if stable, or even longer (up to 3 mos) if INRs have been in range for 3 months. Dose changes per a standardized protocol. •Bleeding: Minor bleeding: Common (eg. petechia, bleeding gums) and is not normally a reason to D/C. Teach or how to prevent and manage. Major bleeds: In most cases, resuming anticoag. is best for pt.(~14 days after GI, within 1 mo. for intracranial)
- **Periprocedural:**
  - **Warfarin:**
    - Maintain stable Vitamin K intake
    - Notify clinic if ill or change in health status (can affect INR)
    - Alcohol can increase INR
  - **DOACs:**
    - Don’t skip doses (short half-life)
  - **LMWH:**
    - Enoxaparin: 1 mg/kg SC q12h (if CrCl ≥30), 1 mg/kg SQ daily (if CrCl <30) •Avoid use with strong P-gp inhibitors if CrCl <30 mL/min* •Avoid use with rifampin •Avoid in pregnancy
    - Initial dose: 5mg is a typical starting dose, but a lower dose may be considered in certain patients (eg. elderly, malnourished, liver disease) •Subsequent dosing based on INR with target range 2-3. •Parenteral tx should be given for at least 5 days and until INR is in range •Avoid in pregnancy
    - Should be taken with food •Twice daily dosing initially •Once daily maintenance dosing
    - Baseline: INR and CBC |
    - INR 3 days after initiation and approx. 7 days after any dose changes. INRs can gradually be spaced out to monthly if stable
    - INRs can be gradually spaced out to monthly if stable
    - Drug of choice in pregnancy
    - Baseline: CBC, creatinine

### Long-term management

- **Follow-up:** at each flu, assess for compliance, sx of bleeding or thromb., interacting meds, and reinforce ed. •DOACs: annually assess CBC, liver, and renal function (more often if renal insufficiency) •warfarin: INRs 3-5 days after re-starting or any changes that can effect INR (ex. med, diet change, or illness) and approx. 7 days after any dose changes. INRs can gradually be spaced out to monthly, if stable, or even longer (up to 3 mos) if INRs have been in range for 3 months. Dose changes per a standardized protocol. •Bleeding: Minor bleeding: Common (eg. petechia, bleeding gums) and is not normally a reason to D/C. Teach or how to prevent and manage. Major bleeds: In most cases, resuming anticoag. is best for pt.(~14 days after GI, within 1 mo. for intracranial)
- **Periprocedural:**
  - **Warfarin:**
    - Maintain stable Vitamin K intake
    - Notify clinic if ill or change in health status (can affect INR)
    - Alcohol can increase INR
  - **DOACs:**
    - Don’t skip doses (short half-life)
  - **LMWH:**
    - Enoxaparin: 1 mg/kg SC q12h (if CrCl ≥30), 1 mg/kg SQ daily (if CrCl <30) •Avoid use with strong P-gp inhibitors if CrCl <30 mL/min* •Avoid use with rifampin •Avoid in pregnancy
    - Initial dose: 5mg is a typical starting dose, but a lower dose may be considered in certain patients (eg. elderly, malnourished, liver disease) •Subsequent dosing based on INR with target range 2-3. •Parenteral tx should be given for at least 5 days and until INR is in range •Avoid in pregnancy
    - Should be taken with food •Twice daily dosing initially •Once daily maintenance dosing
    - Baseline: INR and CBC |
    - INR 3 days after initiation and approx. 7 days after any dose changes. INRs can gradually be spaced out to monthly if stable
    - INRs can be gradually spaced out to monthly if stable
    - Drug of choice in pregnancy
    - Baseline: CBC, creatinine

For patient handouts, visit www.anticoagulationtoolkit.org
References


Drug package inserts

- Apixaban: https://packageinserts.bms.com/pi/pi_eliquis.pdf
- Dabigatran: http://docs.boehringer-ingelheim.com/Prescribing%20Information/PIs/Pradaxa/Pradaxa.pdf
- Edoxaban: http://dsi.com/prescribing-information-portlet/getPIContent?productName=Savaysa&inline=true
- Enoxaparin: http://products.sanofi.us/lovenox/lovenox.html

Disclaimer: This document is for informational purposes only and does not, itself, constitute medical advice. This document is not a replacement for careful medical judgments by qualified medical personnel. There may be information in this document that does not apply to or may be inappropriate for the medical situation at hand.