**Sutter Health COVID-19 Pharmacologic VTE Prophylaxis Guidelines**
Revision Date: 11/9/2020

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**Confirmed COVID-19+ patient**

**Labs on admission:** D-dimer, PT, aPTT, fibrinogen and CBC with differential
- Elevated D-dimer should not be a lone criterion in driving care decisions

**Inpatient labs every 2-3 days:** CBC, PT, aPTT, D-dimer
- If worsening parameters, consider more aggressive critical care support
- Do not use blood products to correct non-bleeding coagulopathy

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**VTE prophylaxis for ALL hospitalized COVID-19+ patients**

**Non-critically ill**

- **BMI < 40:**
  - Enoxaparin 40mg SQ q24h
  - CrCl 15-30 ml/min: Enoxaparin 30 mg SQ q24h
  - CrCl < 15 ml/min: UFH 7,500 units SQ q8h

- **BMI > 40:**
  - Enoxaparin 40mg SQ q12h
  - CrCl 15-30 ml/min: Enoxaparin 40 mg SQ q24h
  - CrCl < 15 ml/min: UFH 7,500 units SQ q8h

**Pregnancy:**
- If infant is non-viable, follow dosing for non-pregnant patients above. If infant is viable, consult Maternal Fetal Medicine for recommendations.
- Hold anticoagulation during active labor or if delivery anticipated within 12-24 hours.

For pts <50 kg, dose adjustment may be needed
- If pharmacologic prophylaxis contraindicated: SCDs

**Critically Ill (see appendix A)**

**Intermediate-Range Prophylaxis Dosing**
(Recommendations based on expert opinion)

- **Normal Renal Function:**
  - Enoxaparin 0.5mg/kg SQ q12h
  - CrCl 15-30 ml/min: Enoxaparin 0.5mg/kg SQ q24h
  - CrCl <15 ml/min: UFH 7,500 units SQ q8h

- **Pregnancy:**
  - If infant is non-viable, follow dosing for non-pregnant patients above. If infant is viable, consult Maternal Fetal Medicine for recommendations.
  - Anti-Xa monitoring should be conducted for ALL patients (see Appendix B)
  - Use LABFXA for enoxaparin monitoring
  - Consider more frequent monitoring in pts: >90 kg, < 50 kg, pregnant, AKI/CKD, high bleeding risk.
  - Target range: 0.2-0.5 units/ml

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**Therapeutic anticoagulation (TX AC)**

**On TX AC prior to admission**

- Use UFH or LMWH for all hospitalized patients who require TX AC. DOACs are not recommended for TX AC in COVID-19.

- **Pregnancy:** If infant is viable, consult Maternal Fetal Medicine for recommendations.

  - aPTT is not accurate in COVID-19; use anti-Xa monitoring
  - Use LABUFHEP for anti-Xa monitoring for UFH
  - Use LABFXA for anti-Xa monitoring for enoxaparin

  - For patients recently on FXa inhibitor (apixaban, rivaroxaban, edoxaban), IV UFH cannot be monitored via anti-Xa
    - Use enoxaparin if CrCl ≥ 15 ml/min
    - If CrCl <15 ml/min, multidisciplinary discussion

**Highly-suspected or confirmed VTE**

- If unable to imaging & high clinical suspicion for VTE, recommend TX AC if no contraindications
- Abnormal PT/PTT are not contraindications to TX AC in COVID-19

- **Options:**
  - Enoxaparin 1.5 mg/kg SQ Q24h (preferred)
  - Or 1 mg/kg SQ 12h
  - CrCl 15-30 ml/min: Enoxaparin 1 mg/kg SQ Q24h
  - CrCl <15 ml/min: use IV UFH ANTIFACTOR XA (VTE-PE/DVT) order sets

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**Post-hospitalization VTE prophylaxis:**

- Severely ill COVID-19+ patients may experience prolonged hospital stay, significant deconditioning, post-ICU syndrome and thus may not fully recover to baseline mobility or health status by time of discharge
- Consideration for extending VTE prophylaxis beyond discharge are reasonable on a case-by-case basis, and may include COVID-19 patients who: were admitted to the ICU, intubated, sedated, and/or paralyzed for multiple days; have ongoing VTE risk factors such as diminished mobility and weakness; have not recovered to baseline physical or mobility status; are discharging to a post-acute care facility; AND have low bleed risk
- Enoxaparin 40 mg SQ q24h OR rivaroxaban 10 mg PO daily for up to 30 days beyond hospitalization is reasonable
- **Post Discharge Recommendations for OB patients:** Antepartum patients need LMWH prophylaxis for total of 4 weeks from COVID-19 diagnosis. Postpartum patients LMWH prophylaxis for 6 weeks after delivery if the COVID diagnosis was < 14 days from delivery.
- Assessment of access to and affordability of extended VTE prophylaxis is required prior to prescribing.

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**Post-hospitalization VTE management:**

- If acute VTE confirmed at time of suspicion, continue TX AC for ≥3 months then reassess
- If VTE unconfirmed & treated empirically, continue TX AC for 3 months regardless of subsequent (negative) imaging findings

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Additional Recommendations for the Management of Anticoagulation in Pregnant COVID-19 patients:

- **ALL Antepartum patients, regardless of disease status, need LMWH prophylaxis for a total of 4 weeks from positive COVID-19 test result.**
- Hold anticoagulation during active labor or if delivery is anticipated within 12-24 hours.
- Guidance for usual dosing in pregnancy:
  - BMI < 40 and determined viable per MFM and LOW risk for urgent delivery -> Lovenox 0.5 mg/kg SQ q24h
  - BMI < 40 and determined viable per MFM and HIGH risk for urgent delivery -> UFH 7,500 units SQ q12h
  - BMI >/= 40 and determined viable per MFM and LOW risk for urgent delivery -> Lovenox 0.5 mg/kg SQ q12h
  - BMI >/= 40 and determined viable per MFM and HIGH risk for urgent delivery -> UFH 10,000 units SQ q12h

Appendix A: Definition and management of critically ill COVID-19 patients

All COVID-19 patients requiring admission to the Intensive Care Unit should receive at least intermediate-dose anticoagulation (middle column). Consider diagnostic testing for systemic venous and arterial thromboses. Empiric therapeutic anticoagulation may be considered in the setting of extremely high D-dimer or fibrinogen (e.g. Pregnancy with D-dimer >3000 ng/ml; Non Pregnant with D-dimer >2000 ng/ml and/or elevated fibrinogen > 800 mg/dL), persistent clotting of lines and/or worsening clinical course, therapeutic anticoagulation may be considered via multidisciplinary discussion with physicians and pharmacists caring for the patient (e.g. critical care, infectious disease, internal medicine, hematology, pharmacy, etc).

Elevation of D-Dimers, fibrinogen and prolonged prothrombin times have been associated with mortality in COVID 19. Higher levels of anticoagulation have been postulated to potentially improve survival. Decisions to escalate to therapeutic anticoagulation in the absence of confirmed VTE/PE should weigh the risks of thrombosis, severity of the patient’s illness, and bleeding risk.

For patients transferring out of intensive care to the general ward environment, appropriate dose and duration of anticoagulation (i.e. full therapeutic dose, intermediate dose, or standard prophylaxis dose) should be a careful multidisciplinary decision, based upon the individual patient’s severity and duration of illness in the intensive care unit, deconditioning, mobility status, risks of thrombosis, and bleeding risk.

Appendix B: Timing for Anti-Xa monitoring when using enoxaparin in critically ill COVID-19 patients

In order to balance the risk of thrombotic and bleeding events in critically ill COVID-positive patients, the following Anti-Xa monitoring schedules are recommended:

- For enoxaparin Q12 hour dosing frequency: first lab draw 4 hours after the 3rd dose; second lab draw 4 hours after the 7th dose
- For enoxaparin Q24 hour dosing frequency: first lab draw 4 hours after the 2nd dose; second lab draw 4 hours after the 4th dose

* References updated weekly based on most current evidence based medicine professional society recommendations. References are available upon request. Please contact: hatfielm@sutterhealth.org
Appendix C: Dose Adjustments for patients outside target range when using enoxaparin in critically ill COVID-19 Patients:

When anti-Xa levels result below the target range for patients on enoxaparin, the following dose adjustment parameters are recommended. All dosage adjustments should be rounded to the nearest 10mg increment available, ensuring doses are rounded **UP** if levels are below target range.

<table>
<thead>
<tr>
<th>Anti Xa level (units/mL)</th>
<th>Dosage Change</th>
<th>Next level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intermediate- Range Prophylactic Dosing</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 0.1 unit/mL</td>
<td>Increase by 20%</td>
<td>4 hours after next dose</td>
</tr>
<tr>
<td>0.11 – 0.19 unit/mL</td>
<td>Increase by 10%</td>
<td>4 hours after next dose</td>
</tr>
<tr>
<td>0.2 – 0.5 unit/mL</td>
<td>NO CHANGE</td>
<td></td>
</tr>
<tr>
<td>0.5 -- 1 unit/mL</td>
<td>Multi-disciplinary discussion of risk vs benefit of dosage adjustment is warranted</td>
<td></td>
</tr>
<tr>
<td>&gt; 1 unit/mL</td>
<td>Decrease by 10-20% per multi-disciplinary discussion of risk vs benefit</td>
<td></td>
</tr>
<tr>
<td>Therapeutic dosing</td>
<td>See Lexi-Comp for Dosage titration to achieve therapeutic dose of 0.5 to 1.1 unit/mL for 1mg/kg q12h dosing</td>
<td></td>
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</tbody>
</table>

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