Anticoagulation Dosing Guideline for Adult COVID-19 Patients

Enoxaparin is the preferred first line anticoagulant for patients diagnosed with COVID-19. The incidence of HIT with enoxaparin is less than 1%.

**VTE Prophylaxis:**
VTE prophylaxis will be considered for COVID-19 patients who are low risk.

**Low risk COVID-19 patient**
1. Not receiving mechanical ventilation
2. D-Dimer < 6 mg/L
3. ESRD on iHD without clotting

<table>
<thead>
<tr>
<th>Kidney Function</th>
<th>BMI (kg/m²)</th>
<th>Dosing of Enoxaparin</th>
<th>Concern for HIT or LMWH Failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>CrCL ≥ 30 mL/min</td>
<td>18.5-39.9</td>
<td>30mg SUBQ Q12H</td>
<td>Consult Hematology</td>
</tr>
<tr>
<td></td>
<td>40-49.9</td>
<td>40mg SUBQ Q12H</td>
<td></td>
</tr>
<tr>
<td></td>
<td>≥ 50</td>
<td>60mg SUBQ Q12H</td>
<td></td>
</tr>
<tr>
<td>CrCL &lt; 30 mL/min OR ESRD/AKI on RRT</td>
<td>18.5-39.9</td>
<td>30mg SUBQ Q24H</td>
<td>Consult Hematology</td>
</tr>
<tr>
<td></td>
<td>≥ 40</td>
<td>40mg SUBQ Q24H</td>
<td></td>
</tr>
<tr>
<td>Special Population: &lt; 18.5 (or weight &lt; 50kg)</td>
<td>Heparin 2500 SUBQ Q8H</td>
<td>Consult Hematology</td>
<td></td>
</tr>
</tbody>
</table>

*Contraindications: Platelets < 25 K/uL or Fibrinogen < 50 mg/dL or active bleeding

**Therapeutic anticoagulation**
Therapeutic anticoagulation will be considered for COVID-19 patients who are considered high risk or diagnosed with an acute VTE.

**High risk COVID-19 patient (any one of the following criteria):**
1. Receiving mechanical ventilation AND D-dimer ≥ 6 mg/L
2. Acute kidney injury (Scr increase 0.3 mg/dL above baseline) +/- CVVHD/AVVHD/SLED or IHD with clotting

**Anti-Xa level goals for enoxaparin therapy (when indicated):**
1. Therapeutic peak LMWH level (Drawn 4 hours after 3rd dose): 0.6-1 anti-Xa units/mL
2. Therapeutic trough LMWH level (Drawn 1 hour prior to 3rd dose): < 0.5 anti-Xa units/mL

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</thead>
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<tr>
<td>CrCL ≥ 30 mL/min</td>
<td>12-49.9</td>
<td>1mg/kg SUBQ Q12H</td>
<td>Bivalirudin infusion (see Anticoagulation COVID-19 guidelines for dosing)</td>
</tr>
</tbody>
</table>
|                | ≥ 50      | 0.8mg/kg SUBQ Q12H | **Monitor peak anti-Xa level with 3rd dose**  
|                |           | **Consult pharmacist to assist with obtaining anti-Xa level and dose adjustment** |
| CrCL < 30 mL/min | 12-49.9   | 1mg/kg SUBQ Q24H | Bivalirudin infusion (see Anticoagulation COVID-19 guidelines for dosing) |
|                | ≥ 50      | 0.8mg/kg SUBQ Q24H | **Monitor peak anti-Xa level with 3rd dose**  
|                |           | **Consult pharmacist to assist with obtaining anti-Xa level and dose adjustment** |
| ESRD or AKI on RRT |            | 0.8mg/kg SUBQ Q24H | Bivalirudin infusion (see Anticoagulation COVID-19 guidelines for dosing) |
|                |           | (MAX dose 1mg/kg Q24H) | **Monitor peak and trough anti-Xa level with 3rd dose**  
|                |           | **Consult pharmacist to assist with obtaining anti-Xa level and dose adjustment** |

If minor bleeding prior to obtaining steady state anti-Xa levels
- Decrease dose to 0.5 mg/kg and monitor anti-Xa peak and trough with 1st dose of new regimen
- Consult pharmacist to assist with obtaining anti-Xa levels and dose adjustment

*Contraindications: Platelets < 50 K/uL or fibrinogen < 100 mg/dL or active bleeding
Intra-dialytic anticoagulation for renal replacement therapy
Nephrology service will determine the need for a booster dose of IV enoxaparin when ordering renal replacement therapy

- Renal replacement therapy (IHD/SLED/CRRT)
  - Enoxaparin 30 mg IV x 1 preferably prior to or within an hour of starting dialysis
  - If HIT positive or enoxaparin failure, recommend switching to bivalirudin

Bivalirudin: Therapeutic anticoagulation
Due to the liver injury that may be seen in patients with COVID-19, bivalirudin is the preferred direct thrombin inhibitor for the treatment of HIT, enoxaparin failure, or patients receiving extracorporeal membrane oxygenation (ECMO).

<table>
<thead>
<tr>
<th>CrCl (ml/min)</th>
<th>Bivalirudin Initial dose (mg/kg/hour)</th>
</tr>
</thead>
<tbody>
<tr>
<td>60</td>
<td>0.15 +/- 0.1</td>
</tr>
<tr>
<td>30-60</td>
<td>0.08 +/- 0.04</td>
</tr>
<tr>
<td>&lt; 30</td>
<td>0.05 +/- 0.02</td>
</tr>
<tr>
<td>IHD (25% clearance by HD filters) or CRRT</td>
<td>0.07 +/- 0.03</td>
</tr>
</tbody>
</table>

IHD - intermittent hemodialysis, CRRT – continuous renal replacement therapy

Dose adjustments:

<table>
<thead>
<tr>
<th>aPTT (seconds)</th>
<th>Dose adjustment</th>
<th>Monitoring recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;50</td>
<td>Increase infusion rate by 20%</td>
<td>Re-check aPTT 4 hours after rate change</td>
</tr>
<tr>
<td>50-80</td>
<td>No change</td>
<td>Re-check aPTT at 4 hours; if 2 consecutive aPTTs are at goal, check aPTT q 24 hours</td>
</tr>
<tr>
<td>&gt;80*</td>
<td>Decrease infusion rate by 20%</td>
<td>Re-check aPTT 4 hours after rate change</td>
</tr>
</tbody>
</table>

* If aPTT >3x baseline, consider holding infusion for 1 hour and re-starting at 50% lower rate

- Monitoring:
  - aPTT q 4 hours following initiation of infusion and following dosing adjustment – target aPTT 50-80
  - If 2 consecutive aPTT are at goal, check aPTT q 24 hours
  - CBC as appropriate based upon clinical status of patient

Bivalirudin: anticoagulation for renal replacement therapy

- CVVH: no loading dose, bivalirudin 2 mg/hour one hour prior to RRT until completion
  - If doses of 2 mg/hour are ineffective, increase bivalirudin dose by 20%

Discontinuation of Therapeutic Anticoagulation

- Patients who are transferred to a general medical floor should be transitioned from therapeutic enoxaparin to a prophylactic enoxaparin
  - Prior to discharge:
    - Patients with normal renal function should receive apixaban 2.5 mg bid x 4-6 weeks
    - Patients with AKI or ESRD should receive apixaban 2.5 mg bid x 2 weeks
      - In patients who do not have insurance coverage for a DOAC or in whom a DOAC may be contraindicated, prophylactic doses of enoxaparin may be used for the time frames listed above
      - Warfarin may be considered in patients who have confirmed HIT
References

1. Rush Anticoagulation Guidelines. Rush University Medical Center. May 2019