CONSIDERATIONS FOR PHARMACOLOGIC TREATMENTS OF PATIENTS WITH CONFIRMED COVID-19 TESTING FOR THE PICU & GENERAL INPATIENT UNIT (GIU)

(This pathway will be reassessed & updated regularly based on experience & emerging data)

Pediatric Patient (≤ 18 Y/O) With Confirmed + COVID-19 Testing
Provide supportive care w/ acetaminophen/NSAIDs pm clinician’s discretion & consider COVID-19 pharmacologic treatment criteria listed below for the GIU & PICU

GIU Criteria
- **Requiring:** ≥ 1 L/min NC O₂ for 24 hrs without being able to wean OR
- **Worsening clinical trajectory** with increasing oxygen support within 24 hrs of starting O₂

PICU Criteria
- **Requiring:**
  - Non-invasive vent support
  - Mechanical ventilation OR
  - ECMO

Contact Pediatric COVID-19 Treatment Team (PCTT) if Considering Treatment
(Find PCTT contact in mobile heartbeat - Available from 8am-5pm, ID fellow available for overnight consults & weekends)

PCTT to review case and determine risks/benefits of investigational treatment on a case-by-case basis

If caregiver & team agree to therapy

Obtain Baseline EKG & Labwork:
- CBC⁺, CRP⁺, Procalcitonin⁺, Ferritin⁺, BMP⁺, Mg⁺, LDH, Troponin, D-Dimer, Fibrinogen, ESR, PT/PTT, cytokine panel

*Priority tests if there is limited blood volume

Consider
- Blood/ETT Cx’s prior to antibiotics - yield highest for PICU pts
- Cardiology consult if abnormal EKG/ cardiac enzymes

Provide Recommended Treatment
(Info on dosing, exclusion criteria, monitoring, & side effects for 1st & 2nd line agents)

For GIU: Repeat labs q 24-hrs if patient not clinically improving
For PICU: Repeat labs q 24-hrs if continues to require PICU support
For Both Units:
- Obtain q 48-hour cytokine panel if meets criteria for q-24 hr labs listed above
- Other monitoring w/ medications (EKGs, additional labwork, monitoring etc.)

Return to Inpatient Pathway when ready for discharge for guidance on home care
Complete treatment course for outpatients as guided by PCTT

For Both PICU & GIU:
May also consider treatment for patients with no oxygen requirement (or lesser degree of resp. support) who have fever and respiratory distress AND a history of:
- Congenital cardiac disease, chronic lung disease, immunosuppression and/or other concerning illness

See Yale COVID information if decision made to utilize adult treatment pathway for inpatients > 18 y/o

Informed verbal or written consent is required for all investigational therapies and should be obtained by either PCTT or by the primary team.

Utilize “COVID-19 Treatment Medications for Pharmacy/ID Provider Entry - Pediatric” Orderset in EPIC

For PICU, add quantiferon gold, may start tx before get result
Consider
- Blood/ETT Cx’s prior to antibiotics - yield highest for PICU pts
- Cardiology consult if abnormal EKG/ cardiac enzymes

References
• For supportive care, it should be safe to use both acetaminophen and NSAIDs on a prn basis per clinician discretion

• There is no firm data to show that NSAIDs worsen the course of COVID-19
  - There is a theoretical risk given the fact that COVID-19 virus uses ACE2 to enter cells and NSAIDs (and ACE inhibitors) may increase ACE2 circulation.
  - However, there is some data to show other coronaviruses that also use ACE2, like SARS, have reduced viral replication with NSAIDs (indomethacin).
  - The WHO and FDA do not recommend against the use of NSAIDs for COVID-19 infections, but will be further investigating the issue - we will update our recs accordingly
• The Pediatric COVID-19 Treatment Team (PCTT) is a multidisciplinary team that will meet to review use of pharmacologic treatment on a case-by-case basis. Members will meet with caregivers and patients/families to review the risks/benefits, review existing evidence and obtain informed consent for use if the decision is reached to pursue pharmacologic therapy.

• PCTT Members:
  ◦ Carlos Oliveira (ID, Chair)
  ◦ Michelle Rychalsky (Pharmacy, Co-Chair)
  ◦ Jaspreet Loyal (Hospitalist Service, member)
  ◦ Adam Berkwitt (Hospitalist Service, member)
  ◦ an Ferguson (Rheumatology, member)
  ◦ Josep Panisello (PICU, member)
  ◦ Tom Murray (ID, member)
  ◦ Elissa Zirinsky (ID, member)
  ◦ ID service team (Fellow and Attending, revolving members)
  ◦ Elijah Paintsil (ID, member)
  ◦ Rebecca Ciaburri (Quality/Safety, member)
  ◦ Matthew Grossman (Quality/Safety, member)
# RECOMMENDED 1st LINE PHARMACOLOGIC TREATMENT FOR PEDIATRIC PATIENTS (≤18Y/O) WITH COVID-19

<table>
<thead>
<tr>
<th>1st LINE AGENT</th>
<th>DOsing</th>
<th>ExCLUSION CRITERIA</th>
<th>MONITORING &amp; LABWORK</th>
<th>SIDE EFFECTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydroxychloroquine (HCQ)</td>
<td>6.5mg/kg/dose q 12 hrs x 1 day (Max 400mg/dose) Then 3.25-3.5mg/kg/dose q 12 hrs x 4 days* (Max 200mg/dose) Use ideal body weight for dosing to reduce side effects</td>
<td>• QTc interval &gt; 500 Use with caution in infants &lt; 6 months - consider 2nd line agent if not critically ill</td>
<td>• Daily EKGs - if concern for prolonged QTc recommend telemetry - consider ICU monitoring, cardiology consult &amp; discuss with PCTT regarding alternative therapies Maintain K &gt; 3.5 &amp; Mg &gt; 1.5 to avoid issues w/ prolonged QTc CBC and CMP at least every 3 days while on treatment (daily if G6PD deficient)</td>
<td>• Risk of cardiotoxicity (QTc prolongation) • Hypoglycemia • Hemolysis in patients with G6PD (very low risk) • Retinopathy and marrow suppression (low risk with 5-days) • Hepatotoxicity: caution in patients with underlying liver disease or if using other hepatotoxic drugs • May increase levels of cyclosporine &amp; digoxin</td>
</tr>
</tbody>
</table>

*Duration may be extended for up to 10 days on a case-by-case basis depending on response and severity of illness.

**Review potential medication interactions with clinical pharmacist prior to initiation**

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**CLICK HERE FOR INFORMATION ON:**
- 2nd line agents for COVID-19 AND
- Managing critically ill patients not responding to therapy
# Recommended 2nd Line Pharmacologic Treatments & For Critically Ill Patients

## Consider 2nd Line Agent If Cannot Tolerate or Meets Exclusion Criteria for HCQ

<table>
<thead>
<tr>
<th>2nd Line</th>
<th>Dosing</th>
<th>Exclusion Criteria</th>
<th>Monitoring &amp; Labwork</th>
<th>Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Lopinavir/ Ritonavir</strong></td>
<td>Age 14 days - 12 months: 18mg/kg/dose of lopinavir twice daily x 7 days**&lt;br&gt;Age ≥ 12 months: 300mg/m²/dose of lopinavir twice daily (max 400mg of lopinavir twice daily) x 7 days**</td>
<td>- Coadministration with drugs that are highly dependent on CYP3A for clearance&lt;br&gt;- Avoid use in combination with QTc/PR prolonging drugs&lt;br&gt;- Avoid use in neonates &lt;14 days of age</td>
<td>- Daily Glucose testing&lt;br&gt;- CBC and CMP at least every 3 days while on treatment&lt;br&gt;- Daily LFTs in patients with underlying hepatic disease&lt;br&gt;- EKG monitoring daily if receiving other drugs that prolong QTc - maintain potassium &gt; 3.5 and magnesium &gt; 1.5 to prevent QTc prolongation&lt;br&gt;- Amylase and Lipase every 3 days if using Lopinavir/ritonavir&lt;br&gt;- All adolescent patients should have HIV testing prior to initiation</td>
<td>- Rash&lt;br&gt;- Hyperglycemia&lt;br&gt;- Nausea, vomiting, diarrhea&lt;br&gt;- May cause hepatitis and/or exacerbate pre-existing hepatic dysfunction&lt;br&gt;- Use Lopinavir/ritonavir with caution in patients with increased triglycerides; pancreatitis has been observed.</td>
</tr>
</tbody>
</table>

**Duration may be extended for up to 14 days on a case-by-case basis depending on response and severity of illness.**

## Consider Remdesivir for Critically Ill Patients Not Responding to 1st or 2nd Line Therapy

<table>
<thead>
<tr>
<th>Remdesivir</th>
<th>Dosing</th>
<th>Exclusion Criteria</th>
<th>Monitoring</th>
<th>Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>If ≥ 12 y/o &amp; ≥ 40kg - eligible for Remdesivir Clinical Trial - Contact PCTT to Obtain&lt;br&gt;if &lt; 12 y/o or &lt; 40kg - obtain via emergency IND</td>
<td>&lt;40 kg: loading dose: 5 mg/kg (max 200 mg) once; followed by maintenance dose (starting 24 hours after loading dose) of 2.5 mg/kg (max 100 mg) every 24 hours x 9 days&lt;br&gt;≥40 kg: loading dose: 200 mg once; followed by maintenance dose (starting 24 hours after loading dose) of 100 mg every 24 hours x 9 days</td>
<td>- Participation in any other clinical trial of an experimental treatment for COVID-19&lt;br&gt;- Concurrent treatment with other agents with actual or possible direct acting antiviral activity against SARS-CoV-2 is prohibited &lt; 24 hours prior to study drug dosing&lt;br&gt;- Evidence of multiorgan failure (severe)&lt;br&gt;- Mechanically ventilated (including V-V ECMO) ≥ 5 days, or any duration of V-A ECMO (severe)&lt;br&gt;- Requiring mechanical ventilation at screening (moderate) (CPAP is accepted)&lt;br&gt;- ALT or AST &gt; 5 x ULN&lt;br&gt;- Creatinine clearance &lt; 50 mL/min (Cockcroft-Gault for ≥ 18 yo and Schwartz for &lt; 18 yo)&lt;br&gt;- Positive pregnancy test&lt;br&gt;- Breastfeeding woman&lt;br&gt;- Known hypersensitivity to the study drug, the metabolites, or formulation excipient</td>
<td>Days 3, 5, 8, 10, and 14 or until discharge (daily while in PICU):&lt;br&gt;- CBC, BUN, creatinine, creatinine clearance, glucose, total bilirubin, ALT, AST</td>
<td>- Not yet FDA approved&lt;br&gt;- Known potential side effects include: elevated transaminases, reversible kidney injury, and hypotension during infusion.</td>
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## Consider Addition of Anakinra & Corticosteroids If Concern for Cytochrome Storm/Clinical Deterioration - Contact Rheumatology for dosing and guidance

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**Back to 1st Line Meds**

**Back to Home**

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Click on this link for further information on protease inhibitor drug-drug interactions.
REFERENCES