Treatment Algorithm for COVID-19

Last Revised 3/27/20

SARS-CoV-2 (COVID-19) positive or strongly suspected

Is patient presently hospitalized or requires inpatient management?

No

- Stay home and avoid close contact with others to minimize spread
- Drink plenty of water
- Symptomatic care for fever, cough, congestion, pain
- Avoid corticosteroids unless required for other condition (e.g. COPD exacerbation)
- If shortness of breath develops, seek immediate medical evaluation

Yes

- Consider antibiotics for secondary bacterial pneumonia if concerned
- Avoid corticosteroids unless indicated for separate process (e.g., septic shock, COPD, asthma, ARDS, etc.)

Patient has any of the following AND confirmed SARS-CoV-2?

- Age ≥ 65 years
- Significant history of lung and/or heart disease
- History of transplantation (solid organ or hematologic)
- Immunocompromising condition and/or receiving immunosuppressive medications
- Moderate to severe infection: Radiographic evidence of pneumonia requiring supplemental oxygen and/or mechanical ventilation

No → **Supportive Care**

Yes → Clinical Status

- Stable supplemental oxygen requirements
- Worsening oxygenation requirements, mechanical ventilation, or expected need for mechanical ventilation within 36 hours

Antiviral therapy may be considered*

Site Specific Criteria

Central Region: ID consult mandatory if initiating therapy.

South Colorado Region: Contact Critical Care boarded providers. Antivirals restricted to critical care boarded or infectious diseases providers

Northern Colorado Region: Contact ID or pulmonology for approval

Contact local antimicrobial stewardship for treatment-related questions

Medications

First-line: Hydroxychloroquine x 5 days

Azithromycin in combination is currently not recommended due to lack of in vitro activity, clinical evidence, and risk of additive adverse events

Second-line: Lopinavir/ritonavir (LPV/r) ± Ribavirin x 5 days

Third-line: Nitazoxanide x 5 days

Remdesivir - currently unavailable for most patients (Page 2)

Antibiotics should be discontinued upon diagnosis of COVID-19 and absence of features consistent secondary bacterial pneumonia

Evidence of severe infection, including hyperinflammatory response?
Consideration of IL-6 inhibition
Assess for agent-specific use criteria

- **Sarilumab Clinical Trial** (Anschutz Only) **Criteria Page 3**
- **Tocilizumab** (All UCHealth) **Criteria Page 2**

*Agents are not FDA approved for COVID-19, and limited evidence supports possible benefit, weigh risks and benefits prior to initiation. Data is rapidly evolving with therapeutics for COVID-19 and recommendations are subject to change rapidly. Please refrain from printing this document.

Medications for Treatment of COVID-19 Infection

<table>
<tr><th>Medication</th><th>Dosing</th><th>Considerations for use</th></tr>
<tr><td>Hydroxychloroquine</td><td>400 mg PO BID for one day, then 200mg PO BID x 4 days
(Duration: 5 days)</td><td>• Pregnancy category C, human data in malaria does not show increased risk
• Caution in liver disease
• Low drug interaction potential
• Monitoring: QTc, visual changes, neuropathy, and cytopenias (anemia may occur and is higher risk among those with G6PD deficiency, no need to send G6PD before starting, consider checking if anemia develops)
• Azithromycin in combination is currently not recommended due to lack of in vitro activity, clinical evidence, and risk of additive adverse events
• Caution using Azithromycin for CAP coverage in patients with baseline QTc prolongation; consideration can be given to doxycycline</td></tr>
<tr><td>Lopinavir/ritonavir (LPV/r)
± Ribavirin</td><td><u>Lopinavir/ritonavir</u>:
400mg/100mg PO BID
<u>Oral Ribavirin:</u>
All patients receive 10 mg/kg load, followed by maintenance dosing for 5 days
Oral Ribavirin Maintenance Dosing
<table><tr><th>CrCl (ml/min)</th><th>Weight (kg)</th><th>Dose</th></tr><tr><td rowspan="4">> 50</td><td>> 120</td><td>1,000 mg TID</td></tr><tr><td>91-120</td><td>800 mg TID</td></tr><tr><td>61-90</td><td>600 mg TID</td></tr><tr><td>40-60</td><td>400 mg TID</td></tr><tr><td>30-50</td><td>All weights</td><td>200 mg TID</td></tr><tr><td><30/HD</td><td>All weights</td><td>200 mg daily</td></tr></table>*Based on limited data</td><td>• LPV/r pregnancy category C, human data does not show increased teratogenic risk
• Ribavirin pregnancy category X
• Significant drug interaction potential with LPV/r
• Consider testing for HIV if has not been done previously or if high-risk behavior placing patient at risk for HIV acquisition
• Monitor: QTc, liver impairment, cytopenias, and diarrhea
• Oral ribavirin preferred; Inhaled ribavirin discouraged, consideration for use in consultation with ID and ID pharmacy</td></tr>
<tr><td>Nitazoxanide</td><td>1,000 mg BID x 5 days</td><td>• In vitro activity only; High cost</td></tr>
</table>

System Criteria for Tocilizumab Use (Based on Drug Availability or Clinical Trial Availability)

- Confirmed COVID-19 positive (No empiric use)
- Critical illness associated with COVID-19 evidenced by: Respiratory failure requiring mechanical ventilation *or* Shock *or* failure of other organs requiring ICU care
- Evidence of ≥2 laboratory abnormalities associated with hyperinflammatory response: D-Dimer > 1 mcg/mL, Serum ferritin > 600 mcg/L, Persistent fever > 38.3°C, C-Reactive Protein > 100 mg/L or 10x ULN, Interleukin-6 ≥ 3x ULN
- Ordered/recommended by Infectious Diseases or Pulmonology Services
- Review and approval by secondary provider(s) not directly involved in the patients care
- ALT/AST < 5x ULN
- Platelet Count is ≥ 50,000/mm3
- Absolute Neutrophil Count (ANC) is ≥ 500/mm^3
- No presence of active or strongly suspected bacterial or fungal infection. Stability of these infections with appropriate antibiotics/antifungals and proceeding with tocilizumab should be carefully weighed by ordering/consulting infectious diseases and/or pulmonology physician.
- Consider avoiding use for significantly elevated procalcitonin levels (i.e > 2 ng/mL), as this may represent an active bacterial infection
- No history of untreated or inadequately treated TB, or latent TB infection
- Caution if high risk of GI perforation (primarily reported as a complication of diverticulitis)
- Not a candidate for Sarilumab Clinical Trial (Anschutz only)

Remdesivir

- As of 3/23/20 individual compassionate use requests for remdesivir can no longer be made to obtain the medication through the manufacturer, Gilead.
  - As an exception, **compassionate use requests may still be made for pregnant women and children < 18 years of age** with confirmed COVID-19 and severe manifestations of disease.
- Gilead is in the process of transitioning to an expanded access program, at which point the medication will be available. There is currently no timeline for when this will occur.

Open COVID-19 Clinical Trials (Anschutz Campus Only)

Sarilumab Clinical Trial: Regeneron 6R88-COV-2040 – An Adaptive Phase 2/3, Randomized, Double-Blind, Placebo-Controlled Study Assessing Efficacy and Safety of Sarilumab for Hospitalized Patients with COVID-19

- Primary objective: Evaluate the clinical efficacy of sarilumab, a monoclonal antibody IL-6 receptor antagonist, relative to the control arm in adult patients hospitalized with severe or critical COVID-19.
- Participants are randomized in a 2:2:1 ratio to a single dose of sarilumab 400 mg IV, 200 mg IV, or placebo.

Requirements to Enter Study:

- Confirmed SARS-Cov-2 infection (up to 14 days prior to enrollment)
- ≥ 18 years
- Hospitalized (or documentation of a plan to admit to the hospital if the patient is in an emergency department)
- Evidence of pneumonia by chest radiograph, chest computed tomography or chest auscultation (rales, crackles)
- Fever documented in the medical record at any time during the admission
- Requires supplemental oxygen administration by nasal cannula, simple face mask, non-rebreather mask or high-flow nasal cannula, invasive or non-invasive ventilation OR requiring treatment in an intensive care unit OR multiorgan system dysfunction
- No known or suspected active bacterial, fungal or mycobacterial infections
- ANC ≥ 2000/mm^3, AST ≤ 195 IU/L and ALT ≤ 260 IU/L, platelets ≥ 50,000/mm^3
- Prior or concurrent hydroxychloroquine is not an exclusion

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