



## GUIDANCE FOR TREATMENT OF COVID-19 IN ADULTS AND CHILDREN

### Patient population:

Adults and pediatric patients with COVID-19 infection, who are admitted on an inpatient floor or to the intensive care unit.

### Key points:

Details regarding isolation/precautions, personal protective equipment, patient movement, family/visitor policy, and cleaning/disinfection can be found [here](#).

### Clinical symptoms:

Range from asymptomatic, uncomplicated upper respiratory tract viral infection to pneumonia, acute respiratory distress syndrome (ARDS), sepsis, and septic shock ([Table 1](#))

### Diagnosis:

See current [COVID-19 testing recommendations](#).

### Treatment:

*Based on data from several randomized control trials, Remdesivir may provide a modest benefit in a subgroup of patients hospitalized with COVID-19. See further details regarding patient populations (see below) and [Table 2](#).*

### Table 1. Potential Treatment Recommendations by Severity of Disease for Patients 18 Years or Older

*Most COVID-19 therapeutics have not been studied in children under 18. The below treatment recommendations may apply to some children, however should be addressed on a case-by-case basis and discussed with Pediatric Infectious Diseases. See specific sections for further details*

| Disease severity   | Potential Treatment Recommendations<br>(per ID consult discretion based on details in <a href="#">Table 2</a> )  |
|--|--|
| Post-exposure prophylaxis  | <ul style="list-style-type: none"> <li>See <a href="#">Post-Exposure Prophylaxis Guidelines</a></li> </ul>   |
| No supplemental oxygen   | <ul style="list-style-type: none"> <li><b>Supportive care</b></li> <li><a href="#">Monoclonal Antibodies</a> may be an option in certain high-risk patients (see eligibility criteria in <a href="#">Table 2</a>) admitted for reasons other than COVID-19 who have mild to moderate symptoms of COVID-19</li> </ul>   |
| Low flow supplemental oxygen   | <ul style="list-style-type: none"> <li><b>Supportive care</b></li> <li><a href="#">Dexamethasone</a> (Exception: Minimal supplemental oxygen (1-2 L) in adults with &lt;7 days of symptoms—uncertain benefit)</li> <li><a href="#">Remdesivir</a></li> </ul>   |
| High flow supplemental oxygen or non-invasive mechanical ventilation | <ul style="list-style-type: none"> <li><b>Supportive Care</b></li> <li><a href="#">Dexamethasone</a></li> <li><a href="#">Tocilizumab</a> (NOTE: currently on shortage and not available for treatment of COVID-19 in patients 18 years an older. <a href="#">Baricitinib</a> is the preferred replacement)</li> <li><a href="#">Remdesivir</a> (uncertain benefit)</li> </ul> |
| Mechanical ventilation or ECMO                                       | <ul style="list-style-type: none"> <li><b>Supportive care</b></li> <li><a href="#">Dexamethasone</a></li> <li><a href="#">Tocilizumab</a> (NOTE: currently on shortage and not available for treatment of COVID-19 in patients 18 years an older. <a href="#">Baricitinib</a> is the preferred replacement)</li> </ul>   |

**Table 2: Therapeutic agents dosing, duration, and details for treatment of COVID-19**

| Therapeutic Agents   | Dosing & Duration  | Comments   |
|--|--|--|
| <p><b>Remdesivir</b></p> <p><i>Patients not hypoxic and those requiring mechanical ventilation or ECMO will not meet the below criteria because existing data does not demonstrate that remdesivir confers a clinical benefit in these patients (clinical recovery or mortality). Exceptions to the below criteria may be considered on an individualized basis.</i></p> <p><u>Guidelines for Use: Patients should meet criteria a &amp; b.</u></p> <p>a. Laboratory confirmed SARS-CoV-2 infection by PCR from nasopharyngeal or respiratory sample and ≤14 days of symptoms</p> <p>b. Severe COVID-19 on admission or during hospitalization: Requires supplemental oxygen, high-flow nasal cannula*, or non-invasive mechanical ventilation*</p> <p><i>*HFNC and NIMV are included as possible indications for remdesivir, but it is uncertain if remdesivir confers a clinical benefit among patients requiring this level of O2 support</i></p> <p><u>Patients &lt; 18 years</u></p> <p>Remdesivir is generally indicated for patients 12-17 years and ≥40 kg who meet the above criteria. For patients &lt;12 years or &lt;40 kg, remdesivir is available through EUA; discuss with Pediatric Infectious Diseases. Remdesivir use is not authorized for patients &lt;3.5 kg.</p> | <p><u>Adult dosing:</u><br/>200 mg IV load, then 100 mg IV q24h</p> <p><u>Pediatric dosing*:</u><br/>3.5 kg to &lt;40 kg:<br/>5 mg/kg IV load, then 2.5 mg/kg q24h<br/>≥40 kg:<br/>200 mg IV load, then 100 mg IV q24h</p> <p><u>Duration:</u><br/>5 days or until hospital discharge whichever comes first. Patients started on remdesivir and progress to requiring higher level of oxygen support (i.e. mechanical ventilation) should still complete a course of remdesivir</p> <p>*pediatric dosing of remdesivir is taken from the <a href="#">WHO recommendations</a> for treatment of Ebola virus, as no specific dosing recommendations exist for COVID-19. Remdesivir is not authorized for patients &lt;3.5 kg.</p> | <ul style="list-style-type: none"> <li>• Please page 30780 for approval prior to first dose of remdesivir between 7 AM and 11 PM (7 days a week).</li> <li>• ID consult is recommended for the following reasons: <ul style="list-style-type: none"> <li>○ Pediatric patient</li> <li>○ Question about Remdesivir should be initiated/ continued</li> <li>○ Patient does not meet criteria for remdesivir but unique clinical circumstances warrant ID evaluation for treatment</li> <li>○ Patient/family request</li> </ul> </li> <li>• CrCl &lt;30 mL/min is not a contraindication to remdesivir. The risk of cyclodextrin accumulation to a toxic level with 5 days of therapy is small &amp; benefit likely outweighs risk</li> <li>• Increased LFTs: daily monitoring of hepatic function is recommended. The risk of hepatotoxicity with a baseline AST/ALT &gt;5x ULN is not known due to patient exclusion from clinical trials; weigh benefit versus risk</li> <li>• Patients &lt;12 years or ≥3.5 kg to &lt;40 kg can qualify under EUA: <ul style="list-style-type: none"> <li>○ Healthcare Providers must review <a href="#">Fact Sheet for Healthcare Providers</a></li> <li>○ Patient/caregiver should be informed of potential risks/benefits and extent to which such risks/benefits are unknown</li> <li>○ Patient/caregiver should be informed of alternative treatments</li> <li>○ Provide the patient/caregiver a copy of the <a href="#">Fact Sheet for Parents and Caregivers</a></li> <li>○ Document in the medical chart the information discussed/provided to the patient/caregiver</li> </ul> </li> </ul> |

| Therapeutic Agents   | Dosing & Duration  | Comments   |
|--|--|--|
| <p><b>Dexamethasone</b></p> <p><u>Patients 18 years and older:</u></p> <ol style="list-style-type: none"> <li><i>Recommended in patients with COVID-19 who require mechanical ventilation or ECMO</i></li> <li><i>Recommended for patients on supplemental oxygen. The benefit of dexamethasone is uncertain in adults on minimal levels of supplemental oxygen (1-2L) with &lt;7 days of symptoms. Decisions should be individualized in such patients with consideration of disease severity in conjunction with risks and benefits of glucocorticoid therapy.</i></li> </ol> <p><i>This recommendation is based on the RECOVERY RCT, NIH and IDSA treatment guidelines for patients with COVID-19 (see references)</i></p> <p><u>Patients &lt;18 years:</u></p> <p><i>Patients &lt;18 years were not represented in the RECOVERY RCT and the mean participant age was 66 years. It is not known if the benefit of dexamethasone will extend to children with COVID-19 who require oxygen, or if there is even the potential for harm, as seen in adults who did not require oxygen. However, it is reasonable to consider dexamethasone for children who require mechanical ventilation, or high levels of oxygen support (e.g., high-flow oxygen or noninvasive ventilation), particularly if they are rapidly progressing toward mechanical ventilation. Recommend consultation with Pediatric Infectious Diseases.</i></p> | <p><u>Adult dosing:</u><br/>6 mg PO or IV q24h</p> <p><u>Pediatric dosing*:</u><br/>0.15 mg/kg/dose IV q24h (max: 6 mg/dose)</p> <p><u>Duration:</u><br/>Maximum 10 days, or until discharge</p> <p><i>Shorter duration is reasonable to consider in patients who have improved rapidly or are experiencing adverse events from steroids. The median duration of therapy in the RECOVERY trial was 6 days.</i></p> <p><i>*Pediatric dosing is based on extrapolation from the adult dose and the RECOVERY protocol but has not been established for COVID-19</i></p> | <p><u>Weigh risks/benefits of use on a case-by-case basis in patients with:</u></p> <ul style="list-style-type: none"> <li>Active bacterial or fungal infection</li> <li>Diabetic ketoacidosis</li> <li>Baseline immunosuppression</li> </ul> <p><u>Not recommended in the following patients:</u></p> <ul style="list-style-type: none"> <li>Not requiring supplemental oxygen. (In RECOVERY, those had a trend towards worse outcomes).</li> <li>No longer COVID-19 PCR positive, but remain intubated. (In RECOVERY, patients were randomized after admission; the risk/benefit of alternative approaches later in the disease course is unknown).</li> </ul> <p><u>Pregnancy, breastfeeding:</u></p> <ul style="list-style-type: none"> <li>Consult OB for gestational age of viability. Alternatives may be prednisone 40 mg PO daily or hydrocortisone 80 mg IV BID.</li> </ul> <p>Dexamethasone is a CYP3A4 substrate, as such drug interactions should be assessed prior to use. Alternatives less prone to interactions are prednisone 40 mg PO daily, methylprednisolone 32 mg IV daily, or hydrocortisone 80 mg IV BID.</p> <p><u>Potential adverse events:</u></p> <ul style="list-style-type: none"> <li>Increased risk for infection</li> <li>Hyperglycemia</li> <li>Peripheral edema</li> <li>Increased appetite</li> <li>Insomnia, irritability, delirium</li> </ul> <p>In the setting of a dexamethasone shortage, an equivalent total daily dose of an alternative glucocorticoid to dexamethasone 6 mg daily can be used (e.g., methylprednisolone 32 mg (&lt;40 kg: 0.8 mg/kg) daily or prednisone 40 mg (&lt;40 kg: 1 mg/kg) daily)</p> |

| Therapeutic Agents   | Dosing & Duration  | Comments  |
|--|--|---|
| <p><b>SARS-COV-2 Neutralizing Antibodies</b><br/>Available via FDA issued Emergency Use Authorization</p> <p><b>Casirivimab + Imdevimab</b></p> <p><u>Eligibility Criteria</u><br/>Patients with mild or moderate COVID-19 who meet criteria #1-4 AND #5 or #6</p> <ol style="list-style-type: none"> <li>1) Admitted for a reason not related to COVID</li> <li>2) No requirement for supplemental oxygen (or no increase from baseline supplemental oxygen)</li> <li>3) Symptoms ≤10 days</li> <li>4) Not received convalescent plasma</li> <li>5) Adult ≥18 years old and ≥40 kg <u>AND</u> one of the following:               <ol style="list-style-type: none"> <li>a) BMI ≥25 kg/m<sup>2</sup></li> <li>b) Age ≥50 years</li> <li>c) Pregnancy</li> <li>d) Chronic respiratory disease (e.g., COPD, Asthma, Bronchiectasis, CF, ILD)</li> <li>e) Cardiovascular disease (e.g., HTN, valvular disease, CVA, PAD, CHF)</li> <li>f) Diabetes</li> <li>g) CKD</li> <li>h) Sickle cell disease</li> <li>i) Immunosuppressed: congenital or acquired immunodeficiency, SOT, active malignancy receiving chemotherapy, BMT, or autoimmune diseases requiring immunosuppressive therapy</li> <li>j) Neurodevelopmental disorder (e.g., cerebral palsy)</li> <li>k) Medical-related technological dependence (e.g., tracheostomy, gastrostomy)</li> </ol> </li> <li>6) Pediatric 12-17 years ≥40 kg <u>AND</u> one of the following:               <ol style="list-style-type: none"> <li>a) BMI ≥95% for age on CDC growth chart</li> <li>b) Immunosuppressed: congenital or acquired immunodeficiency, SOT, active hematologic malignancy receiving chemotherapy, BMT, or autoimmune diseases requiring immunosuppressive therapy</li> <li>c) Pregnancy</li> </ol> </li> </ol> | <p><u>Adult and Pediatric Dosing</u></p> <p><b>Casirivimab</b> 600 mg IV x1<br/><b>+ Imdevimab</b> 600 mg IV x1</p> <p><i>Note: Monoclonal antibodies are not authorized for patients &lt;12 years or &lt;40 kg, regardless of other indications</i></p> | <p><b>ID approval is required. ID consultation is recommended and can only be ordered by ID consultants</b></p> <p>See <a href="#">Post-exposure prophylaxis guidelines</a> if patient has been exposed, but is not symptomatic</p> <p>At the discretion of the ID consultant, monoclonal antibody therapy may be given for patients not meeting the eligibility criteria listed but who are still deemed high risk for progression to severe disease.</p> <p>Healthcare Providers must review: <a href="#">Casirivimab + Imdevimab Fact Sheet for Healthcare providers</a></p> <p>Healthcare Providers must provide recipients with the Fact Sheet for Patients/Caregivers and communicate the following information to the recipients: <a href="#">Casirivimab plus Imdevimab Fact Sheet for Patients/Caregivers</a></p> <ol style="list-style-type: none"> <li>1. FDA has authorized emergency use of (<b>Casirivimab + Imdevimab</b>), which is not an FDA-approved therapy</li> <li>2. The patient or caregiver has the option to accept or refuse administration</li> <li>3. The significant known and potential risks and benefits of the therapy and the extent to which such risks and benefits are unknown</li> <li>4. Information on available alternative treatments and the risks and benefits of those alternatives.</li> </ol> |

| Therapeutic Agents  | Dosing & Duration  | Comments  |
|---|--|---|
| <p><b>Tocilizumab</b></p> <ul style="list-style-type: none"> <li>NOTE: currently on shortage and not available for treatment of adult patients with COVID-19.</li> <li>Patients &lt;18 years may continue to use tocilizumab.</li> <li>Patients 18 years and older, see <a href="#">alternative suggested therapies below</a></li> <li>ID APPROVAL NEEDED, ID consult is recommended for all patients with critical COVID</li> </ul> <p>Recommend <b>Tocilizumab</b> (in addition to <b>dexamethasone</b>) in patients:</p> <ol style="list-style-type: none"> <li>Newly on mechanical ventilation (&lt;48 hours)</li> <li>On high flow supplemental oxygen or noninvasive mechanical ventilation</li> </ol> <p><b>Tocilizumab</b> is <b>NOT</b> recommended in the following scenarios:</p> <ol style="list-style-type: none"> <li>Patients requiring lower levels of respiratory support than high flow support, noninvasive ventilation, or mechanical ventilation.</li> <li>High concern for systemic bacterial or fungal co-infection</li> <li>Receiving mechanical ventilation for longer than 48 hours</li> <li>Patients who significantly improve with the initiation of enhanced oxygen support or corticosteroids; monitoring such patients for 12-24 hours is reasonable</li> <li>Unlikely to survive &gt;48 hours</li> <li>Receiving baricitinib* (see comment)</li> </ol> <p><i>Recommendations are primarily based on preliminary findings from the REMAP-CAP and RECOVERY trials (see references 14 and 16). Pediatric patients were not represented in these trials. It is not known if the benefit will extend to children with COVID-19. Recommend consultation with Infectious Diseases.</i></p> | <p>** Dose rounding currently built into Epic order. Doses should be rounded to nearest available full vial (80 mg, 200 mg, 400 mg vials)**</p> <p><u>Adult Dosing (≥18 years):</u><br/>8 mg/kg (max: 800 mg/dose)</p> <p><u>Pediatric Dosing (2 to 17 years):</u><br/>&lt;30 kg:<br/>12 mg/kg<br/>≥30 kg:<br/>8 mg/kg<br/>(max: 800 mg/dose)</p> <p><u>Duration:</u><br/>One dose</p> <p><i>There are no data to inform risk vs. benefit of a second dose. Based on local experience a second dose is <b>NOT</b> recommended.</i></p> | <p><u>Pregnancy and Nursing Mothers:</u></p> <ul style="list-style-type: none"> <li>Maternal-Fetal Medicine at Michigan Medicine has endorsed the use of tocilizumab in pregnancy</li> <li>Tocilizumab may be harmful to newborns, and mothers should stop breastfeeding if receiving tocilizumab but may resume after discontinuation and discussion with provider</li> <li>*Tocilizumab benefit has been shown in studies with concomitant corticosteroid therapy. The combination of tocilizumab + baricitinib has not been rigorously studied and both the safety and efficacy of this combination is unclear. Thus, when tocilizumab is administered, it should be in combination with dexamethasone or an equivalent corticosteroid. Prior use of baricitinib is not a contraindication to using tocilizumab</li> </ul> <p><u>Serious adverse events:</u></p> <ul style="list-style-type: none"> <li>Gastrointestinal perforation</li> <li>Anemia</li> <li>Hepatitis</li> <li>Infusion reaction</li> <li>Neutropenia</li> <li>Infection</li> </ul> <p>Healthcare Providers must review FDA <a href="#">Fact Sheet for Health Care Providers</a></p> <p>Healthcare Providers must provide recipients with the <a href="#">Fact Sheet for Patients/Caregivers</a> and communicate the following information to the recipients:</p> <ol style="list-style-type: none"> <li>FDA has authorized emergency use of Tocilizumab for patients 2 years and older with COVID-19, which is not an FDA-approved indication for use</li> <li>The patient or caregiver has the option to accept or refuse administration of Tocilizumab</li> <li>The significant known and potential risks and benefits of Tocilizumab and the extent to which such risks and benefits are unknown</li> <li>Information on available alternative treatments and the risks and benefits of those alternatives.</li> </ol> |



| Therapeutic Agents   | Dosing & Duration  | Comments  |
|--|--|---|
| <p><b>Alternatives to Tocilizumab for patients 18 years and older:</b></p> <p><u>NOTES:</u></p> <ol style="list-style-type: none"> <li><b>Baricitinib</b> is the preferred alternative to tocilizumab<sup>17</sup>.</li> <li><b>Sarilumab</b><sup>14</sup> should only be utilized in candidates for baricitinib but who cannot receive baricitinib due to: <ul style="list-style-type: none"> <li>Enteral administration is not possible or reliable</li> <li>Baricitinib is contraindicated if eGFR <math>\leq 15</math> or IHD, but is acceptable if patient is on CRRT</li> <li>Pregnant (sarilumab preferred)</li> </ul> </li> <li>Consideration of either agent <i>requires ID consultation</i></li> <li>The FDA has authorized emergency use of Baricitinib, requiring steps to be followed (see comments)</li> <li>Pediatric patients were not represented in the RCT informing these recommendations. It is not known if the benefit will extend to children with COVID-19 and use is currently not recommended in patients &lt;18 years</li> </ol> | <p><b>Baricitinib</b></p> <p>(NOTE: renal dosing uses MDRD equation, which is not available in MiChart. MDRD calculator is available <a href="#">here</a>.)</p> <p><u>eGFR <math>\geq 60</math> mL/min/1.73 m<sup>2</sup>:</u><br/>4 mg PO q24h</p> <p><u>eGFR 30- &lt;60 mL/min/1.73 m<sup>2</sup>:</u><br/>2 mg PO q24h</p> <p><u>eGFR 15- &lt;30 mL/min/1.73 m<sup>2</sup> or CRRT:</u><br/>1 mg PO q24h</p> <p><u>eGFR <math>\leq 15</math> mL/min/1.73 m<sup>2</sup> or HD:</u><br/>Not recommended, use Sarilumab instead (see below)</p> <p><u>Duration:</u><br/>Maximum 14 days, or until discharge</p> <p><b>Sarilumab:</b><br/>**Sarilumab is available as pre-filled syringes for SC administration but clinical trials have validated the use of this product given intravenously**</p> <p><u>Dosing:</u><br/>400 mg IV</p> <p><u>Duration:</u><br/>One dose</p> | <p>The combination of sarilumab + baricitinib has not been studied and both the safety and efficacy of this combination is unclear. Cases in which patients are initiated on baricitinib but develop contraindications for use prior to completion of treatment course may arise, and case-by-case considerations for sarilumab should be discussed with Infectious Diseases.</p> <p><b>Baricitinib Considerations:</b></p> <p><u>Potential adverse events:</u></p> <ul style="list-style-type: none"> <li>Thromboembolic events: VTE, PE (prophylactic anticoagulation recommended except if contraindicated)</li> <li>Increased risk for infection</li> <li>Transaminitis</li> <li>Neutropenia, lymphopenia, and anemia. Evaluate at baseline and during therapy. Treatment interruption/discontinuation may be considered in consultation with Infectious Diseases if baricitinib thought to be causing/exacerbating such abnormalities.</li> </ul> <p>Healthcare Providers must review FDA <a href="#">Fact Sheet for Health Care Providers</a></p> <p>Healthcare Providers must provide recipients with the <a href="#">Fact Sheet for Patients/Caregivers</a> and communicate the following information to the recipients:</p> <ol style="list-style-type: none"> <li>FDA has authorized emergency use of Baricitinib for patients 2 years and older with COVID-19, which is not an FDA-approved indication for use</li> <li>The patient or caregiver has the option to accept or refuse administration of Baricitinib</li> <li>The significant known and potential risks and benefits of Baricitinib and the extent to which such risks and benefits are unknown</li> <li>Information on available alternative treatments and the risks and benefits of those alternatives.</li> </ol> <p><b>Sarilumab Considerations:</b></p> <p><u>Pregnancy and Nursing Mothers:</u></p> <ul style="list-style-type: none"> <li>Maternal-Fetal Medicine at Michigan Medicine has endorsed the use of IL-6 inhibitors in pregnancy</li> <li>Sarilumab may be harmful to newborns, and mothers should stop breastfeeding if receiving sarilumab but may resume after discontinuation and discussion with provider</li> </ul> <p><u>Serious adverse events:</u></p> <ul style="list-style-type: none"> <li>Gastrointestinal perforation</li> <li>Anemia</li> <li>Hepatitis</li> <li>Infusion reaction</li> <li>Neutropenia</li> <li>Infection</li> </ul> |

**Do not use** (therapies without any supportive evidence and/or associated with potential harm): hydroxychloroquine, hydroxychloroquine + azithromycin, lopinavir/ritonavir, nitazoxanide, oseltamivir, baloxavir, interferon, ribavirin, IVIG

## Antibiotic Management for Pneumonia in PUI and Confirmed COVID-19 Patients

### Recommendations:

1. In patients admitted with suspected COVID-19 pneumonia (testing pending), decisions whether to initiate antibiotic therapy should be based on guidance provided in the institutional pneumonia treatment and procalcitonin usage guidelines.
2. Continuation/initiation of antibiotic therapy *solely* due to confirmation of COVID-19 pneumonia is not indicated as described below.
3. In patients with confirmed COVID-19 pneumonia, community-onset bacterial co-infection is uncommon, even in critically ill patients, and elevated procalcitonin levels are not reliably associated with bacterial infection, especially in the setting of concomitant renal dysfunction. Empiric antibiotic therapy should generally be discontinued once a patient is confirmed COVID-19 positive, but may be indicated in patients with leukocytosis and/or hemodynamic instability. De-escalation/discontinuation of antibiotics should be considered based on clinical and microbiological data. Note that an extended duration of fevers is typical in COVID-19 patients.
4. In patients who test negative for COVID-19 pneumonia, antibiotic therapy should be based on guidance provided in the institutional pneumonia treatment and procalcitonin usage guidelines.

Reports thus far have not identified unusual associations between COVID-19 infection and bacterial co-infection. Additionally, no unique association with resistant pathogens, including MRSA or *Pseudomonas*, has been made.

In an observational analysis by Somers et al of 154 patients with severe COVID-19 infection requiring mechanical ventilation at Michigan Medicine:

- 40% developed a bacterial superinfection, with 32% developing bacterial pneumonia. The median time to development of infection was 8-10 days after initiation of mechanical ventilation.

In a review of studies reporting bacterial co-infections in patients with COVID-19, Lansbury et al reported that the proportion of co-infection in ICU patients was 14%, compared to a proportion of 4% in studies which grouped ICU and floor-status together. Timing of onset of infection was not reported. Similarly, Vaughn et al reported that 3.5% of all patients hospitalized with COVID-19 had a community-onset bacterial co-infection and that 11% of patients admitted directly to the ICU had a community-onset bacterial co-infection<sup>11</sup>.

In the study of adult patients by Zhou et al.:

- 15% of hospitalized COVID-19 patients developed a secondary bacterial infection (definition: clinical symptoms or signs of pneumonia or bacteremia with a positive culture).
- The median time to secondary bacterial infection was 17 days (13 to 19 days).
- Of all COVID-19 patients in their cohort, 79% had a WBC <10.
- Only 1% of survivors developed a secondary bacterial infection, yet the median duration of fever in survivors was 12 days and cough persisted for 19 days. Thus, 'just in case' treatment of bacterial infection can result in prolonged durations of therapy.

Data in pediatric patients are limited, but one small study (Xia et al.) suggests that procalcitonin may be higher in children with COVID-19, regardless of suspected bacterial superinfection. Decisions about antibiotic management for children should continue to be guided by clinical judgment.

Adult pneumonia treatment guidelines are summarized here, and adult and pediatric pneumonia treatment guidelines are available in their entirety at:

- [Pneumonia Treatment \(Adult\)](#)
- [Community-Acquired Pneumonia Treatment \(Pediatrics\)](#)
- [Procalcitonin Use Guidelines](#)

## Procalcitonin

- Although PCT levels should not be used in isolation to decide whether to initiate antibiotics in patients with suspected bacterial pneumonia, **bacterial co-infection is unlikely in a confirmed COVID-19 patient with a low procalcitonin (<0.25), and antibiotics can be safely withheld<sup>11</sup>. In addition, PCT levels >0.25 are not uncommon in patients with COVID-19 pneumonia, and do not appear to be a reliable marker of bacterial superinfection. Importantly, patients with CKD and AKI have falsely elevated PCT levels, and as such PCT is not reliable in such settings.** Procalcitonin should also NOT be routinely used to *extend* treatment duration.

## Adult Pneumonia Treatment Summary Recommendations

| Indication   | 1 <sup>st</sup> Line Empiric Therapy<br>(see guidelines for alternatives)  | Duration of Therapy  |
|--|--|--|
| <b>Pathway A</b> – Inpatient community-acquired with no risk factors   | <b>Ampicillin-sulbactam</b> 3 g IV q6h<br>+ Azithromycin 500 mg IV/PO x1 day, then 250 mg q24h x4 days   | <u>Uncomplicated pneumonia:</u><br>5 days for patients who defervesce within 72 hours and have <b>no more than 1</b> sign of CAP instability at the time of antibiotic discontinuation |
| <b>Pathway B</b><br>-Community onset pneumonia with risk factors for drug resistant pathogens (see risk factors below) | <b>Cefepime</b> 2 g IV q8h<br>(+ <b>Tobramycin</b> IV if admitted to ICU)<br>+ <b>Vancomycin*</b> IV (see <a href="#">nomogram</a> )<br><br>*Discontinue vancomycin if no evidence of MRSA colonization/infection (negative MRSA nasal swab or respiratory culture). | <u>Uncomplicated pneumonia:</u><br>7 days  |
| <b>Pathway C</b><br>Hospital-acquired Pneumonia<br><br>Ventilator-associated pneumonia                                 | <b>Cefepime</b> 2 g IV q8h<br>(+ <b>Tobramycin</b> IV if admitted to ICU)<br>+ <b>Vancomycin*</b> IV (see <a href="#">nomogram</a> )<br><br>*Discontinue vancomycin if no evidence of MRSA colonization/infection (negative MRSA nasal swab or respiratory culture). | <u>Uncomplicated pneumonia:</u><br>7 days  |

### PATHWAY B RISK FACTORS

- History of infection or colonization with *Pseudomonas* spp., MRSA, or pathogens resistant to standard CAP therapy (ampicillin-sulbactam or ceftriaxone) within previous 12 months
- Severe community-acquired pneumonia (septic shock **OR** requiring mechanical ventilation **OR** high clinical concern for needing ICU care<sup>3</sup>), AND meeting 1 of the following criteria:
  - Hospitalization for at least 48 hours AND use of any intravenous antibiotic, fluoroquinolone, or linezolid within previous 90 days **OR**
  - Immunocompromised, defined as:
    - AIDS (CD4 <200)
    - Neutropenia (ANC <1000)
    - Kidney or liver or heart transplant recipient within previous 1 year
    - Solid organ transplant recipient treated for rejection within previous 6 months
    - Lung transplant recipient
    - Allogeneic stem cell transplant within previous 1 year or those with chronic GVHD
    - Autoimmune disorders on biologic agents (TNF $\alpha$  inhibitors, rituximab, etc.)

### Concomitant use of NSAIDs and/or ACE-I/ARBs:

There are conflicting theories regarding the risk and benefit of non-steroidal anti-inflammatory drugs (NSAIDs) or angiotensin converting enzyme inhibitors/ angiotensin II receptor blockers (ACE-I/ARBs) in patients with COVID-19 infection. Currently, there are no robust data demonstrating beneficial or adverse outcomes with use of these drugs in COVID-19 infections or specifically in COVID-19 infected patients taking these medications for cardiovascular disease. The American Heart Association, American College of Cardiology, and Heart Failure Society of America do not recommend stopping ACE-I or ARBs in COVID-19 infected patients. In addition, a clinical trial (NCT04312009) is investigating whether adjunctive ARB therapy can improve outcomes in COVID-19 patients. Pending this data, we do not endorse stopping or starting such therapies solely because of COVID-19 infection.



**References:**

1. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. [Lancet. 2020 Mar 28;395\(10229\):1054-1062.](#)
2. Beigel JH, et al. Remdesivir for the Treatment of Covid-19 —Final Report. [N Engl J Med. 2020 Oct 8;NEJMoa2007764.](#)
3. Goldman JD, et al. Remdesivir for 5 or 10 Days in Patients With Severe Covid-19. [N Engl J Med 2020 \[Online ahead of print\]](#)
4. Group RC, Horby P, Lim WS, et al. Dexamethasone in hospitalized patients with COVID-19—preliminary report. [N Engl J Med. 2020 Jul 17;NEJMoa2021436.](#)
5. NIH COVID-19 Treatment Guidelines, <https://www.covid19treatmentguidelines.nih.gov/antiviral-therapy>
6. IDSA COVID-19 Treatment Guidelines, <https://www.idsociety.org/practice-guideline/covid-19-guideline-treatment-and-management/>
7. Lansbury L, et al. Co-infections in people with COVID-19: a systematic review and meta-analysis. [J Infect. 2020 Aug;81\(2\):266-275.](#)
8. Committee on Drugs, American Academy of Pediatrics. The transfer of drugs and other chemicals into human milk. [Pediatrics 2001;108:776–89.](#)
9. Vaughn VM, Gandhi T, et al. Empiric Antibacterial Therapy and Community-onset Bacterial Co-infections in Patients Hospitalized with COVID-19: A Multihospital Cohort Study. [Clin Infect Dis. 2020 Aug 21;ciaa1239.](#)
10. Pan H, Peto R, et al. Repurposed antiviral drugs for COVID-19 – interim WHO Solidarity trial results. medRxiv 2020.10.15.2029817; doi: <https://doi.org/10.1101/2020.10.15.2029817>
11. Agarwal A, Mukherjee A, et al. Convalescent plasma in the management of moderate covid-19 in adults in India:open label phase II multicentere randomized controlled trial (Placid Trial). [BMJ 2020;371:m3939](#)
12. Chen P et al. SARS-CoV-2 Neutralizing Antibody LY-CoV555 in Outpatients with Covid-19. [NEJM. 2020 Oct 28;NEJMoa2029849.](#)
13. Weinreich DM et al. REGN-COV2, a neutralizing cocktail, in outpatients with COVID-19. [NEJM 2020 Dec 17;NEJM oa2035002.](#)
14. Effectiveness of Tocilizumab, Sarilumab, and Anakinra for critically ill patients with COVID-19 The REMAP-CAP COVID-19 Immune Modulation Therapy Domain Randomized Clinical Trial. medRxiv 2021: <https://www.medrxiv.org/content/10.1101/2021.06.18.21259133v2>.
15. Libster R et al. Early High-Titer Plasma Therapy to Prevent Severe Covid-19 in Older Adults [NEJM. 2021 Jan 6;NEJMoa2033700.](#)
16. RECOVERY Collaborative Group. Tocilizumab in patients admitted to hospital with 3 COVID-19 (RECOVERY): preliminary results of a 4 randomised, controlled, open-label, platform trial. MedRxiv 2021: <https://www.medrxiv.org/content/10.1101/2021.02.11.21249258v1>
17. Marconi VC et al. Efficacy and safety of baricitinib in patients with COVID-19 infection: Results from the randomised, double-blind, placebo-controlled, parallel-group COV-BARRIER phase 3 trial. MedRxiv 2021: <https://www.medrxiv.org/content/10.1101/2021.04.30.21255934v2>

|   |                       |
|---|-----------------------|
| Antimicrobial Subcommittee Approval: N/A  | Originated: 03/2020   |
| P&T Approval: N/A   | Last Revised: 08/2021 |
| <p>Revision History:</p> <ul style="list-style-type: none"> <li>3/16/20: Removed testing recommendations - added link to testing document</li> <li>3/17/20: Added tocilizumab, adjusted pediatric hydroxychloroquine dosing</li> <li>3/19/20: Revised tocilizumab criteria, added pneumonia guidance</li> <li>3/20/20: Revised tocilizumab dosing to weight based due to changes in Epic dose rounding capabilities, added limited data for corticosteroids in ARDS</li> <li>3/24/20: Added guidance on azithromycin, revised tocilizumab dosing, added clinical study enrollment appendix</li> <li>3/25/20: Revised criteria for HCQ use.</li> <li>3/26/20: Revised tocilizumab criteria &amp; included sarilumab study caveat</li> <li>3/27/20: Removed study flow diagram</li> <li>3/31/20: Removed recommendation for routine HCQ, removed nitazoxanide and lopinavir/ritonavir options, revised ACE/ARB/NSAID recommendations, recommendations re: combination HCQ/Azithromycin, revised pregnancy/breastfeeding recommendations and Remdesivir compassionate use criteria, deleted Tocilizimab re-dosing</li> <li>4/2/20: Added suggested labs, revised remdesivir clinical trial information</li> <li>4/3/20: Added hyperlink to Appendix A - review of HCQ data</li> <li>4/6/20: Revised testing guidance hyperlink</li> <li>4/7/20: Revised tocilizumab criteria</li> <li>4/10/20: Revised tocilizumab criteria</li> <li>4/15/20: Revised tocilizumab criteria</li> <li>5/15/20: Revised tocilizumab criteria, revised remdesivir comments</li> <li>6/3/20: Revised secondary infection information, revised remdesivir obtainment information</li> <li>7/10/20: Added dexamethasone section</li> <li>8/3/20: Added remdesivir criteria</li> <li>9/15/20: Added convalescent plasma section</li> <li>10/5/20: Removed tocilizumab, updated remdesivir comments, updated convalescent plasma comments</li> <li>10/14/20: Revised remdesivir criteria</li> <li>10/28/20: Revised Table 1, revised remdesivir section</li> <li>11/19/20: Revised remdesivir comments</li> <li>12/3/20: Revised remdesivir criteria</li> <li>12/8/20: Added neutralizing antibodies section, revised remdesivir criteria.</li> <li>12/17/20: Revised neutralizing antibodies criteria</li> <li>12/23/20: Revised neutralizing antibodies criteria</li> <li>1/5/21: Revised neutralizing antibodies criteria</li> <li>1/13/21: Revised neutralizing antibodies criteria</li> <li>1/17/21: Added tocilizumab section</li> <li>1/27/21: Updated convalescent plasma criteria</li> <li>2/25/21: Revised tocilizumab criteria, added new reference</li> <li>3/15/21: Added bamlanivimab + etesevimab to mAb section</li> <li>3/22/21: Added criteria and comments for tocilizumab, updated vancomycin nomogram hyperlink</li> <li>4/7/21: Removed bamlanivimab monotherapy from mAb section</li> <li>5/26/21: Revised mAb criteria</li> <li>6/9/21: Revised casirivimab + imdevimab dosing and provider fact sheet</li> <li>6/29/21: Revised mAb product availability</li> <li>8/10/21: Added Post-exposure Prophylaxis hyperlink</li> <li>8/25/21: Removed convalescent plasma section, revised tocilizumab section, revised alternative to tocilizumab section, updated pneumonia treatment recommendations.</li> </ul> |                       |

*The recommendations in this guide are meant to serve as treatment guidelines for use at Michigan Medicine facilities. If you are an individual experiencing a medical emergency, call 911 immediately. These guidelines should not replace a provider’s professional medical advice based on clinical judgment, or be used in lieu of an Infectious Diseases consultation when necessary. As a result of ongoing research, practice guidelines may from time to time change. The authors of these guidelines have made all attempts to ensure the accuracy based on current information, however, due to ongoing research, users of these guidelines are strongly encouraged to confirm the information contained within them through an independent source.*

*If obtained from a source other than med.umich.edu/asp, please visit the webpage for the most up-to-date document.*