TREATMENT GUIDELINE FOR PATIENTS WITH COVID-19
This is a living document that will be updated as more data emerge.
Last updated: 1/27/23

Table 1. Overview of Treatment Recommendations Based on Hospitalization and Severity of Disease

<table>
<thead>
<tr>
<th>Not Hospitalized (supportive care is the mainstay of treatment)</th>
<th>Hospitalized</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Oral Treatment Options:</strong></td>
<td><strong>Recommended Treatment</strong></td>
</tr>
<tr>
<td>• Preferred: Nirmatrelvir/ritonavir (Paxlovid™) if within 5 days of symptom onset for patients who meet EUA criteria (see Table 2)</td>
<td>• Supportive Care, AND</td>
</tr>
<tr>
<td>• Alternative: Molnupiravir (Lagevrio™) if within 5 days of symptom onset for patients 18 yo and older who meet EUA criteria</td>
<td>• One of the following for patients who meet criteria (see Table 2):</td>
</tr>
<tr>
<td></td>
<td>o Paxlovid for 5 days (restricted to ID physicians - except for continuation of prior to admission medication), OR</td>
</tr>
<tr>
<td></td>
<td>o For patients admitted for reasons not related to COVID-19 AND meet all criteria for use:</td>
</tr>
<tr>
<td></td>
<td>• Remdesivir for 3 days (restricted to ID physicians)</td>
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<tr>
<td></td>
<td>• Anticoagulation: refer to COVID-19 Anticoagulation and Coagulopathy Management for Adults</td>
</tr>
<tr>
<td>No supplemental oxygen (or if on chronic oxygen therapy, not requiring an increase in baseline oxygen flow rate due to COVID-19)</td>
<td>Low-flow supplemental oxygen (i.e., persistent SpO2 ≤ 94% on room air AND requiring supplemental oxygen)</td>
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<tr>
<td></td>
<td>• Remdesivir (restricted to ID physicians) for 5 days or until discharge, whichever comes first, AND</td>
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<tr>
<td></td>
<td>• Dexamethasone 6 mg IV/PO daily for up to 10 days or until discharge, whichever comes first, AND</td>
</tr>
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<td></td>
<td>• Anticoagulation: refer to COVID-19 Anticoagulation and Coagulopathy Management for Adults</td>
</tr>
<tr>
<td>Non-invasive ventilation or high-flow oxygen devices</td>
<td>Non-invasive ventilation or high-flow oxygen devices</td>
</tr>
<tr>
<td></td>
<td>• Dexamethasone 6 mg IV/PO daily for up to 10 days or until discharge, whichever comes first (consider higher dose in select patients – refer to Table 2), AND</td>
</tr>
<tr>
<td></td>
<td>• Consider remdesivir (clinical benefit uncertain - restricted to ID physicians) for 5 days or until discharge, whichever comes first, AND</td>
</tr>
<tr>
<td></td>
<td>• Baricitinib or tocilizumab (restricted to ID physicians), AND</td>
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<tr>
<td></td>
<td>• Anticoagulation: refer to COVID-19 Anticoagulation and Coagulopathy Management for Adults</td>
</tr>
<tr>
<td>Mechanical ventilation or ECMO</td>
<td>Mechanical ventilation or ECMO</td>
</tr>
<tr>
<td></td>
<td>• Dexamethasone 6 mg IV/PO daily for up to 10 days or until discharge, whichever comes first (consider higher dose in select patients – refer to Table 2), AND</td>
</tr>
<tr>
<td></td>
<td>• If &lt; 48h of mechanical ventilation: tocilizumab or baricitinib (restricted to ID physicians), AND</td>
</tr>
<tr>
<td></td>
<td>• Anticoagulation: refer to COVID-19 Anticoagulation and Coagulopathy Management for Adults</td>
</tr>
</tbody>
</table>

SUGGESTED LABORATORY MONITORING
Obtain at baseline and with any sudden decline in oxygenation status
• Complete blood count with differential (leukopenia and lymphopenia common)
• Comprehensive metabolic panel (moderately elevated AST/ALT described)
• Lactate dehydrogenase (elevation associated with increased mortality)
• Ferritin (extreme elevation associated with severe illness and mortality)
• C-reactive protein (extreme elevation associated with severe illness and mortality)
• Procalcitonin (refer to Table 3)
• D-dimer (commonly elevated; should NOT be used in isolation to prescribe therapeutic anticoagulation- refer to COVID-19 Anticoagulation and Coagulopathy Management for Adults)
Table 2. Recommended Agents for Therapeutic Management of COVID-19

<table>
<thead>
<tr>
<th><strong>Paxlovid (nirmatrelvir/ritonavir)</strong> - Restricted to Infectious Disease physicians (except for continuation of PTA medication)</th>
</tr>
</thead>
</table>

**Restricted to Infectious Disease Prescribers for inpatient use.** Prescriber must complete all EUA requirements.

*The concomitant use of Paxlovid with certain other drugs may result in potentially significant drug interactions. Consult the EUA Fact Sheet and/or a web-based interaction checker for potential drug interactions.*

**Dosage regimen (based on renal function):**

- eGFR ≥ 60 mL/min: 3 tablets (two 150 mg tablets nirmatrelvir with one 100 mg ritonavir tablet) PO BID for 5 days
- eGFR 30 to < 60 mL/min: 2 tablets (one 150 mg tablet nirmatrelvir with one 100 mg ritonavir tablet) PO BID for 5 days
- eGFR < 30 mL/min: Not recommended

<table>
<thead>
<tr>
<th><strong>Inclusion Criteria</strong></th>
<th><strong>Exclusion Criteria</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive SARS-CoV-2 test (i.e., RT-PCR or antigen, not antibody test), AND Symptom onset within the last 5 days, AND High risk for progression to severe COVID-19 based on CDC risk factors</td>
<td>Pediatric patients &lt; 12 yo OR &lt; 40 kg, OR Requiring supplemental oxygen (or if on chronic oxygen therapy, requiring an increase in baseline oxygen flow rate due to COVID-19), OR eGFR &lt; 30 mL/min, OR Severe hepatic impairment (Child-Pugh Class C), OR Significant drug interactions (i.e., interactions associated with serious and/or life-threatening reactions or interactions that result in a significant reduction in nirmatrelvir or ritonavir plasma concentrations and may result in the potential for loss of virologic response and possible resistance)</td>
</tr>
</tbody>
</table>
Remdesivir (Restricted to Infectious Disease physicians. Use will be audited by the Antimicrobial Stewardship Team)

### 3-day Regimen Criteria

**Inclusion:**
- Admitted for reasons not related to COVID-19, **AND**
- Symptom onset ≤ 7 days, **AND**
- Positive SARS-CoV-2 test (i.e., RT-PCR or antigen, not antibody test), **AND**
- Oxygen saturation > 94% on room air, **AND**
- At least 1 risk factor for severe disease, which include the following:
  - Older age (e.g., age ≥ 60 years of age)
  - BMI ≥ 30
  - Pregnancy
  - Chronic kidney disease (CKD)
  - Chronic liver disease
  - Diabetes
  - Immunosuppressive disease or immunosuppressive treatment
  - Cardiovascular disease (including congenital heart disease) or hypertension
  - Cerebrovascular disease
  - Chronic lung diseases (e.g., COPD, interstitial lung disease)
  - Sickle cell disease

**Exclusion:**
- Weight < 3 kg, **OR**
- Patients being transferred/awaiting transfer

### 5-day Regimen Criteria

**Inclusion:**
- Positive SARS-CoV-2 test (i.e., RT-PCR or antigen, not antibody test), **AND**
- Symptom onset ≤ 14 days, **AND**
- Persistent SpO2 ≤ 94% on room air and requiring supplemental oxygen or on non-invasive ventilation or high-flow oxygen devices

**Exclusion:**
- Mechanical ventilation (MV) or extracorporeal membrane oxygenation (ECMO), **OR**
- Weight < 3 kg, **OR**
- Patients being transferred/awaiting transfer

### Precautions

- eGFR < 30 mL/min: the pharmacokinetics have not been evaluated in patients with eGFR < 30 mL/min. The risk of toxicity in these patients is low and benefit of remdesivir likely outweighs this risk.
- ALT ≥ 5 x ULN at baseline: risk of hepatotoxicity in these patients is not known due to exclusion from clinical trials. Use of remdesivir should be based on potential risk versus benefit considerations.

### Adult Dosing

200 mg IV x 1 on day 1, then 100 mg IV daily for days 2 – 5 or until hospital discharge, whichever comes first. **For 3-day regimen:** if progress to hypoxia, therapy can be extended to a total of 5 days. **For 5-day regimen:** if progress to requiring mechanical ventilation/ECMO, can still complete the 5-day course.

**Pediatric Dosing (12 yo and weighing at least 40 kg):** 200 mg IV load on day 1, then 100 mg IV q24hr for days 2-5
**Pediatric Dosing (>/=28 days of age AND 3 kg to < 40 kg):** 5 mg/kg IV load on day 1, then 2.5 mg/kg IV q24hr for days 2-5

### Laboratory Monitoring

- Prior to initiation: Scr/BUN, hepatic function, prothrombin time
- **During therapy:** Scr/BUN and prothrombin time should be monitored as clinically appropriate, hepatic function panel should be monitored as follows:
  - 3-day therapy: If baseline ALT is < 2.5 x ULN: no additional monitoring is required, if baseline or follow-up ALT is > 2.5 x ULN: hepatic function panel should be checked daily
  - 5-day therapy: If baseline ALT is < 2.5 x ULN: check on day 3 of therapy, if baseline or follow-up ALT is > 2.5 x ULN: hepatic function panel should be checked daily
- Consider discontinuing if ALT > 10 x ULN; discontinue if ALT elevation accompanied by signs or symptoms of liver inflammation
  - Pharmacists can order necessary labs listed above for patients receiving remdesivir

### Infusion-related reactions

(e.g., hypotension, hypertension, tachycardia, bradycardia, hypoxia, fever, dyspnea, wheezing, angioedema, rash, nausea, diaphoresis, and shivering): Slow infusion rate, with a maximum infusion time up to 120 minutes, to potentially prevent these signs and symptoms. If clinically significant infusion-related reactions occur, immediately discontinue & initiate appropriate treatment.
Steroids*

Recommended in adult patients with **persistent** SpO2 ≤ 94% on room air AND requiring supplemental oxygen (i.e., on low- or high-flow nasal oxygen, non-invasive or invasive mechanical ventilation, or ECMO):

- **Preferred:** Dexamethasone 6 mg IV/PO q24h **for up to 10 days (or until discharge if earlier)**
- **Pregnant Patients:**
  - COVID-19: Dexamethasone 6 mg IV/PO q24h **for up to 10 days (or until discharge if earlier)**
  - COVID-19 and fetal lung maturity: Dexamethasone 6 mg IV/PO q12h x 4 doses, then dexamethasone 6 mg IV/PO q24h to complete a total of 10 days or until discharge (whichever comes first)
- Alternatives if dexamethasone is unavailable:
  - Methylprednisolone 40 mg IV q24h for up to 10 days (or until discharge if earlier)
  - Prednisone 40 mg PO q24h for up to 10 days (or until discharge if earlier)

- **For select** patients on high-flow nasal oxygen, non-invasive or invasive mechanical ventilation, or ECMO (**based on physician discretion**):
  - Consider high-dose steroids (maximum recommended dose dexamethasone 20 mg/day or methylprednisolone 80 mg/day):
    - Dexamethasone 20 mg IV/PO q24h x 5 days, then 10 mg IV/PO q24h x 5 days --OR--
    - Methylprednisolone 40 mg IV q12h x 5 days, then 40 mg IV q24h x 5 days

- **Monitor:**
  - Oxygenation status, CRP, ferritin, and LDH. If no improvement, rule out secondary bacterial infection.
  - Blood glucose in high-risk individuals. Consider point-of-care blood glucose monitoring 4 times per day for 24-48 hours to monitor for steroid induced hyperglycemia, hyperglycemic crises, and new onset diabetes or for chronic diabetes management.

- For adult patients with refractory septic shock and COVID-19 the recommendation is to follow surviving sepsis guidelines with consideration for use with hydrocortisone 200 mg IV per day divided.

- **Drug-drug interactions:** The combination of dexamethasone and direct oral anticoagulants (DOACs: apixaban, rivaroxaban, dabigatran, edoxaban and betrixaban) **should be avoided**. Dexamethasone is believed to be a combined P-glycoprotein and strong CYP 3A4 inducer. When used in combination with DOACs there is a potential for reduced DOAC drug concentration and increased risk of thrombosis.

- **Stress ulcer prophylaxis:** Consider in patients also on therapeutic anticoagulation, mechanical ventilation, and/or patients with coagulopathy

**Pediatric patients:** Methylprednisolone IV (at an appropriate weight-based dose) may be initiated in pediatric ICU patients by the Pediatric Intensivist on a case-by-case basis. As literature evolves, recommendations and dosing in pediatric patients will be updated.

*for patients with a contraindication to steroids, consult Infectious Diseases to determine possible alternatives*
Baricitinib (Restricted to Infectious Disease physicians)

Inclusion Criteria:
- Positive SARS-CoV-2 test (i.e., RT-PCR or antigen, not antibody test), AND
- Receiving high-flow oxygen or noninvasive ventilation or < 48h of mechanical ventilation if administering with steroids. Baricitinib may also be administered as a steroid alternative in those patients with a contraindication to steroids, AND
- Age ≥ 2 years old (prescriber must complete EUA requirements for patients 2-17 yo)

Exclusion Criteria:
- Mechanical ventilation > 48 hours, OR
- Absolute neutrophil count (ANC) < 0.5 bil/L, OR
- Absolute lymphocyte count (ALC) < 0.2 bil/L, OR
- Age 9 yo and older: eGFR < 15 ml/min/1.73 m² or on dialysis, OR
- Age 2 to < 9 yo: eGFR < 30 ml/min/1.73 m² or on dialysis, OR
- Received tocilizumab, OR
- Active tuberculosis, OR
- Receipt of live vaccine within the past 14 days

Precautions (prescribers will have to discuss risk vs benefit with patient)
- Active serious infections other than COVID-19
- Suspected or confirmed DVT/PE
- Patients at risk for GI perforations
- Severe hepatic impairment
- Pregnancy

Required Laboratory Monitoring
A pharmacist may order the appropriate laboratory tests using the order mode of "Within Scope: No co-sign required" if not ordered by the prescriber.

<table>
<thead>
<tr>
<th>eGFR (ml/min/1.73 m²)</th>
<th>Recommendation</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 60</td>
<td>9 yo and older: 4 mg once daily</td>
<td>14 days or until discharge, whichever comes first</td>
</tr>
<tr>
<td></td>
<td>2 to &lt; 9 yo: 2 mg once daily</td>
<td></td>
</tr>
<tr>
<td>30 to &lt; 60</td>
<td>9 yo and older: 2 mg once daily</td>
<td>14 days or until discharge, whichever comes first</td>
</tr>
<tr>
<td></td>
<td>2 to &lt; 9 yo: 1 mg once daily</td>
<td></td>
</tr>
<tr>
<td>15 to &lt; 30</td>
<td>9 yo and older: 1 mg once daily</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2 to &lt; 9 yo: Not recommended</td>
<td></td>
</tr>
<tr>
<td>&lt; 15, on dialysis or ESRD</td>
<td>Not recommended</td>
<td></td>
</tr>
</tbody>
</table>

Dosage Adjustments based on Age and eGFR

<table>
<thead>
<tr>
<th>eGFR (ml/min/1.73 m²)</th>
<th>Recommendation</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
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<td></td>
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<td></td>
<td>2 to &lt; 9 yo: 1 mg once daily</td>
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</tr>
<tr>
<td>15 to &lt; 30</td>
<td>9 yo and older: 1 mg once daily</td>
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</tr>
<tr>
<td></td>
<td>2 to &lt; 9 yo: Not recommended</td>
<td></td>
</tr>
<tr>
<td>&lt; 15, on dialysis or ESRD</td>
<td>Not recommended</td>
<td></td>
</tr>
</tbody>
</table>

Frequency of Laboratory Test

<table>
<thead>
<tr>
<th>Baseline</th>
<th>Prior to first dose of baricitinib:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Hepatic function panel</td>
</tr>
<tr>
<td></td>
<td>• Scr and BUN</td>
</tr>
<tr>
<td></td>
<td>• CBC with differential</td>
</tr>
<tr>
<td></td>
<td>Prescriber should make any necessary renal dose adjustments based on GFR</td>
</tr>
<tr>
<td></td>
<td>Limited information regarding use in patients with any of the following findings:</td>
</tr>
<tr>
<td></td>
<td>o ANC &lt; 1 bil/L</td>
</tr>
<tr>
<td></td>
<td>o ALC &lt; 0.2 bil/L</td>
</tr>
<tr>
<td></td>
<td>o Hemoglobin &lt; 8 g/dL</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Monitoring while on Treatment</th>
<th>Hepatic function panel</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Every 2-3 days or daily if AST/ALT elevated</td>
</tr>
<tr>
<td></td>
<td>Scr and BUN</td>
</tr>
<tr>
<td></td>
<td>• Every 2-3 days or daily if unstable renal function</td>
</tr>
<tr>
<td></td>
<td>CBC with differential</td>
</tr>
<tr>
<td></td>
<td>• Every 2-3 days or daily if ALC/ANC low</td>
</tr>
<tr>
<td></td>
<td>Prescriber should make any necessary renal dose adjustments based on GFR</td>
</tr>
<tr>
<td></td>
<td>It is recommended to discontinue if:</td>
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<tr>
<td></td>
<td>o ALC &lt; 0.2 bil/L or ALC &lt; 0.5 bil/L. Can restart once above these thresholds.</td>
</tr>
<tr>
<td></td>
<td>o AST or ALT ≥ 10 x ULN or if drug-induced liver injury (DILI) is suspected, then hold therapy until DILI is excluded</td>
</tr>
</tbody>
</table>
**Tocilizumab** (Restricted to Infectious Disease physicians - *Prescriber must complete all EUA requirements*)

**Inclusion Criteria:**
- Positive SARS-CoV-2 test (i.e., RT-PCR or antigen, not antibody test), **AND**
- Receiving high-flow oxygen or noninvasive ventilation or < 48h of mechanical ventilation, **AND**
- Receiving systemic corticosteroids, **AND**
- Age ≥ 2 years old

**Exclusion Criteria:**
- Mechanical ventilation > 48 hours, **OR**
- ALT/AST > 10 x upper limit of normal, **OR**
- ANC < 1000 cells/mm³, **OR**
- Platelet count < 50,000 cells/mm³, **OR**
- Active tuberculosis (see precaution section for LTBI), **OR**
- Receiving baricitinib, **OR**
- Previously received an IL-6 inhibitor during hospitalization or is on long-term therapy with an IL-6 inhibitor, **OR**
- Patient has already received any dose of one or more of any form of tocilizumab, or sarilumab during this hospitalization or is on long-term therapy with any of these agents prior to this hospital admission, **OR**
- Receipt of live vaccine within the past 14 days
- For solid organ transplant patients, ID prescriber can consult Dr. Dilip Samarapungavan regarding risk of administration (Pager: 248-992-8057)

**Precautions** *(prescribers will have to discuss risk vs benefit with patient)*
- Active serious infections other than COVID-19
- Patients at risk for GI perforations
- Latent tuberculosis (LTBI)
- Pregnancy
- Not studied in patients CrCl < 30 mL/min (but unlikely to be significantly renally eliminated)

**Laboratory Monitoring:** LFTs and CBC

**Pediatric patient:** tocilizumab has not been studied in children with COVID-19; EUA granted for ≥ 2 yo based on extensive safety and dosing information for approved indications and adult efficacy data for COVID-19

**Pregnancy and Nursing Mothers:** Discussion of risk versus benefit with the patient’s care team, OB/GYN and Infectious Disease physicians should occur prior to administration in a pregnant patient

**Adverse Reactions:** Headache, hypertension, infusion reactions (rash, pruritus, nausea, hyper- or hypotension), LFT elevations, cytopenias, diarrhea, and allergic reaction (rare), and secondary bacterial and fungal infections

<table>
<thead>
<tr>
<th>Patients at or above 30 kg</th>
<th>8 mg/kg/dose (max: 800 mg) x 1 dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients &lt; 30 kg</td>
<td>12 mg/kg/dose x 1</td>
</tr>
</tbody>
</table>

- A second dose of tocilizumab is not recommended due to increased risk of possible secondary infection and lack of proven benefit
- For patients >40 kg, doses should be rounded as follows:
  - > 90 kg: 800 mg
  - > 65 to 90 kg: 600 mg
  - > 40 to 65 kg: 400 mg
Table 3. Bacterial Co-infections and Other Treatment Considerations

### Bacterial Co-Infections with COVID-19

Bacterial co-infections are uncommon in patients presenting with COVID-19 infection. A meta-analysis by Langford et al and Michigan cohort study (n = 1705 patients) found only 3.5% of hospitalized patients had community-onset bacterial co-infection and risk was slightly higher in patients admitted directly to the ICU at 11%. Secondary bacterial infections occurred in about 14% of COVID-19 patients. A study by Zhou and colleagues found the median duration of fever to be 12 days (8-13 days) and cough persisted for 19 days in survivors.

Procalcitonin: Low procalcitonin can be used to help rule-out bacterial co-infection (PCT < 0.25), but PCT > 0.25 should not be used as the only reason to initiate or continue antibiotic therapy. PCT > 0.25 is common in patients with COVID-19 pneumonia, especially in patients with more severe disease (possibly due to systemic inflammation); therefore, it appears to be an unreliable marker of bacterial superinfection. Also, patients with CKD and AKI have falsely elevated PCT levels, and as such PCT is not reliable in these patients.

### Strongly Suspected or Confirmed MRSA pneumonia:

For patients with moderate to severe COVID-19 with suspected MRSA pneumonia:
- Anti-staphylococcal therapy is generally unnecessary, since concomitant bacterial infection appears to be uncommon
- For sites using AUC-guided dosing for vancomycin (i.e., RYO, TRY, GRP):
  - For any infection in which a vancomycin AUC goal of 400 – 600 is currently recommended switch to trough monitoring with a goal ~15 mg/L for patients with COVID-19
- If MRSA pneumonia is suspected: suggest oral linezolid instead of vancomycin to help decrease fluid volume and required blood draws
  - Check MRSA nasal swab and discontinue if negative
  - Check for drug-drug interactions prior to starting linezolid
  - Caution in patients with pre-existing myelosuppression
- For pediatric patients: linezolid is restricted to Infectious Diseases physicians
  - Infants & children < 12 years old: linezolid 10 mg/kg/dose (max: 600 mg/dose) PO every 8 hours
  - Children & adolescents ≥ 12 years: linezolid 600 mg PO every 12 hours or as recommended by Infectious Diseases

Current evidence does not support use of the agents below for treatment of hospitalized patients with COVID-19 (due to lack of efficacy and/or potential toxicity)
- Hydroxychloroquine ± azithromycin
- Lopinavir/ritonavir (Kaletra)
- Osel tamivir
- Ribavirin
- Immune globulin (IVIG)
- Interferon
- Ivermectin (current clinical and pharmacokinetic data does not support use for prevention or treatment; last reviewed 2.16.22)
- Oral Vitamin C
- Colchicine (insufficient data at this time; last reviewed 2.15.21)
- Vitamin D (insufficient data at this time; last reviewed 5.3.21)
- Fluvoxamine (insufficient data for hospitalized patients; last reviewed 11.4.21)
Other Treatment Considerations

ACEi/ARBs therapy: Patients chronically taking ACEi/ARBs should continue therapy. It is unclear if ACEi/ARBs will worsen or improve outcomes in patients with COVID-19.

Oral Vitamin C: Oral vitamin C does not achieve high enough concentrations in the serum for any potential therapeutic benefit due to saturable absorption. Also, oral vitamin C has the potential to cause harm, specifically AKI and/or kidney stones secondary to the accumulation of oxalate. Therefore, we do not recommend the use of oral vitamin C as adjuvant therapy for the treatment of COVID-19.

Statins: Due to the lack of data, we do not recommend COVID-19 be the sole indication for statin therapy.

Other Treatment Considerations (continued)

Stress ulcer prophylaxis: Consider in patients on steroids and therapeutic anticoagulation, mechanical ventilation, and/or patients with coagulopathy.

Table 4. BH Investigational Studies

<table>
<thead>
<tr>
<th>Study Agent</th>
<th>Location</th>
<th>Study Coordinator</th>
<th>Study Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nirmatrelvir/ritonavir</td>
<td>RYO</td>
<td>Susan Highers</td>
<td>An Interventional Efficacy And Safety, Phase 2, Randomized, Double-Blind, 3-Arm Study To Investigate Nirmatrelvir/Ritonavir in Nonhospitalized Participants at Least 12 Years Of Age With Symptomatic COVID-19 Who Are Immunocompromised</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><strong>Primary Objective:</strong> Comparison of 5, 10, or 15 days of active therapy.</td>
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</tbody>
</table>
|                      |          |                   | **Key Inclusion Criteria:**  
|                      |          |                   | • Participants aged 12 years or older and weighing ≥40 kg at screening.                                                                                             |
|                      |          |                   | • Confirmed SARS-CoV-2 infection as determined by RT-PCR or other acceptable test method in any specimen collected.                                                       |
|                      |          |                   | • ≥1 sign/symptom attributable to COVID-19 present on the day of randomization.                                                                                     |
|                      |          |                   | • Immunocompromised.                                                                                                                                                |
|                      |          |                   | **Key Exclusion Criteria:** Current or anticipated hospitalization                                                                                        |
| Nirmatrelvir/ritonavir | RYO      | Susan Highers     | An Interventional, Efficacy and Safety, Phase 2, Double-Blind, 2-Arm Study To Investigate Orally Administered Nirmatrelvir/Ritonavir Compared with Placebo/Ritonavir for the Treatment of Severe COVID-19 in Hospitalized Participants Who are Immunocompromised or at Increased Risk for Severe COVID-19 Outcomes |
|                      |          |                   | **Primary Objective:** Comparison of 15 days of active versus placebo therapy.                                                                                 |
|                      |          |                   | **Key Inclusion Criteria:**  
|                      |          |                   | • Participants aged 12 years or older and weighing ≥40 kg at screening.                                                                                             |
|                      |          |                   | • Confirmed SARS-CoV-2 infection as determined by RT-PCR or other acceptable test method in any specimen collected.                                                       |
|                      |          |                   | • Immunocompromised or having more 2 or more risk factors.                                                                                                        |
|                      |          |                   | • Hospitalized                                                                                                                                                    |
|                      |          |                   | • Requires oxygen supplementation                                                                                                                             |
|                      |          |                   | • Expected to require hospitalization for > 72 hours                                                                                                            |
|                      |          |                   | **Key Exclusion Criteria:** ECMO or mechanical ventilation                                                                                                    |
References


2. Young BE, Ong SWX, Kalimuddin S et al. Epidemiologic Features and Clinical Course of Patients Infected with SARS-CoV-2 in Singapore. JAMA. Published online March 03, 2020.


