### Treatment Guidance for Hospitalized Patients with COVID-19

*This is a living document that will be updated based as more data emerge.*

*Last updated: 7/15/20*

There are no FDA-approved therapies to treat COVID-19 at this time. For more specific medication information, please refer to a drug information resource such as LexiComp® online or contact Pharmacy.

<table>
<thead>
<tr>
<th>Mild Disease (No supplemental oxygen)</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Supportive care (Current literature, internal data, and recommendations from professional organizations and public health agencies do not support the routine use of hydroxychloroquine for patients with confirmed COVID-19 infection)</td>
<td>Routine treatment with investigational therapies (including hydroxychloroquine) is not recommended outside clinical trials. COVID-19 infected patients will be screened for eligibility in ongoing clinical trials.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Adjunctive Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anticoagulation:</td>
</tr>
<tr>
<td>- Adult patients: refer to COVID-19 Anticoagulation and Coagulopathy Management for Adults</td>
</tr>
<tr>
<td>- Pediatric patients: VTE prophylaxis with enoxaparin (at an appropriate weight-based dose) may be initiated on a case-by-case basis in pediatric patients with confirmed COVID-19 (or a suspected COVID-19 patient with risk factors for thrombosis) as determined by the patient’s Pediatric Hospitalist, Pediatric Intensivist and/or Pediatric Hematologist.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Moderate to Severe Disease (Receiving supplemental oxygen or requiring mechanical ventilation)</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Supportive care (Current literature, internal data, and recommendations from professional organizations and public health agencies do not support the routine use of hydroxychloroquine for patients with confirmed COVID-19 infection)</td>
<td>Routine treatment with investigational therapies (including hydroxychloroquine) is not recommended outside clinical trials. COVID-19 infected patients will be screened for eligibility in ongoing clinical trials.</td>
</tr>
</tbody>
</table>

| Remdesivir (Investigational agent) x 5-10 days if inclusion/exclusion criteria are met (Refer to Treatment Dosing Recommendations) |

<table>
<thead>
<tr>
<th>Adjunctive Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prophylactic Anticoagulation:</td>
</tr>
<tr>
<td>- Adult patients: refer to COVID-19 Anticoagulation and Coagulopathy Management for Adults</td>
</tr>
<tr>
<td>- Pediatric patients: VTE prophylaxis with enoxaparin (at an appropriate weight-based dose) may be initiated on a case-by-case basis in pediatric patients with confirmed COVID-19 (or a suspected COVID-19 patient with risk factors for thrombosis) as determined by the patient’s Pediatric Hospitalist, Pediatric Intensivist and/or Pediatric Hematologist.</td>
</tr>
</tbody>
</table>

| Therapeutic Anticoagulation: refer to COVID-19 Anticoagulation and Coagulopathy Management for Adults |
**Steroids**: recommended in adult patients with new or worsening hypoxemia and requiring supplemental oxygen

- **Low-dose steroids for up to 10 days (or until discharge if earlier):**
  - Dexamethasone 6 mg IV/PO q24h --OR--
  - Methylprednisolone 40 mg IV q24h --OR--
  - Prednisone 40 mg PO q24h

- **For select patients on high flow nasal oxygen, non-invasive or invasive mechanical ventilation, or ECMO (based on physician discretion):**
  - Consider high-dose steroids:
    - 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, and consider administering tocilizumab (Refer to Tocilizumab criteria below).
  - 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, new onset diabetes or for chronic diabetes management.

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

- **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.

- **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.

**Tocilizumab**: Consider in patients with rapidly worsening gas exchange/respiratory status over 24-48 hours, high suspicion of cytokine storm, and progressive elevation in inflammatory markers (e.g., CRP, ferritin, D-dimer, IL-6), and PaO2/FiO2 ≤ 300 or SpO2 ≤ 93%. Patient should meet inclusion/exclusion criteria and use must be authorized by Tocilizumab Approval Group (Refer to Treatment Dosing Recommendations below).

**Suggested laboratory monitoring**

- CBC with diff (lymphocytes): Leukopenia: 17-45%; Lymphopenia: 33-85%
- CMP: LFTs (generally elevated)
- LDH (increased 27-75%)
- D-dimer (generally increased)
- Ferritin (generally increased)
- CRP (generally increased)
- Procalcitonin (generally low, but nonspecific)
- Creatine Kinase (generally elevated)
- Severe/ICU patients: IL-6 levels

*BNP: brain natriuretic peptide; CBC: complete blood count; CMP: comprehensive metabolic panel; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; IL-6: interleukin 6; LDH: lactate dehydrogenase; LFTs: liver function tests*
<table>
<thead>
<tr>
<th>Treatment Dosing Recommendations</th>
</tr>
</thead>
</table>
| **Remdesivir**  
(Investigational Agent)  
Available through: 1) **Compassionate Use:** pregnant and pediatric patients  
2) **Emergency Use Authorization:** received a limited number of doses for Beaumont Health |
| **Adult Dosing:**  
200 mg IV x 1 dose, then 100 mg IV q24hr through day 5-10 |
| **Pediatric Dosing***:  
< 40 kg: 5 mg/kg IV load, then 2.5 mg/kg IV q24hr  
≥ 40 kg: 200 mg IV load followed by 100 mg IV q24hr |
| **Pregnancy and Nursing Mothers:** Consider in pregnant women if criteria for compassionate use are met (refer to the Treatment Guidance for Pregnant and Breastfeeding Mothers with COVID-19 for more information) |
| **Tocilizumab**  
Patient must meet inclusion criteria and use must be authorized by Tocilizumab Approval Group (see below) |
| **Key Inclusion Criteria:**  
- Authorization from Tocilizumab Approval Group  
- Confirmed SARS-CoV-2 test  
- Persistent or increasing oxygenation requirements of 6 L or more with a SpO2 ≤ 93% or PaO2/FiO2 ≤ 300 mmHg  
- Abnormal chest imaging consistent with COVID-19  
- Progressive elevation of laboratory criteria supportive of cytokine storm in addition to clinical decline:  
  - Ferritin >300 ug/L (or surrogate) with doubling within 24 hours  
  - Ferritin >600 ug/L at presentation and LDH >250 U/L  
  - Elevated D-dimer (>1 mg/L) |
| **Key Exclusion Criteria:**  
- Mechanical ventilation > 48 hours  
- ALT/AST > 5 x upper limit of normal  
- Absolute neutrophil count < 500 cells/mm³  
- Platelet count < 50,000 cells/mm³  
- For solid organ transplant patients, the site level ID physician from the tocilizumab approval group can consult Dr. Dilip Samarapungavan regarding risk of administration (Pager: 248-992-8057)  
- Hypersensitivity to tocilizumab or any excipients  
- Patients with active pulmonary tuberculosis or strongly suspected bacterial or fungal infection |
| **Adult Dosing:**  
8 mg/kg/dose (max: 800 mg; infused over 1 hour) x 1 dose  
- Doses should be rounded to nearest available full vial  
- A second dose of tocilizumab is strongly discouraged due to increased risk of possible secondary infection and lack of proven benefit |
| **Pediatric Dosing:**  
8 mg/kg/dose (max: 400 mg; infused over 1 hour) x 1 dose |
| **Expected Clinical Improvement:** Based on the limited literature available for COVID-19 at this time, tocilizumab effects are generally not seen until around 48-72 hours after administration. |
| **Laboratory Monitoring:** LFTs and CBC  
**Precaution:** Not studied in patients CrCl < 30mL/min; use caution in patients with diverticulitis (increased risk for GI perforation)  
**Pregnancy and Nursing Mothers:** Discussion of risk versus benefits with the patient’s care team, Infectious Diseases physician, and the Tocilizumab Approval Group should occur prior to administration in a pregnant patient (refer to the Treatment Guidance for Pregnant and Breastfeeding Mothers with COVID-19 for more information)  
**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 |
### Tocilizumab Approval Group (contact your site specific Infectious Diseases physician listed below)

<table>
<thead>
<tr>
<th>Site</th>
<th>Contacts</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dearborn, Taylor, Trenton, and Wayne</td>
<td>Cecilia Big, MD</td>
</tr>
<tr>
<td>Farmington Hills</td>
<td>Wiley Fan, MD</td>
</tr>
<tr>
<td>Grosse Pointe</td>
<td>Joel Fishbain, MD; Renee Jiddou-Yaldoo, MD</td>
</tr>
<tr>
<td>Royal Oak</td>
<td>Matthew Sims, MD; Carl Lauter, MD</td>
</tr>
<tr>
<td>Troy</td>
<td>Sachi Gowda, MD</td>
</tr>
</tbody>
</table>

### 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)
- Oseltamivir
- Baloxavir
- Ribavirin
- Immune globulin (IVIG)
- Interferon
- Ivermectin
- Oral Vitamin C

*List subject to change

### Other Treatment Considerations

#### 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

#### 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.

#### Melatonin:

- Insufficient data for the use of melatonin as an adjunctive agent in the treatment of COVID-19
COVID-19 Investigational Studies at Beaumont Health

<table>
<thead>
<tr>
<th>Study Agent</th>
<th>Location</th>
<th>Study Coordinator</th>
<th>Inclusion Criteria</th>
</tr>
</thead>
</table>
| Naltrexone and Ketamine (SINK study) | RYO      | Maureen Cooney, RN | 1) ≤ 6L O\textsubscript{2} by nasal cannula randomized to low-dose naltrexone vs placebo, ketamine if O\textsubscript{2} requirements increase  
2) > 6L O\textsubscript{2} by nasal cannula enrolled as open label low-dose naltrexone & directly into the ketamine rescue group |
| Gimsilumab                         | RYO      | Susan Highers, RN  | > 6L oxygen with SpO\textsubscript{2} <93% or PaO\textsubscript{2}/FiO\textsubscript{2} ratio <300 or on mechanical ventilation for < 24 hours |
| Sirukumab                          | RYO      | Lauren Brown, RN   | > 4L oxygen with SpO\textsubscript{2} <92% or PaO\textsubscript{2}/FiO\textsubscript{2} ratio <300 or on mechanical ventilation < 72 hours |
| Convalescent Serum                 | All sites| Lydia Kosovich, RN | > 6L nasal cannula O\textsubscript{2} or on mechanical ventilation                                                                               |

References