Table 1. Risk Factors for Severe COVID-19

<table>
<thead>
<tr>
<th>Patient History/Exam(^1,2)</th>
<th>Age ≥60, Immunocompromised, Comorbidities (Cardiac, Pulmonary, Renal, Hepatic, Heme), Obesity (BMI &gt;35), Long Term Care Facilities. Respiratory Rate &gt;24. HR &gt;125. SpO2&lt;92% on Room Air.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lab Identifiers of Severity / Mortality(^1)</td>
<td>D-Dimer &gt; 1 mg/L, Ferritin &gt; 300ng/mL, Lymphopenia (ALC&lt;600), LDH &gt;250, SOFA&gt;4. Baseline and Q1-3d depending on severity. Baseline and PRN CPK, CRP, Troponin, EKG; Procalcitonin</td>
</tr>
</tbody>
</table>

Table 2. Therapy Recommendations

See Appendix 1 for treatment recommendations based on disease severity

<table>
<thead>
<tr>
<th>Therapy, Dose, Toxicity, NIH Evidence level (if available)</th>
<th>Place in Therapy / Other Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Remdesivir</td>
<td>FDA approved for treatment of COVID-19 in hospitalized adult and pediatric patients (age ≥12y; wt ≥40kg). Available through EUA for hospitalized pediatric patients weighing 3.5 kg to 40kg. Requirements for use are aligned across AAH. If remdesivir supply is constrained, then changes may be made to these use criteria.</td>
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<tr>
<td><strong>200mg IV x 1 then 100mg IV q24h on days 2-5, or until hospital discharge, whichever comes first.</strong></td>
<td><strong>NIH 2020</strong> guidelines recommend remdesivir in combination with corticosteroids in hospitalized COVID-19 patients who are on supplemental oxygen, including high-flow oxygen and non-invasive ventilation (B-III). For patients recently placed on mechanical ventilation, remdesivir may be considered in combination with corticosteroids (C-III).</td>
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<td>Absence of clinical improvement: may extend to 10days.</td>
<td>• <strong>IDSA 2020</strong> guidelines recommend remdesivir in hospitalized COVID-19 patients with hypoxemia (SpO2 ≤94% on room air), including those requiring mechanical ventilation or ECMO, and corticosteroids in hospitalized COVID-19 patients with severe disease.³</td>
</tr>
</tbody>
</table>
| Ventilated/ECMO: recommended duration 10 days | • **WHO 2020** recommends against the use of remdesivir in hospitalized patients, regardless of disease severity (conditional recommendation). This does not change our internal recommendation to use remdesivir. 
Baseline assessment of renal function, ALT, & prothrombin time recommended. Daily assessment of SrCr & ALT during therapy. Pharmacists may order ALT daily during RDV therapy per AAH P&T. |
| * In clinically improved patients otherwise medically stable for discharge, shorter courses may be acceptable. Per NIH Guidelines – usual duration of remdesivir therapy for patients on supplemental O2: 5 days or until hospital discharge, whichever comes first. | Remdesivir is not recommended if CrCl <30mL/min. Treating MD must assess risk vs benefit and monitor renal function daily. |
| Remdesivir is not recommended if CrCl <30mL/min. Treating MD must assess risk vs benefit and monitor renal function daily. | ALT>10x ULN: Discontinue remdesivir. Reassess per MD. |
| **Toxicity:** Transient elevations in AST/ALT. No dose adjustment needed for moderate hepatic dysfunction. | * |
Steroids with Severe Pneumonia / COVID-related ARDS

1. IV or oral dexamethasone 6mg daily for 10 days.
   PREFERRED OPTION, other options listed below

2. IV methylprednisolone* 20mg Q12hours for 10 days
   OR
   IV methylprednisolone** 40mg Q12hours for 10 days –
   for patients >80kg and/or receiving mechanical ventilation

3. Oral prednisone 40mg daily

*Consider a conversion to oral prednisone in those who qualify for enteral therapy. **May consider dose escalation in severe morbid obesity.

NOTE: For patients with prolonged hypoxemia or who clinically deteriorate, may consider dose escalation. For patients with COVID-related ARDS (P:F<150): See Comments Below.

NIH Ratings
A-I: for patients on mechanical ventilation, high-flow oxygen or noninvasive ventilation
B-III/B-I: for patients on supplemental oxygen (with/without remdesivir)
A-IIa: avoid steroids in inpatients not on supplemental oxygen

WHO 2020 recommends systemic corticosteroid for 7-10 days in patients with severe (SpO2 <90% on room air, RR >30, or signs of respiratory distress) and critical (ARDS, sepsis/shock, vasopressors, mechanical ventilation) COVID-19.

NIH 2020 recommends corticosteroid therapy for COVID-19 patients who require supplemental oxygen, including patients on high-flow deives, mechanical ventilation and ECMO.

IDSA 2020 recommends glucocorticoid therapy for hospitalized patients with severe COVID-19 infection (SpO2 ≤ 94%, supplemental oxygen or mechanical ventilation).


In the RECOVERY trial, dexamethasone 6mg once daily for up to 10 days reduced 28-day mortality among COVID-19 patients compared to usual care (21.6% vs. 24.6%; aRR=0.83; 95%CI 0.74, 0.920).

This effect was pronounced in patients receiving invasive mechanical ventilation (RR=0.65, 95% CI 0.51, 0.82) and patients requiring supplemental oxygen (RR=0.80, 95% CI 0.70, 0.92).

A meta-analysis of 7 randomized trials of corticosteroid therapy (N=1703 patients) found that 28-day mortality was lower with corticosteroid therapy (32.7%) than standard of care (41.5%) - OR, 0.66 [95% CI, 0.53-0.82]. There was minimal inconsistency between studies and serious adverse event rates were similar between groups.

Comments: Corticosteroids in Severe ARDS.

ARDS P:F<150 – Dexamethasone 20mg IV days 1-5, 10mg IV days 6-10 for patients with ARDS may be considered by critical care on a case by case basis. CoDEX: Open label RCT from Brazil in COVID (+), mechanically ventilated adults with P:F ≤200 randomized within 48hours of intubation to Dexamethasone 20mg IV days 1-5, 10mg IV days 6-10 (n=151) or placebo (n=148) – both groups received available standard of care. No patients received remdesivir (not available); vasopressor use in 66%; prone position in 22%. Mean P:F ration 131. Primary outcome: at 28-days, dexamethasone treatment resulted in an increase in number of ventilator-free days (alive and free of mechanical ventilation) compared to standard of care alone (6.6 days vs 4days) p=0.04. No difference in secondary outcomes of 28-day all-cause mortality (56.3% vs 61.5% p=0.85), six-point ordinal scale, or duration of mechanical ventilation. Similar adverse effects between dexamethasone and placebo.

COVID-19 Convalescent Plasma (CCP) (LIMITED Access)

Emergency Use Authorization (EUA): CCP is available to treat hospitalized patients with COVID-19 using EPIC and CareConnection order sets for CCP. Please refer to AAH internal CCP guidance.

CCP data emanate from a non-randomized, non-peer reviewed study in which CCP was most effective when given within 3 days of diagnosis.

• NIH 2020 determined there are insufficient data to recommend either for or against the use of convalescent plasma for the treatment of COVID-19.
| Therapy Considerations: | Baricitinib (TOC) is NOT recommended for management of COVID-19 outside of clinical trials (IDA 2020, NIH 2020).<sup>a,b</sup> Preliminary, unpublished data from a randomized, controlled trial failed to demonstrate benefit. Additional clinical trials are needed to inform research on the effectiveness of treatment with TOC for patients with COVID-19.<sup>c</sup> See AAH criteria for use.

Doses greater than 400mg and repeat doses are not recommended and must be approved by ID physician leadership.

Repeat doses were associated with higher rates of secondary infections within AAH (internal review April – June 2020; data/summary available upon request)

Must assess for concurrent non-COVID related infection (viral, fungal, bacterial) prior to administration.

HSV prophylaxis advised:
- Valacyclovir 500mg PO BID or Acyclovir 200mg IV daily.
- Duration: 4 weeks.

| NOT Recommended but NOT Prohibited | Therapies NOT Recommended: See updated table from Drug Policy Committee |

References:

12. Busani S, Bedini A, Biagioli E, et al. Two fatal cases of acute liver failure due to HSV-1 infection in COVID-19 patients following immunomodulatory therapies [published online a


## Appendix 1. Suggested COVID-19 Treatment Based on Patient Severity of Illness

<table>
<thead>
<tr>
<th>WHO Ordinal&lt;sup&gt;a&lt;/sup&gt;</th>
<th>1-2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
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<tr>
<td>Ordinal Description/Therapy</td>
<td>Ambulatory ± limitation of activities</td>
<td>Hospitalized, no oxygen therapy</td>
<td>Oxygen by mask or nasal cannula</td>
<td>Non-invasive ventilation or high-flow oxygen</td>
<td>Intubation and mechanical ventilation</td>
<td>Ventilation + additional organ support (vasopressors, RRT, ECMO)</td>
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<tr>
<td>IV Remdesivir</td>
<td><em>See below</em></td>
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<td>Convalescent Plasma</td>
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<td>Corticosteroids</td>
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<td>Tocilizumab&lt;sup&gt;b&lt;/sup&gt;</td>
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<tr>
<td>Baricitinib</td>
<td>Not recommended but not prohibited. Formal ID and Pulm/Critical Care consults required.</td>
<td>Consider with formal ID and Pulm/Critical Care consults required.</td>
<td>Not recommended but not prohibited. Formal ID and Pulm/Critical Care consults required.**</td>
<td>Not recommended but not prohibited. Formal ID and Pulm/Critical Care consults required.**</td>
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<td>Monoclonal Antibody Preparations</td>
<td>For patients with mild to moderate symptoms within 10 days of positive test result (AAH use criteria)</td>
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<sup>b</sup> Tocilizumab may be considered for patients with cytokine-induced organ failure under direction of Infectious Diseases and Pulmonary/Critical Care only. See AAH criteria for use.

* NIH Guidelines (Dec 4, 2020) - For Patients with COVID-19 Who Are Not Hospitalized or Who Are Hospitalized With Moderate Disease but Do Not Require Supplemental Oxygen:
  - NIH does not recommend any specific antiviral or immunomodulatory therapy for the treatment of COVID-19 in these patients. Patients are considered to have moderate disease if they have clinical or radiographic evidence of lower respiratory tract infection and a saturation of oxygen (SpO2) ≥94% on room air at sea level.
  - There are insufficient data for NIH to recommend either for or against the use of remdesivir for the treatment of COVID-19.
  - NIH recognizes there may be situations in which a clinician judges that remdesivir is an appropriate treatment for a hospitalized patient with moderate disease (e.g., a person who is at a particularly high risk for clinical deterioration).

** Preliminary ACTT-2 data do not demonstrate a mortality benefit of Baricitinib + Remdesivir for mechanically ventilated patients.