This document was prepared (in March, 2020-April, 2021) by and for MGH medical professionals (a.k.a. clinicians, care givers) and is being made available publicly for informational purposes only, in the context of a public health emergency related to COVID-19 (a.k.a. the coronavirus) and in connection with the state of emergency declared by the Governor of the Commonwealth of Massachusetts and the President of the United States. It is neither an attempt to substitute for the practice of medicine nor as a substitute for the provision of any medical professional services. Furthermore, the content is not meant to be complete, exhaustive, or a substitute for medical professional advice, diagnosis, or treatment. The information herein should be adapted to each specific patient based on the treating medical professional’s independent professional judgment and consideration of the patient’s needs, the resources available at the location from where the medical professional services are being provided (e.g., healthcare institution, ambulatory clinic, physician’s office, etc.), and any other unique circumstances. This information should not be used to replace, substitute for, or overrule a qualified medical professional’s judgment.

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- This document was developed by members of the Infectious Diseases (ID) division at MGH in conjunction with pharmacy, radiology, and other medicine divisions to provide guidance to frontline clinicians caring for adult patients with COVID-19.
- This document covers potential emergency use, off-label and/or experimental use of medications and immunosuppression management for transplant patients as well as a suggested laboratory work up. It does NOT cover recommendations for infection control, personal protective equipment (PPE), management of hypoxemia or other complications in patients with COVID-19.
- This is a living document that will be updated in real time as more data emerge.

What’s New in the April 28, 2021 update:

- Based on RECOVERY and REMAP-CAP, tocilizumab may be administered for patients progressing on dexamethasone +/- remdesivir. For patients progressing to or towards high-flow oxygen, after assessment of eligibility, tocilizumab may be authorized by agreement of pharmacy with pulmonary/critical care.
- MGB guidance for emergency use authorization monoclonal antibodies has been updated and applies mostly for outpatients. Rarely, inpatients may qualify if they were hospitalized for reasons other than COVID-19.
- We are aware of reports regarding benefits related to anticoagulation for severely ill but not critically ill patients; however, insufficient details are available at this time to deploy this therapy.
- Routine consultation of pulmonary no longer recommended for patients with underlying lung disease.
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**Table 1: Work-up for diagnosis, prognosis / risk stratification, and/or safety of therapeutics**

**Suggested for hospitalized patients with confirmed COVID-19**

<table>
<thead>
<tr>
<th>Recommended daily labs (until stable):</th>
<th>For acute kidney injury (i.e. serum creatinine &gt;0.3 above baseline)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• CBC with diff (esp. total lymphocyte count)</td>
<td>• Urinalysis and spot urine protein:creatinine</td>
</tr>
<tr>
<td>• Complete metabolic panel²</td>
<td>When MAS/sHLH suspected (rising LFTs, falling fibrinogen, hypotension, see <strong>Immunomodulation</strong>):</td>
</tr>
<tr>
<td>• CPK (creatinine kinase)</td>
<td>• ESR, Ferritin</td>
</tr>
<tr>
<td>• CRP (first week of hospitalization, non-ICU)³</td>
<td>Viral serologies for all patients unless done recently:</td>
</tr>
<tr>
<td><strong>Recommended at baseline then every other day (if in ICU or elevated check daily):</strong></td>
<td>• HBV serologies (sAb, cAb, and sAg)</td>
</tr>
<tr>
<td>• PT/PTT/fibrinogen</td>
<td>• HCV antibody, unless positive in past</td>
</tr>
<tr>
<td>• D-dimer</td>
<td>• HIV 1/2 Ab/Ag</td>
</tr>
<tr>
<td><strong>Link to <a href="#">Guidance from MGH Hematology</a></strong></td>
<td><strong>If clinically indicated:</strong></td>
</tr>
<tr>
<td><strong>For risk stratification:</strong></td>
<td>• Blood cultures (2 sets) if bacteremia suspected</td>
</tr>
<tr>
<td>• LDH (repeat daily if elevated)</td>
<td>• β-HCG for women of childbearing age</td>
</tr>
<tr>
<td>• Troponin⁵ (see below if elevated)</td>
<td><strong>Following infection control/PPE guidelines:</strong></td>
</tr>
<tr>
<td>• Baseline ECG (<a href="#">QTc monitoring algorithm</a>)</td>
<td>• SARS-CoV-2 test, if not already performed.</td>
</tr>
<tr>
<td><strong>With clinical deterioration, repeat risk stratification labs.</strong></td>
<td>• The Pandemic Response Viral Order used to order COVID-19 PCR test will order additional viral testing (i.e. influenza and RSV, or an expanded panel) based on order question responses and MGH protocols.</td>
</tr>
<tr>
<td><strong>Radiology:</strong></td>
<td>• If bacterial superinfection highly suspected, routine sputum for Gram stain and culture, Legionella urinary antigen. If immunocompromised, see next page.</td>
</tr>
<tr>
<td>• Portable CXR at admission</td>
<td></td>
</tr>
<tr>
<td>• High threshold for PA/lateral, consider only if low suspicion for COVID-19 and result would change management or affect PUI status.</td>
<td></td>
</tr>
<tr>
<td>• Non-contrast CT is of limited utility in definitively diagnosing COVID-19 and should only be considered if it is likely to change management or PUI status; check <a href="#">CORAL tool</a>.</td>
<td></td>
</tr>
</tbody>
</table>

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1 The prognostic value of some of these labs is being defined or is not yet proven. For PUI, please refer to [COVID-19 Testing Criteria](#) or [Infection Control page for biothreats resolution pathways](#).

2 For a primer on liver issues related to COVID19 and treatment, please see our [supporting liver document](#).

3 If beyond 1 week of hospital stay or admitted to ICU setting, inflammatory markers are hard to interpret. CRP may be useful in determining candidacy for tocilizumab.

4 Viral serologies assist for interpretation of ALT elevations, present in ~25% of presentations. Note: follow-up molecular testing for HIV/HBV/HCV may have longer turnaround times than usual.

5 See note on next page regarding elevated troponins.
**Suggested for immunocompromised patients:** If clinically indicated, consider sending *Pneumocystis* DFA from sputum (*no induced sputum* given risk of aerosolization). If unable to send sputum, consider sending serum beta-d-glucan. If clinically indicated, consider sending fungal/AFB sputum cultures.

**Additional diagnostic considerations for candidates for corticosteroids or immunotherapy:**
If starting steroids or immunotherapy AND if the patient is foreign-born from a resource-limited country, experiencing homelessness, or has a history of incarceration AND if there is no past history of active TB or latent TB infection (LTBI), send T-Spot. Routine screening for TB is unnecessary for most COVID patients. More explanation is found here, accompanied by a separate flowchart.

**Procalcitonin is not recommended for most patients admitted with COVID-19.** It may have limited utility in those with intermediate risk for bacterial superinfection. Note that from studies to date, procalcitonin remains low in the first 7-10 days of COVID-19 infection and can rise later on, even without bacterial superinfection. Repeating PCT is less specific late in the course of COVID-19 and generally unnecessary. See FAQ.

**Considerations for elevated troponin:**
Biomarkers of cardiac injury may be elevated due to of COVID-19, an acute cardiac issue such as an MI or heart failure, or both. Significant degree of troponin elevation and rising values both predict in-hospital mortality. For elevated high-sensitivity troponin (> 2 times upper limit of normal) without hemodynamic compromise, can repeat troponin in 24 hours; echocardiogram not routinely necessary unless otherwise indicated, e.g. unexplained hypotension or reduced central venous O2 saturation. Markedly elevated troponin (e.g. > 5-10x ULN), up-trending troponin with hemodynamic compromise or other concerning cardiovascular symptoms/signs should prompt consideration of obtaining a point of care ultrasound (POCUS), a transthoracic echocardiogram or cardiology consultation. Note: interpretation of troponin elevation in the setting of renal dysfunction can be challenging.
Determine severity: The severity of COVID-19 is categorized into **mild** (symptoms but no dyspnea or abnormal imaging), **moderate** (lower respiratory disease w/ SpO2 >94% on room air), **severe** (SpO2 ≤ 94% on room air, a ratio of arterial partial pressure of oxygen to fraction of inspired oxygen (PaO2/FiO2) <300 mmHg, respiratory frequency >30 breaths per minute, or lung infiltrates >50%), or **critical** (ICU, respiratory failure, septic shock, and/or multiple organ dysfunction). Note these definitions vary in the literature; the choice of cutoff of ≤ 94% is based on the ACCT-1 trial. 

*When classifying the severity of COVID-19 based on SpO2, please note whether the hypoxemia is new (as opposed to at or near baseline) or due to other causes (such as volume overload).*

Determine prognosis: The following risk factors may predict COVID-19 disease progression to more severe manifestations. Patients with multiple risk factors may warrant closer monitoring or, on a case-by-case basis for moderate disease, be considered for remdesivir.

<table>
<thead>
<tr>
<th><strong>Table 2: Risk Factors for COVID-19 Disease Progression</strong></th>
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</thead>
<tbody>
<tr>
<td><strong>Epidemiological – Category 1</strong></td>
</tr>
<tr>
<td>Age &gt; 50</td>
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<tr>
<td>Pre-existing pulmonary disease</td>
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<tr>
<td>Chronic kidney disease</td>
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<tr>
<td>Diabetes with A1c &gt; 7.6%</td>
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<tr>
<td>History of hypertension</td>
</tr>
<tr>
<td>History of cardiovascular disease</td>
</tr>
<tr>
<td>Obesity (BMI &gt; 30)</td>
</tr>
<tr>
<td>Pregnancy</td>
</tr>
<tr>
<td>Use of biologics*</td>
</tr>
<tr>
<td>History of transplant or other immunosuppression*</td>
</tr>
<tr>
<td>HIV, CD4 cell count &lt;200 or unknown CD4 count*</td>
</tr>
</tbody>
</table>

*Not yet proven as risk factors for progression, inferred from other infections. Other factors include poverty, racism, recent cancer chemotherapy, recent surgery, sickle cell disease. For more information about COVID-19 severity, see our [supporting risk factors document](#).
Algorithm based on severity

1. Confirm COVID Positive, Admitted as Inpatient
   - Clinical trials team considers candidacy for all admissions†
   - 1. Assess severity of illness§
   - 2. Assess prognosis*
   - 3. Do not routinely start antibiotics

Asymptomatic, mild or moderate disease
- No specific COVID-19 therapy
- Supportive care, close monitoring, especially for those with multiple risk factors for progression
- Repeat labs at regular intervals
- Remdesivir may be considered for select patients with multiple risk factors for progression
- Monoclonal antibodies can be considered per EUA / MGB criteria if COVID-19 is not the primary reason for hospitalization
- If progresses to severe disease, may reassess candidacy for clinical trials and other therapies*

Severe disease
- SpO2 ≤ 94% on RA, P/F ratio < 300, RR > 30

- If eligible‡, ensure PT, eGFR, ALT; remdesivir 200 mg IV x 1, then 100 mg IV daily for 4 days
- If on supplemental oxygen, dexamethasone 6 mg PO or IV daily for up to 10 days
- Consider statin if CV indication
- Supportive care, close monitoring especially for those with multiple risk factors for progression

- Repeat labs at regular intervals
- If on RDV, follow daily LFTs and eGFR if on RDV
- Dexamethasone strongly recommended
- Decisions about alternative steroids, off-label immunomodulatory (such as tocilizumab) or other therapies can be considered on a case-by-case basis by the ICU team

Critical disease (ICU, respiratory failure, septic shock, and/or multiple organ dysfunction)

- Refer to MGH ICU COVID management guidance
- Follow daily LFTs and eGFR if on RDV
- Dexamethasone strongly recommended
- Decisions about alternative steroids, off-label immunomodulatory (such as tocilizumab) or other therapies can be considered on a case-by-case basis by the ICU team

- Repeat labs at regular intervals
- If on RDV, follow daily LFTs and eGFR
- If not on RDV, may reconsider via the ID antibiotic approval pager*
- RDV/DEX can be d/c’d upon discharge
- If clinically deteriorating on dexamethasone and CRP ≥ 75 mg/L, tocilizumab can be considered with guidance from critical care

§: When assessing severity, consider whether hypoxia is a new requirement or due to another cause (such as CHF)
*: See risk factors table on previous page
†: Current list of clinical trials is found at this link.
ID strongly recommends referral to clinical trials, which occurs automatically for all admissions
‡: Check RDV criteria on next page. Guidance from ID regarding use of remdesivir (e.g. eGFR<30), off-label use, is available 8am to 8pm via the antibiotic approval pager.
❖: If not on RDV (eg declined or not qualified earlier in admission), regardless of clinical trial enrollment status, patient may be reconsidered for RDV should they qualify.
COVID-19 Specific Management:
Guidance is available from NIH and IDSA. MGH-specific recommendations are below.

The above algorithm provides guidance based on available information to-date regarding possible and investigational treatments. As appropriate, these recommendations will be updated to include new or emerging data.

Antibody-Based Therapies

Monoclonal antibodies (mAbs). Anti-spike SARS-CoV-2 monoclonal antibodies bind to the S protein receptor binding domain (RBD) and block interaction with the ACE2 receptor. For outpatients, reports from RCTs of certain monoclonal antibodies suggest benefit by ~70% reduction of hospitalizations and medically attended visits. Bamlanivimab, bamlanivimab + etesevimab, and a combination of casirivimab + imdevimab are authorized for high-risk outpatients; recently the NIH endorsed combination therapies. MGB providers can assess eligibility for symptomatic high-risk outpatients through the table below and further access instructions are available at this link.

Inpatient monoclonal therapy use may be indicated for patients admitted for non-COVID-related reasons who develop COVID-19 symptoms and diagnosis as an inpatient (e.g. admitted for elective surgery or nosocomially acquired). For selected patients who do not qualify via EUA, specifically those with significant humoral immunity deficits such as those induced by anti-CD20 agents (eg rituximab), casivirimab + imdevimab may be obtained via a compassionate use mechanism. Please consult the inpatient ID service for potential use.

<table>
<thead>
<tr>
<th>EUA criteria for outpatients</th>
<th>Additional criteria for inpatients</th>
</tr>
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<tbody>
<tr>
<td>• Confirmed COVID-19 (by PCR or antigen testing)</td>
<td>Admitted for reason unrelated to COVID-19 with rationale documented</td>
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<tr>
<td>• Mild to moderate symptoms (cannot be asymptomatic)</td>
<td>• Oxygen saturation of ≥94% on room air for those without baseline hypoxemia, or at baseline for those with baseline hypoxemia</td>
</tr>
<tr>
<td>• Infusion must be completed within 10 days of symptom onset after the positive SARS-CoV-2 test is performed (for outpatients, this means referral must be placed no later than day 9 of symptoms)</td>
<td>• Documented approval by antibiotic stewardship team or ID consult</td>
</tr>
<tr>
<td>• Do NOT require oxygen therapy, or an increase of baseline oxygen flow rate, due to COVID-19</td>
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</tr>
<tr>
<td>• Have at least one of the following high-risk characteristics:</td>
<td></td>
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<tr>
<td>• Age ≥ 65 years</td>
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<tr>
<td>• Body mass index (BMI) ≥ 35</td>
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<tr>
<td>• Chronic kidney disease</td>
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<tr>
<td>• Diabetes</td>
<td></td>
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<tr>
<td>• Immunosuppressive disease</td>
<td></td>
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<tr>
<td>• Currently receiving immunosuppressive treatment</td>
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<tr>
<td>• Age ≥ 55 years and cardiovascular disease</td>
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<tr>
<td>• Age ≥ 55 years and hypertension</td>
<td></td>
</tr>
<tr>
<td>• Age ≥ 55 years and chronic obstructive pulmonary disease or other chronic lung disease</td>
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</tbody>
</table>

Note: Vaccination should be deferred for 90 days following administration of anti-spike mAbs.
Note on variants: Laboratory studies suggest that monoclonal antibodies have variable activity against worldwide circulating variant strains. Members of the ID Division and others are closely monitoring the prevalence of variants that may affect decisions regarding monoclonal antibodies.

*Intravenous immunoglobulin.* IVIG preparations would not be expected to have sufficient antibody titers against SARS-CoV-2 to offer effective passive immunity. Clinical trial data are not conclusive to promote routine use; may be considered for patients with IgG levels < 400.

*Convalescent plasma.* The EUA for convalescent plasma is based on possible benefit and specifically states that it is not the standard of care for COVID-19. At this time (March 2021), *convalescent plasma/sera/hyperimmune globulin* products are generally not available for off-label administration at MGH. A clinical trial is available. For patients with B cell immunity defects, prolonged illness and evidence of ongoing viral replication, convalescent plasma has been considered on a case-by-case basis with input from ID and approval from the Blood Bank (pager 21829).
**Remdesivir (RDV):** Remdesivir is FDA-approved for hospitalized adults and children (≥12 years and ≥40 Kg). RDV is currently available at MGH via the algorithm below. RDV is available under Emergency Use Authorization (EUA) for pediatric patients under 12 years old (≥3.5 kg) and pediatric patients under 40 kg.

Data regarding remdesivir include a large randomized control trial showing efficacy in reducing duration of hospital stay and a trend toward mortality benefit and a larger open-label trial suggesting no mortality benefit. Data for moderate disease are available from a large open-label RCT indicating a small benefit in improved clinical status at 11 days for the 5 day group compared to standard of care, but no benefit for the 10 day group.

**Under the MGB guidance, remdesivir may be given to:**
Patients hospitalized at an acute care facility or awaiting hospitalization in the emergency department with documented positive SARS-CoV-2 PCR AND one of the following criteria:

- SpO2 ≤ 94% on room air, requiring supplemental oxygen, or mechanical ventilation OR
- COVID-19 is a primary contributor to current hospitalization OR
- Patient is at high risk for clinical deterioration due to severe immunocompromise, recent major surgery, or severe pre-existing cardiopulmonary disease

Remdesivir should not be initiated or should be stopped if ALT is ≥ 10x ULN. For patients with eGFR < 30 ml/min, remdesivir may be considered on an individual basis considering risk/benefit with input from infectious diseases and nephrology and a clinical trial is currently open at MGH. Treatment of moderate COVID-19 with remdesivir may be considered on a case-by-case basis but should not be done routinely. Definitions of moderate, severe, or critical COVID-19 are found earlier in the document at this link. **Patients must have ALT, eGFR and PT assessed prior to infusion.**

To discuss new starts of remdesivir: 1) check eligibility above; then 2) please contact Infectious Diseases via the antibiotic approval pager. See detailed checklist below. Remdesivir is a restricted antimicrobial that may be started overnight without approval; approval will be required to continue its use the following day. **Given different antiviral mechanisms of action, remdesivir may be used in settings of prior or concurrent monoclonal antibody administration, unless prohibited by a clinical trial.**
Dexamethasone is recommended for hospitalized patients with severe COVID-19 who require supplementary oxygen. Systemic corticosteroids should be avoided for patients with mild or moderate disease (no oxygen support) unless there is another indication.

A report from the RECOVERY RCT in the UK indicates survival benefit of low dose dexamethasone for patients with severe or critical COVID-19, but no benefit in those not requiring oxygen support. Specifically, the mortality benefit was greater in a pre-specified subgroup of patients receiving mechanical ventilation (RR 0.64) than in those on supplemental oxygen (RR 0.82), with a non-statistically significant trend towards harm in those not on oxygen (RR 1.19). Notably the group on supplemental oxygen in RECOVERY was heterogeneous, and whether there is equal benefit for those patients on a low-level of oxygen compared to high levels is uncertain.

Notes for use at MGH:

- Given no benefit in those who are off oxygen, whether an oxygen requirement is new from a baseline requirement or due to other causes should be considered in the decision to start dexamethasone. Also, subgroup analysis suggests less benefit if administered ≤7 days after symptom onset.
- Both PO and IV formulations of dexamethasone are currently in stock at MGH. Alternatives to dexamethasone include:
  - Hydrocortisone IV 50mg q8hrs (or q6h for refractory shock co-indication)
  - Methylprednisolone IV 30mg daily
  - Prednisone PO 40mg qd
- Dexamethasone has no mineralocorticoid effect, unlike the above alternatives
- No data are available for the combination of dexamethasone and remdesivir at this time.
- Dexamethasone is a moderate CYP3A4 inducer; review of potential drug-drug interactions is recommended before initiation. Coadministration with remdesivir is allowable.
- Dexamethasone has fetal effects; please refer to pregnancy section for specific guidance.
- Please refer to the MGH critical care guidelines, once updated, for more specific guidance in this population. See FLARE on the RECOVERY trial.
- Contraindications to dexamethasone use include previous hypersensitivity and uncontrolled fungal infection.
- Close monitoring for hyperglycemia is recommended, particularly in a person with diabetes mellitus.
- Duration is 10 days or until discharge, whichever comes first. There are no data supporting use beyond 10 days for COVID-19 treatment even if the patient is not improving.
- With at-risk patients, consider adrenal insufficiency after discontinuation.

Corticosteroid administration is associated with reactivation of latent infections. Please check section for further guidance regarding HBV, Strongyloides, and tuberculosis. Routine prophylaxis for herpesviruses and Pneumocystis is not recommended at this time.
Modulating Host Immunity (tocilizumab, sarilumab, baricitinib)

Hyperinflammation is a hallmark of severe and worsening COVID-19. Dexamethasone is recommended for severe or critical COVID-19 (see above section).

**Tocilizumab 8 mg/kg (maximum dose 800 mg) may be considered on a case-by-case basis for patients with COVID-19 progressing on dexamethasone, oxygen ≤92% RA and/or on escalating oxygen requirements and CRP ≥ 75 mg/L.**

- Earlier trials of IL-6R blockade with sarilumab or tocilizumab were negative for mortality benefit but were conducted before dexamethasone’s efficacy was established and were generally underpowered. Results from the open-label REMAP-CAP and RECOVERY adaptive platform trials indicate mortality benefit of tocilizumab with dexamethasone for certain populations, including those admitted to the ICU within 24 hours and a select group of worsening patients with escalating oxygen requirements.
- For patients admitted to ICU settings, please refer to critical care guidelines.
- For patients with progressive COVID-19 in floor settings, the RECOVERY trial showed mortality benefit and a lower rate of mechanical ventilation associated with receipt of tocilizumab. However, it is difficult to identify the precise subset of patients who were randomized into the tocilizumab arm of RECOVERY.
- To be eligible for tocilizumab in floor settings at MGH,
  - Escalating oxygen requirements may be defined as rapid increase of 6L/min or more in <24 hours or a 10L/min or more requirement, or escalating beyond nasal cannula
  - The patient must already be on dexamethasone;
  - The patient’s respiratory status must be due to progressive COVID-19 and not due to other causes (such as bacterial or fungal superinfection, fluid overload, pulmonary embolism, or asthma exacerbation);
  - The patient should not have an uncontrolled and serious non-COVID-19 infection;
  - The patient’s labs must demonstrate a contemporaneous CRP level ≥ 75 mg/L.
  - If the patient does not meet all of these criteria, defer seeking tocilizumab.

**Caution should be applied for immunocompromised patients, uncontrolled viral, bacterial, or fungal infection, ALT/AST > 5x ULN, ANC < 1000 cells/mm³, platelets < 50K, those at high risk for intestinal perforation. Prior hypersensitivity to tocilizumab is a contraindication.**

- Tocilizumab may be approved by the critical care consult (pager 26955), who will assist the primary team in assessing and managing respiratory compensation and eligibility for tocilizumab.
- Generally, the medical senior on for the house (pager 22337) should be contacted about tocilizumab eligible patients on the floors as they are at risk for eventual transfer.
- Once authorized, the primary team should document discussion of the risk/benefit with the patient and/or proxy and assent in the record. Sample language: “Tocilizumab is not FDA
approved for treatment of COVID-19 but may have benefit when used with dexamethasone. The patient and/or proxy have assented to administration after discussion of risk/benefits.”

- Tocilizumab dosing is weight-based. Weight >90 kg = 800 mg; >65 to 90 kg = 600 mg; >40 to 65 kg = 400 mg; ≤40 kg = 8 mg/kg
- Repeat doses of tocilizumab are not recommended at this time.
- Data for sarilumab are less robust and thus sarilumab is not recommended.
- Cases of strongyloides reactivation were associated with dexamethasone and tocilizumab; please ensure that ivermectin is administered for patients from endemic areas (see below).

Other immunomodulatory agents

- Baricitinib. In the ACTT-2 trial, a benefit of the Janus kinase inhibitor baricitinib when added to remdesivir is suggested, but there are not enough data to recommend its use.
  - This trial was performed largely before dexamethasone was widely used for the treatment of COVID-19. It is unknown whether baricitinib has equivalent benefit as dexamethasone, or whether there is additive benefit, or, conversely, toxicity when used in combination.
  - In a patient who requires supplemental oxygen (but is not ventilated), and in whom corticosteroids are contraindicated, baricitinib in combination with remdesivir may be considered. Note: hyperglycemia and delirium are NOT absolute contraindications to corticosteroids.
- For additional immunomodulatory therapies we strongly prefer that the team refer the patient to a clinical trial, if available. See link for details.
- Corticosteroids, IVIG and/or anakinra may be considered for adults who present with multisystem inflammatory syndrome (MIS-A). For MIS-C, refer to pediatric guidance.
- Decisions regarding off-label use of immunomodulatory agents should be made with agreement of both the primary and recommending teams.
Medication considerations:

Anti-infectives

Do not start empiric antibiotics if COVID-19 confirmed or high likelihood
Consider antibiotics only if CXR displays lobar infiltrate and/or ICU admission
Sputum GS & Culture & Legionella urinary antigen
ceftaxone 1 gm IV QD + doxycycline 100 mg PO BID
If ICU/sepsis, consider MRSA / MDRO coverage

- **Routine empiric antibiotics are not recommended.** MGH has detected low rates of bacterial superinfection in COVID-19 patients, consistent with studies from other centers. Unnecessary antibiotic use increases risks of multi-drug resistant organisms and C. difficile.

- If empiric antibiotics are given, recommend:
  - Ceftriaxone 1 gm IV daily + either doxycycline 100 mg PO BID x 5 days or azithromycin 500 mg PO x 1 then 250 mg PO daily for 4 days.
  - For nonpregnant patients, doxycycline is preferred over azithromycin.
  - Azithromycin is preferred for pregnant women and patients unable to be upright for 30m to prevent pill esophagitis related to doxycycline.
  - Azithromycin is not proven as a treatment for COVID-19 and should be given only if there is another indication.
  - If antibiotics started, maximum duration is 5 days. May discontinue if concern for bacterial pneumonia low (confirmed COVID-19, classic presentation, PCT<0.2)

- **Regularly reassess need for ongoing antibiotics.** For all patients with suspected bacterial pneumonia on empiric antibiotics, reassess for clinical improvement at 48-72h as well as risk factors for MDROs. For guidance on risk factors for MRSA/MRDO and for antibiotic de-escalation after 48-72h of empiric broad spectrum antibiotics in suspected hospital-acquired or ventilator-associated pneumonia, please check link to algorithm.

- Due to low rates of influenza coinfection at MGH, we do not currently recommend starting oseltamivir on most patients with COVID-19.

Cardiovascular medications

**ACE-Inhibitors (ACEi) / Angiotensin Receptor Blockers (ARBs):**

- **Continue ACEi/ARBs if already prescribed.** Note there is interest in the potential role of ACE-inhibitors (ACEi) / angiotensin receptor blockers (ARBs) in the pathophysiology of this disease since the SARS-CoV-2 virus binds to the ACE2 receptor for cellular entry. Current data do not support stopping ACEi/ARBs on patients with COVID-19.

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7 If a known flu contact or high suspicion for flu, request approval for testing and start oseltamivir 75 mg BID in adult patients with normal renal function. Adjust for renal insufficiency. Stop oseltamivir if testing is negative.

8 Lopes et al. JAMA 2021
However, if acute kidney injury, hypotension or other contraindication develops, we recommend stopping them at that time. After a person is recovering from their viral syndrome, their home medications can be restarted, and new ACEi/ARBs can be started if they have a primary indication such as new persistently reduced ejection fraction.

**Statins:**

- **Continue statins if already prescribed.** Cardiovascular disease is a major risk factor for COVID-19 disease severity. Additionally, statins may help promote antiviral innate immune response. For a brief discussion of statins and COVID-19, see our [statin rationale document](#).
- Several retrospective studies suggest that baseline statin use is associated with better hospital outcomes but randomized controlled trial data regarding new initiation of statins are not available. For those who have a guideline indication for a statin and no contraindication, consider starting atorvastatin 40 mg daily. When major drug-drug interactions with atorvastatin are expected, pitavastatin 4 mg daily (or pravastatin 80mg daily if pitavastatin not available) are alternatives. If already on a statin, no need to change to these agents. If elevated CPK >/= 500 U/L or if ALT > 3x upper limit of normal, consider not starting a statin. Monitor CPK daily if on both statin and azithromycin.

**Antithrombotic medications:**

- All patients should be routinely placed on routine standard LMWH prophylaxis, with the exception of pregnant women ≥ 20 weeks gestation who should receive unfractionated heparin. Please see link for further guidance from MGH Hematology

**Other medications:**

- NSAIDs. See [FDA statement on NSAIDs](#) dated 3/19/20. Acetaminophen is the suggested first-line anti-pyretic. If NSAIDs are used, lowest effective dose is suggested.
- **Inhaled medications should be given by metered dose inhaler rather than nebulization.** If nebulized medications are given, patients need to have a recent negative COVID test (within 3 days), given the risk of aerosolizing the virus with nebulizers (see [MGB Policy](#)). For those without pre-existing pulmonary disease, the risk/benefit of inhaled steroids for inpatients remains unknown; a randomized study of inhaled budesonide suggests benefit for outpatients.
- **Systemic corticosteroids.** See discussion under COVID-19 specific management in the next section regarding dexamethasone, which is recommended for patients on oxygen support but avoided for patients with mild or moderate disease (no oxygen support). Corticosteroids may be considered if indicated for another reason (e.g. refractory septic shock, multisystem inflammatory syndrome, pregnancy for fetal benefit, or specific to [lung transplant guidelines](#), as delineated below). For those prescribed long-term corticosteroids, discuss with prescribing physician the management of the underlying condition and whether / how to continue corticosteroids while hospitalized.

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9 Links to observational studies regarding statins: [Hubei Province](#), [The Bronx](#), [Manhattan, Illinois](#), [California](#).
**Suggested Treatment Algorithm Based on Clinical Severity:**

(See [figure](#) at end of document for schematic layout of algorithm)

**Table 3:**

<table>
<thead>
<tr>
<th>Clinical Situation</th>
<th>Recommendation</th>
<th>Notes / Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>All hospitalized patients</td>
<td>All patients should receive standard prophylactic anticoagulation with LMWH in the absence of any contraindications[10]</td>
<td>For pregnant patients ≥ 20 weeks gestation, UFH is preferred to LMWH.</td>
</tr>
<tr>
<td>For patients with mild or moderate disease</td>
<td>Supportive care with close monitoring.</td>
<td>See Table 2 for list of risk factors</td>
</tr>
<tr>
<td>Mild disease is defined as mild symptoms (e.g. fever, cough, change in taste or smell, no dyspnea).</td>
<td><strong>Dexamethasone:</strong> Do not start dexamethasone unless the patient progresses to oxygen requirement (severe disease) or has an alternate indication for corticosteroids</td>
<td>A trend towards harm was seen in the sub-group of patients with the RECOVERY trial who were not on oxygen</td>
</tr>
<tr>
<td>Moderate disease is defined as clinical or radiographic evidence of lower respiratory tract disease; oxygen saturation &gt;94% on RA</td>
<td><strong>Remdesivir:</strong> Remdesivir is not routinely recommended in this patient population at this time; consider on a case-by-case basis in people at high risk of clinical deterioration.</td>
<td>Remdesivir may have efficacy in moderate disease.</td>
</tr>
<tr>
<td></td>
<td>Application for a clinical trial. Please check <a href="#">link</a> for basics of clinical trial inclusion and exclusion criteria.</td>
<td>A Spanish language video regarding clinical trials for patients and families is found at this <a href="#">link</a>.</td>
</tr>
<tr>
<td></td>
<td><strong>Monoclonal antibody through EUA or compassionate use:</strong> These may be sought for select situations, eg patients who were hospitalized for non-COVID-19 reasons or acquired COVID-19 nosocomially, or for</td>
<td></td>
</tr>
</tbody>
</table>

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[10] Contraindications include active bleeding or platelet count less than 25,000; monitoring advised in severe renal impairment; abnormal PT or APTT is not a contraindication. If LMWH contraindicated due to renal failure (Creatinine Clearance <30mL/min), UFH can be used as an alternative. For clarifications, contact Rachel Rosovsky from Hematology, pager 37021.
For patients with severe* or critical disease

Severe disease is defined as SpO2 ≤ 94% on room air, a ratio of arterial partial pressure of oxygen to fraction of inspired oxygen (PaO2/FiO2) <300 mmHg, respiratory frequency >30 breaths per minute, or lung infiltrates >50%

*For patients who are hypoxemic (SpO2 ≤ 94% on room air) but are at their baseline or who are hypoxemic due to other causes (such as volume overload), consider whether they should be classified as

<table>
<thead>
<tr>
<th>Compassionate use patients with severely compromised humoral immunity. Consult or curbside ID to discuss.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Remdesivir (RDV) is FDA approved for COVID-19 as of October 22, 2020 for adults and children ≥12 years of age and at least 40 Kg. MGB remdesivir policy is at this link.</td>
</tr>
<tr>
<td>1. Check eligibility and confirm eligible under MGB Guidance</td>
</tr>
<tr>
<td>2. Ensure PT, ALT, and eGFR are measured</td>
</tr>
<tr>
<td>3. Contact ID Approval pager 21884 to discuss candidacy and availability</td>
</tr>
<tr>
<td>4. If approved by ID, order via order panel.</td>
</tr>
<tr>
<td>5. Dosing of remdesivir is 200 mg IV loading dose following by 100 mg IV daily for a maximum of 5 days; extension to 10 days may be considered in certain patients, please consult ID to discuss.</td>
</tr>
<tr>
<td>6. Monitor ALT and eGFR daily, discuss with ID if eGFR&lt; 30 ml/min, discontinue RDV if ALT ≥ 10x ULN</td>
</tr>
</tbody>
</table>

RDV may be available through the clinical trial ACCT.

Key links regarding remdesivir:
- [Partners / MGB Remdesivir Guidance](#)
- [Info for providers](#)
- [Info for patients/families](#)
- [English](#) or [Spanish](#)
- [Educational slide set](#)

Assess for [drug–drug interactions](#) before starting.

Discontinue remdesivir upon discharge regardless of duration.
**Dexamethasone** at a dose of 6 mg PO / IV daily for up to 10 days is recommended for patients with an oxygen requirement and/or requiring mechanical ventilation.

Greater benefit was observed for patients requiring mechanical ventilation compared to those receiving oxygen and for those with >7 days of symptoms. Refer to critical care guidelines for patients in ICU.

**Tocilizumab** at a single dose (weight >90 kg = 800 mg; >65 to 90 kg = 600 mg; >40 to 65 kg = 400 mg; ≤40 kg = 8 mg/kg) may be considered for patients with rapid progression of COVID-19 and CRP ≥75 mg/L already on dexamethasone. Rapid progression may be defined as >6L/min change in oxygen requirement over 24 hours or 10 or more L by nasal cannula, or use of high-flow oxygen.

The patient’s respiratory status must be due to progressive COVID-19 and not due to other causes (such as bacterial or fungal superinfection, fluid overload, pulmonary embolism, or asthma exacerbation).

**Assess for** [drug-drug interactions](#) before starting. Dexamethasone has fetal effects; please refer to [pregnancy section](#) for specific guidance.

Candidates for corticosteroids / immunomodulation with risk for endemic infections, click [here](#).

Discontinue dexamethasone upon discharge regardless of duration, unless previously used as maintenance medications for another indication or continuation required as part of a clinical protocol/trial.

**Tocilizumab** may be considered in the ICU setting per Critical Care guidance. For selected floor patients (see above), tocilizumab may be approved after review by the critical care consult service (pg26955). Medical senior should generally be contacted as this population would overlap with those at risk for transfer.

Before administration, please document that a risk / benefit discussion was performed with the patient and/or proxy. Benefit is potential improvement in mortality; risks include bacterial or fungal superinfection, hepatitis, neutropenia, intestinal perforation.
<table>
<thead>
<tr>
<th>Application for a clinical trial. Please check <a href="#">link</a> for basics of clinical trial inclusion and exclusion criteria.</th>
<th>A Spanish language video regarding clinical trials for patients and families is found at this <a href="#">link</a>.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>For patients with evidence of secondary hemophagocytic lymphohistiocytosis (sHLH)</strong></td>
<td>With ID input, <strong>anakinra</strong> (Kineret) can be considered</td>
</tr>
<tr>
<td><strong>For patients with evidence of multisystem inflammatory syndrome</strong></td>
<td>Consult infectious diseases, consider rheumatology consult. Corticosteroids, IVIG and/or anakinra can be considered</td>
</tr>
<tr>
<td><strong>Not recommended</strong></td>
<td>Current case definition includes persons &lt;21 years of age but may occur at older ages.</td>
</tr>
<tr>
<td><strong>Baricitinib</strong> should not be routinely used as data are lacking regarding whether it may be beneficial when used instead of or in combination with dexamethasone. <strong>Hydroxychloroquine</strong> (HCQ) should not be initiated. Chloroquine has safety concerns and should not be used. Neither <strong>azithromycin</strong> nor <strong>ivermectin</strong> are proven treatments for COVID-19. Only use azithromycin or ivermectin for other indications. Ribavirin, lopinavir/ritonavir, sarilumab are not recommended</td>
<td>In a patient who requires supplemental oxygen (but is not ventilated), and in whom corticosteroids are contraindicated, baricitinib in combination with remdesivir may be considered. Note: hyperglycemia and/or delirium are not absolute contraindications. Chloroquine antagonizes remdesivir in vitro against RSV. Chloroquine and HCQ should not be co-administered with remdesivir.</td>
</tr>
</tbody>
</table>
Table 4: Special Populations

<table>
<thead>
<tr>
<th>Special Population</th>
<th>Recommendation</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pregnancy and postpartum</td>
<td>Protocols for treating non-pregnant women should be followed, unless there is an intervention specifically excluded by pregnancy.</td>
<td>Physiology late in pregnancy and postpartum may potentially place women at risk for more rapid deterioration.</td>
</tr>
<tr>
<td>Link to COVID-19 L+D antepartum/MFM management</td>
<td>Multidisciplinary evaluation should include obstetric, infectious disease and critical care providers. Obstetricians, working with this team, will consider when in the context of a woman’s health status, fetal well-being and gestational age, delivery should be undertaken.</td>
<td>Treating recommendations for pregnant women should be discussed with Maternal-Fetal Medicine.</td>
</tr>
</tbody>
</table>
For a patient meeting criteria for steroids due to increased risk for preterm birth and due to COVID (usually weeks 24-<34)

- Dexamethasone 6mg IM q12h x 4 doses (When used for both indications, the higher dose required for fetal benefit should be used in the first 48 hours)
- After the initial 48 hours of dexamethasone, patients can be switched to hydrocortisone, methylprednisolone, or prednisone to reduce fetal exposure for the remainder of the 10-day course.

For a patient meeting criteria for steroids for COVID who do not require corticosteroids for fetal benefit (generally < week 24 or ≥ week 34)

- Recommend hydrocortisone, methylprednisolone, or prednisone to minimize fetal effects.

For breastfeeding women: Recommend hydrocortisone, methylprednisolone, or prednisone due to limited evidence regarding dexamethasone and breastfeeding.

Extended exposure to dexamethasone has known adverse fetal effects. Different steroid dosing regimens can be designed to balance maximizing maternal COVID recovery, maximizing fetal benefit in the setting of possible preterm delivery, and minimizing unnecessary fetal exposures. See corticosteroid section for alternative regimens (hydrocortisone, prednisone or methylprednisolone).

Remdesivir is available to pregnant persons as for non-pregnant persons.
Nitric oxide therapy may be considered. Clinical guidelines are available at this link.

Compassionate use remdesivir is no longer available.
Adjunctive medications:
For DVT prophylaxis, pregnant women ≥ 20 weeks gestation should receive unfractionated heparin rather than LMWH.

If antibiotics given for concern of bacterial pneumonia, azithromycin is preferred to doxycycline.

On a case-by-case basis, may discuss statin use with the MFM service.

See MGH hematology guidelines
Azithromycin has better safety data in pregnancy compared to doxycycline
Limited data on tocilizumab

<table>
<thead>
<tr>
<th>Patients who are foreign-born from resource-limited countries (at risk for reactivation of tuberculosis or Strongyloides)</th>
<th>If receiving steroids or immunotherapy AND if no prior history of latent or active TB, please send T-Spot. Click here for further management advice.</th>
<th>For Strongyloides, treat empirically with ivermectin for those receiving steroids and/or immunomodulation.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients who are experiencing homelessness, history of incarceration (at risk for tuberculosis reactivation)</td>
<td>If receiving steroids or immunotherapy AND if no prior history of latent or active TB, please send T-Spot and see below for further management advice.</td>
<td></td>
</tr>
<tr>
<td>Patients with underlying lung disease (including asthma or COPD of any severity, ILD, etc. Additional guidance for lung transplantation below)</td>
<td>Do not stop or change chronic pulmonary-related medications for any PUI or COVID+ patient with underlying lung disease unless for a non-COVID reason.</td>
<td>Discontinuation of medications such as inhaled steroids may precipitate exacerbation of underlying lung disease. For inhaled corticosteroids, please discuss the risk / benefit of discontinuing this medication with Pulmonary.</td>
</tr>
<tr>
<td>Patients with myasthenia gravis</td>
<td>Please contact outpatient neurologist or consult inpatient Neurology for any PUI or COVID+ patients with myasthenia gravis</td>
<td>Avoid azithromycin and HCQ in patients with myasthenia gravis; discuss risk / benefit of COVID-19 related medications with Neurology</td>
</tr>
<tr>
<td>People living with HIV</td>
<td><strong>Please call/consult Infectious Diseases.</strong> HIV with CD4 count &lt;200 is a risk factor for complications of other respiratory infections. Additional caution in this group is warranted. Because people with HIV may also have other conditions (lung disease, smoking) or vulnerabilities, they may be at higher risk for complications regardless of CD4 cell count.</td>
<td><strong>Resource for crushing HIV-medications</strong>&lt;br&gt;<strong>medications for intubated patients</strong>&lt;br&gt;<strong>Resource for ARV drug-drug interactions</strong></td>
</tr>
<tr>
<td>---</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>If IgG &lt;400</td>
<td>Consider IVIG at dose of 25 grams x1 (unclear benefit)</td>
<td>Note: Titers against SARS-CoV-2 are likely to be low in commercial IVIG</td>
</tr>
<tr>
<td>For patients on biologic medications, disease-modifying anti-rheumatic drugs DMARDs, neurologic disease modifying therapies (DMTs) and other non-transplant immunosuppressive medications</td>
<td><strong>Please contact the primary prescribing provider about management of the underlying condition and medications</strong>&lt;br&gt;Do not abruptly stop prednisone for patients who are on long term prednisone; consider taper.</td>
<td>If the primary prescribing physician is unavailable, please contact the respective inpatient consult team&lt;br&gt;Abrupt cessation may precipitate a flare of underlying conditions</td>
</tr>
<tr>
<td>Heart/Liver/Kidney Transplant Recipients</td>
<td><strong>Guided by transplant and transplant ID teams – please call/consult</strong>&lt;br&gt;Consider decreasing tacrolimus/cyclosporine by 50%, stop mycophenolate (CellCept/Myfortic) and Azathioprine in kidney/liver transplant patients and reduce dose by 50% in heart transplant patients. Kidney patients approximate target tacrol level 3.5 ng/ml, cyclosporine level target 25-50 ng/ml.</td>
<td>Screen for drug-drug interactions with anti-viral agents, if they are being used</td>
</tr>
</tbody>
</table>
In the setting of ground glass opacities can consider switching mTor to CNI (tacrolimus) given possibility of pneumonitis w/ mTor; discuss with heart transplant before making switch

Critical illness – in liver and kidney – stop all immunosuppression except for prednisone if they are on it at baseline

For outpatients on belatacept, consider switching to tacrolimus or cyclosporine starting 28 days after last dose, to avoid clinic visit. Levels will need to be checked and thus institute plan to draw them without exposing community.

For inpatients on belatacept, do not administer any further belatacept. 28 days after last dose, consider adding low dose CNI. For CNI intolerant, consider increasing daily prednisone dose from 5 mg to 7.5-10 mg daily.

Continue low dose prednisone (5 mg) in all patients who were on it before hospitalization for mild or moderate COVID-19; for severe COVID-19, consider dexamethasone and/or remdesivir.

Request bronchoscopy only if significant decompensation, versus lung biopsy as may be lower risk for aerosolization and exposure to staff.
| Lung transplant recipients | **Guided by transplant and transplant ID teams - please call/consult.** Immunosuppression requires case-by-case approach. | Screen for [drug-drug interactions](#) with anti-viral agents, if they are being used |
### Table 5: Brief Overview of Agents Discussed

Note listing below does not indicate endorsement for use. For a more detailed overview of trials at MGH, please refer to the [Apollo Clinical Trials page](#).

<table>
<thead>
<tr>
<th>Agent (link to package insert)</th>
<th>Classification</th>
<th>Target / Mechanism</th>
<th>Dosing</th>
<th>Key toxicities</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Antivirals</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>remdesivir</td>
<td>FDA-approved for adults and children 12 years of age and older and ≥ 40 Kg</td>
<td>RNA dependent RNA polymerase inhibitor</td>
<td>200 mg IV x1, then 100 mg IV daily, 5 days for most patients</td>
<td>Nausea, vomiting, ALT elevations</td>
</tr>
<tr>
<td>bamlanivimab + etesevimab</td>
<td>Investigational, emergency use authorization (high-risk outpatients)</td>
<td>Anti-spike antibodies</td>
<td>700 mg IV (BAM) 1400 mg IV (ETE)</td>
<td>Hypersensitivity reactions (rare)</td>
</tr>
<tr>
<td>casirivimab + imdevimab</td>
<td>Investigational, Emergency use authorization (high-risk outpatients)</td>
<td>Anti-spike antibodies</td>
<td>1200 mg IV (CAS) 1200 mg IV (IMD)</td>
<td>Hypersensitivity reactions (rare)</td>
</tr>
<tr>
<td>Inhaled nitric oxide</td>
<td>Off-label, investigational</td>
<td>Vasodilator, <em>in vitro</em> virucidal properties</td>
<td>Variable</td>
<td>Methemoglobinemia</td>
</tr>
</tbody>
</table>

### Immune modulators:

<table>
<thead>
<tr>
<th>Agent (Decadron)</th>
<th>Classification</th>
<th>Target / Mechanism</th>
<th>Dosing</th>
<th>Key toxicities</th>
</tr>
</thead>
<tbody>
<tr>
<td>dexamethasone</td>
<td>Off-label</td>
<td>Corticosteroid</td>
<td>6 mg PO/IV once daily for up to 10 days</td>
<td>Hyperglycemia, Avascular necrosis (rare), Reactivation of latent infections</td>
</tr>
<tr>
<td>tocilizumab</td>
<td>Off-label, investigational</td>
<td>Monoclonal antibody to IL6 receptor</td>
<td>Dosing by weight: &gt;90 kg = 800 mg; &gt;65 to 90 kg = 600 mg; &gt;40 to 65 kg = 400 mg; ≤40 kg = 8 mg/kg</td>
<td>ALT elevations; decline in neutrophils, bowel perforation if history of diverticulitis</td>
</tr>
<tr>
<td>sarilumab</td>
<td>Off-label, investigational</td>
<td>Monoclonal antibody to IL-6 receptor</td>
<td>Dosing for COVID/CRS to be determined</td>
<td>ALT elevations; decline in neutrophils, bowel perforation if history of diverticulitis</td>
</tr>
<tr>
<td>Drug Name</td>
<td>Status</td>
<td>Type</td>
<td>Dosage/Protocol</td>
<td>Side Effects</td>
</tr>
<tr>
<td>---------------------------</td>
<td>-------------------------------</td>
<td>-------------------------------</td>
<td>--------------------------------------------------------------------------------</td>
<td>--------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>ruxolitinib (Jakafi)</td>
<td>Investigational</td>
<td>Janus kinase inhibitor</td>
<td>10 mg BID for 14 days, possible extension to 28 days</td>
<td>Cytopenias, ALT elevations, increased infection risk including herpesvirus reactivation</td>
</tr>
<tr>
<td>baricitinib (Olumiant)</td>
<td>Investigational, emergency use authorization</td>
<td>Janus kinase inhibitor</td>
<td>Per research protocol</td>
<td>Cytopenias, ALT elevations, increased infection risk including herpesvirus reactivation, venous/arterial thrombosis</td>
</tr>
<tr>
<td>anakinra (Kineret)</td>
<td>Off-label</td>
<td>IL-1 receptor antagonist</td>
<td>Dosing for COVID/CRS to be determined</td>
<td>Injection site reactions, decline in neutrophils</td>
</tr>
</tbody>
</table>

### Selected Adjunctive Medications

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Status</th>
<th>Type</th>
<th>Dosage/Protocol</th>
<th>Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>atorvastatin (Lipitor)</td>
<td>Off-label</td>
<td>Cardioprotection; immunomodulatory</td>
<td>40-80 mg PO daily</td>
<td>Avoid if using LPV/r</td>
</tr>
<tr>
<td>pravastatin (Pravachol)</td>
<td>Off-label</td>
<td>Cardioprotection; immunomodulatory</td>
<td>80 mg PO daily</td>
<td></td>
</tr>
<tr>
<td>ivermectin (Stromectol)</td>
<td>FDA-approved</td>
<td>Treatment of Strongyloidias Not recommended for COVID-19</td>
<td>200 mcg/kg rounded to the nearest 3 mg x 1 (as tablets are 3 mg each), then repeat dose next day</td>
<td>Caution with those from filarial endemic areas (West or Central Africa) Maximum dose is 21 mg</td>
</tr>
</tbody>
</table>

Infections, Steroids & Immunomodulation

Immunomodulation may be associated with increased risk of infections. Corticosteroids as part of the armamentarium of treatments for Covid-19 should be used according to the criteria used in the RECOVERY trial. Subspecialty consultation may be required when utilizing steroids for other indications. It is unknown whether data from longer term exposure from steroids or other immunomodulators can be extrapolated to the shorter term use associated with COVID-19.

Reactivation of viruses such as hepatitis B virus (HBV) or herpesviruses (HSV, CMV, VZV) may occur in patients receiving steroids or immunomodulation. Also, parasites such as Strongyloides and intracellular pathogens such as M. tuberculosis may activate years to decades after leaving countries with higher prevalence of these infections. COVID-19 related Strongyloides hyperinfection has been reported.

Screen for HBV: All patients with COVID-19 should be screened for active HBV with HBsAg regardless of country of origin. Contact ID or hepatology for guidance if receiving steroids/immunomodulatory therapy.

Empirically Treat Strongyloides: We favor empiric treatment in patients who are foreign-born (resource-limited settings) with ivermectin prior to steroids/immunotherapy rather than checking serology due to long turnaround times. Ivermectin is safe and recommended treatment is 1 dose of 200 ug/kg rounded to nearest 3 mg increment PO x 1 (maximum dose 21 mg), then repeat the same dose a day later.

If a patient is West or Central African, do not give empiric ivermectin due to the potential rare complication of larval migration with certain filarial nematodes. Screen the patient with a microfilarial smear (order as a miscellaneous micro test, 2 large purple top tubes) to exclude concomitant high-titer filarial nematodes. If questions, contact Infectious Diseases.

Note there is a report of in vitro inhibition of SARS-CoV-2 by ivermectin. It would require 50-100x standard dosing to achieve in vivo concentrations necessary to inhibit SARS-CoV-2. Ivermectin is therefore not recommended for COVID-19.

Consider Tuberculosis: For patients who are foreign-born from resource-limited countries or for patients who are experiencing homelessness or have a history of incarceration, if there is no history of prior active TB disease or infection, we favor checking a T-spot prior to starting immunotherapy. Proceed with immunomodulation while that result is pending. Thus far, there are scant data but no indication that TB reactivation occurs more frequently during COVID-19 illness. If there are concerns for development of active TB disease during a hospital admission, please contact ID for further guidance.

If a patient at risk is considering or has started steroids or off-label immunomodulatory agent, or the patient is entering into a clinical trial of an immunomodulatory agent, please click here for a flowsheet that has more details and guidance. Apply algorithm even if the patient may be receiving a placebo.
When should I consult Infectious Diseases?

At MGH, Infectious Disease consultation is not necessary for most hospitalized patients with COVID-19.

All infection control issues should be referred to this page, which contains a comprehensive guide to CORAL (resolution of COVID-19 status), FAQs, and Whom to Call. Calls to the ID consult pager will be directly referred to this resource.

https://apollo.massgeneral.org/coronavirus/clinicians/infection-control/

Before paging / consulting, please examine relevant sections of this document before consulting ID. Reasons to contact ID for either advice or consultation for COVID-19 patients include:

- Hospital-associated infections for which ID evaluation would be helpful (e.g. VAP, HAP)
- Uncertainty whether an individual requires RDV (e.g. alternate explanation for hypoxemia)
- Relative contraindication to RDV when indicated (e.g. reduced eGFR)
- Pregnancy
- Concern for Multisystem Inflammatory Syndrome in Adults (MIS-A)
- New HIV infection
- Positive HBSAg and/or TB screening and candidate for dexamethasone / other immunomodulation (please read above section and consult algorithm before contacting)
- Concern for re-infection (documented positive test > 90 days prior to the current presentation with a compatible syndrome)
- Concern that persistent PCR positivity may represent prolonged illness in an immunocompromised patient
- Management of COVID-19 associated pulmonary aspergillus (CAPA)
- **For patients with impaired B cell immunity, consideration of monoclonal antibody or convalescent plasma**