

UCLA Infectious Disease COVID-19 Team Clinical Guidance

Contact Information:

Please page the service specific pager. All patients who have had a transplant must be evaluated by the transplant ID team. For isolation precautions, please contact the Infection Control pager 94040

Pharmacy support

Infectious Disease Pharmacists: Ethan Smith, Meganne Kanatani, Christine Pham, Lynn Chan Clinical Trials Pharmacists: Christina Shin

During after-hours/weekends --Kerry Menmuir, Director of Inpatient Pharmacy

General Approach to Treatment of Patients with COVID-19

Remdesivir is the 1st line agent for all patients with a SpO2 <94% who meet our eligibility criteria

Dexamethasone 6mg po/IV daily for up to 10 days is recommended for patients who require oxygen support, particularly those that are on high-flow nasal cannula or mechanically ventilated and should be considered for those with worsening hypoxia on any supplemental O2. Steroids are not recommended for patients who do not require supplemental oxygen.

JAK inhibitors (baricitinib, tofacitinib) and IL-6 inhibitors (tocilizumab, sarilumab) are recommended for patients with early, critical disease requiring high-flow nasal cannula or mechanical ventilation/ECMO with elevated/worsening inflammatory markers. See Section 3 below for specific criteria.

Please also see DHHS guidance at: https://www.covid19treatmentguidelines.nih.gov/whats-new/



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Section 1. Diagnostic Testing for Patients with Suspected or Confirmed COVID-19

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Table 1. Diagnostic Testing

Recommended daily labs (can be discontinued at primary team's discretion if no longer needed):	
• CBC with diff (trend total lymphocyte count) • CMP	Commented [PKK1]: I don't feel strongly but considering removing this, as I think that it has been well over a year since RT has done a mini-BAL for a suspected covid patient We are removing this option from the covid order set as a result
If clinically indicated: For acute kidney injury (i.e. serum creatinine >0.3 above baseline) urinalysis with microscopy spot urine protein:creatinine For cardiac disease/cardiomyopathy CK-MB CK Troponin-I BNP TTE if BNP elevated or other clinical concern EKG Continuous telemetry	
	If clinically indicated: For acute kidney injury (i.e. serum creatinine >0.3 above baseline) urinalysis with microscopy spot urine protein:creatinine For cardiac disease/cardiomyopathy CK-MB CK Troponin-I BNP TTE if BNP elevated or other clinical concern EKG Continuous telemetry 16



 Radiology

 Portable CXR at admission

 High threshold for PA/lateral in ambulatory patients, consider only if low suspicion for COVID-19 and result would change management or affect PUI status.

 Would NOT get CT Chest as part of routine diagnostic tests per American College of Radiology recommendations.

 Consider CTA PE protocol if concerned for pulmonary embolism

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Section 2. Treatment Guidance for COVID-19 Positive Patients NOTE: Supportive care is crucial for management of cases

Table 2. General Principles of Treatment

All COVID-19 Positive Patients

- Remdesivir should be considered for all symptomatic patients who meet the window (see eligibility)
- <u>Monitor high risk patients</u>: including those who are immunosuppressed and have had Lung Transplant/BMT/other SOT (<u>All transplant patients</u> <u>should get ID consult</u>)
- Screen for drug interaction via Liverpool chart
- Place all adult patients on pharmacologic VTE prophylaxis such as enoxaparin or heparin SC if no contraindications. Otherwise place on mechanical VTE prophylaxis such as TEDs/SCDs. (<u>American Society of Hematology</u>). Therapeutic heparin can be considered in select patients.

Outpatient care				
COVID+, clinically stable	 Advise patients on self-isolation per LACDPH guidelines: http://publichealth.lacounty.gov/acd/ncorona2019/covidisolation/ Oral therapies are available for high-risk patients at <u>select pharmacies and clinics in LA County</u> Dexamethasone or other steroids are not recommended for outpatient use See Outpatient Guidance for critieria and process to obtain outpatient remdesivir 			
Low risk – SpO2 >94% on room air	 If antibiotics are started, reassess need based on cultures/clinical condition Remdesivir can be used for mildly symptomatic high-risk patients with SpO2>94 if sx onset <a href="https://www.symptomaticscommutationscommut</th>			
Moderate risk, SpO2 <u><</u> 94% but stable	 Remdesivir if SpO2_94% if sx onset <10d, review eligibility criteria Consult ID for transplant patients for evaluation of treatment options 			
	Certain trials or compassionate use agents may be considered			
	 Dexamethasone is NOT recommended for patients who do not require supplemental oxygen. It is also not recommended if respiratory failure is due to a condition other than COVID-19 (pulmonary edema, aspiration pneumonia, etc). 			
	 Discontinue dexamethasone after 10 days or when patients no longer require supplemental oxygen, whichever is sooner 			
	Convalescent plasma can be considered in immunosuppressed patients			

Commented [PKK2]: I don't think that we are still doing convalescent plasma or monoclonal Ab trials for outpatients but I could be wrong

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Step-Down/ICU level care- Consult Infectious Diseases and Pulmonology			
Moderate-High Risk SpO2<94% on RA AND requiring increased supplemental O2 OR	 Consider Remdesivir, review eligibility criteria Dexamethasone 6mg po/IV daily for up to 10 days if progressive oxygen requirements and in particular mechanical ventilation unless contraindications. Please see Table 1 for additional screening considerations. 		
RR > 30 OR PaO2/FiO2 ≤ 300mmHg OR Mechanical ventilation	 Tocilizumab or baricitinib may be considered for select patients who are critically ill (ID consultation is needed-see guidance below) In the setting of drug shortages, tofacitnib and sarilumab may be considered Routine supportive care, including blood and respiratory cultures and antibiotics as clinically indicated 		
	If refractory hypotension, increased pressor requirement		
Please obtain blood cultures, sputum cultures and chest x-ray as needed Consider TTE Consider pulmonary embolism on differential, CTA PE protocol Empiric broad spectrum antibiotics as appropriate			

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Guidance regarding tocilizumab or baricitinib in combination with dexamethasone

Recent data have suggested that tocilizumab in conjunction with dexamethasone can result in a reduction in days of organ support and mortality if used within 24 hours of receiving organ support. Baricitinib has also been shown to reduce mortality among patients who are not undergoing mechanical ventilation. Given this, use of tocilizumab (single intravenous dose of 8 mg/kg of actual body weight, up to 800 mg) or baricitinib (4mg¹ po daily for maximum of 14 days) can be considered **in combination with dexamethasone** in certain hospitalized patients who are exhibiting rapid respiratory decompensation due to COVID-19 meeting the following inclusion/exclusion criteria below:

Inclusion:

- Admitted to ICU < 24 hours and:
 - mechanical ventilation (tocilizumab or baricitinib)
 - o noninvasive mechanical ventilation (tocilizumab or baricitinib)
 - high-flow nasal canula oxygen (>0.4 FiO₂/30 L/min of oxygen flow) (tocilizumab or baricitinib)

OR

- Recently hospitalized patients (not in an ICU) with:
 - Rapidly increasing oxygen needs who require NIV or HFNC <u>and</u> have significantly increased markers of inflammation. (Tocilizumab or baricitinib).

Exclusion: Without high suspicion of bacterial/fungal/mycobacterial infection; Risks and benefits of therapy should be weighed prior to initiation for patients with pre-existing VTE/PE (baricitinib), lymphocytopenia (ALC < 500 cells/mL), neutropenia (ANC < 1000 cells/mL), severe anemia Hgb < 8g/dL.

ID consultation is needed for the use of tocilizumab or baricitinib for Covid-19. In rare circumstances, baricitinib can also be considered alone when dexamethasone cannot be used. In extreme shortages, sarilumab 400mg x 1 dose may be used in lieu of tocilizumab, and tofacitinib² 10 mg po twice daily for up to 14 days or hospital discharge (whichever comes first) can be used in lieu of baricitinib.

Pediatric Considerations: Tocilizumab is not recommended for the majority of pediatric patients who have mild or moderate COVID-19. For children with severe or critical illness, use of tocilizumab or baricitinib should be evaluated on a case-by-case basis in consultation with the Pediatric Infectious Diseases team

¹ Dose reduction from baricitinib 4 mg to 2 mg PO daily is recommended for eGFR ≥30 mL/min to <60 mL/min and to 1 mg PO daily for eGFR of 15 mL/min to <30 mL/min. Baricitinib is not recommended for patients with eGFR <15 mL/min.

² Dose reduction from tofacitinib 10 mg to 5 mg PO twice daily is recommended for eGFR<60 ml/min. Afternoon doses should be given after dialysis for HD-dependent patients, no supplemental doses required for pre-HD doses.







The FDA has approved remdesivir for use in adult patients (as of, October 22, 2020) and pediatric patients who are at least 28 days of age and older and weighing at least 3 kg (as of, April 25, 2022) with COVID-19 requiring hospitalization. Remdesivir reduced the time to recovery by 29% compared with placebo (10 v 15 days) among patients with COVID-19 infection in the NIH-sponsored ACTT-1 Trial. Remdesivir appears to have the most benefit in patients who have low-flow oxygen requirements and has no benefit for individuals who are mechanically ventilated >48 hours.

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For patients not on oxygen we recommend a 3-day course if their symptom onset is <7 days. For all others we recommend a 5 day course. Any longer courses of remdesivir require an ID consult.

At this time, we recommend remdesivir for patients meeting the below criteria:

- 1. Positive SARS-CoV-2 RT-PCR result within 7 days of admission
- 2. Symptom onset within 10 days prior to initiation of treatment
- 3. Hypoxia defined as:
 - a) SpO₂ <94% on room air OR
 - b) Requiring supplemental oxygen (low-flow/highflow) OR
 - c) Mechanically ventilated <48 hours
- 4.

Patients who are not hypoxic but high risk (anticipatory chemotherapy, lung transplant) may be considered on a case-by-case basis.

If remdesivir is given via EUA (for pediatrics < 12 years or weighing 3.5-40kg), a patient fact sheet must be reviewed with the patient/caregiver prior to use.

If supply becomes severely limited (i.e. when demand > supply), those with terminal illness will not be considered. Modifiers for the definition of terminal illness considered include:

- Clinical Frailty Score >8
- Advanced progressive incurable neurologic disease requiring ventilatory support or Rankin scale ≥5
- Metastatic cancer with expected survival <1 year despite treatment

Commented [PKK4]: I believe that this order was rescinded with the end of the public health emergency

Commented [KI5]: Please delete this part. EUA is evoked.

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Guidance Regarding Use of COVID-19 Convalescent Plasma (CCP) via Emergency Use Authorization

On December 28, 2021, the Federal Drug Administration (FDA) reissued an Emergency Use Authorization (EUA) for the use of COVID-19 convalescent plasma (CCP) as a passive immune therapy and restricted CCP for the treatment of patients with immunosuppressive disease or receiving immunosuppressive treatment with COVID-19. CCP is human plasma collected by FDA registered blood establishments from individuals who have recovered from a COVID-19 infection and whose plasma contains anti SARS-CoV-2 antibodies. These donors must meet all standard donor eligibility requirements. Each donor/CCP unit undergoes testing for anti SARS-CoV-2 antibody titers to determine that there are sufficient antibody levels before being released into inventory. However, at UCLA, these titer determinations were not performed using the EUA assay and therefore will be labeled with a "low titer" tag to meet the EUA specifications. It is important to note, certain clinical trials will exclude patients if they have received CCP and it is important to address all the possible therapeutic regimens available at this time.

The EUA was granted based on retrospective, observational data that suggested a potential clinical benefit is associated with high-titer units of CCP administered early in the course of disease (within 72 hours of diagnosis for inpatient, within 8 days of symptom onset for outpatient based on the Mayo Clinic National Convalescent Plasma Expanded Access Protocol). Three large randomized clinical trials (RECOVERY, REMAP-CAP, CONCOR-1) each failed to demonstrate clinical benefit on mortality or duration of organ support outcomes in the inpatient setting. Although these trials did not exclude patients with impaired humoral immunity, most patients did not report immunodeficiency or receipt of immunosuppressive therapy. Based on these data, the NIH COVID-19 guidelines recommend against convalescent plasma in patients without impaired humoral immunity (**A-I**).

At this time, we recommend considering the administration of 1-2 CCP units administered within 72 hours of diagnosis under guidance from ID consultation for select hospitalized patients and within 7 days of symptom onset for outpatients who meet the following criteria:

- Impaired humoral immunity either by an immune compromising condition or immunosuppressive agents
- Select patients with profound cell mediated immunodeficiencies (such as those who have received a bone marrow transplant or with chronic lymphocytic leukemia), CCP can be considered

Dosage considerations should be made based on patient weight/TBV (if >85 kg, consider 2 units of CCP). Patients with impaired cardiac function and heart failure may require a smaller volume or transfusion over a longer period. CCP may be contraindicated in patients with a history of severe allergic reactions or anaphylaxis to plasma transfusion.

Prior to CCP order entry and transfusion, <u>the standard Consent to Blood Transfusion must be obtained</u>. The patient must be provided with the state required brochure "A Patient's Guide to Blood Transfusion" per hospital policy HS1320, and the "Fact Sheet for Patients and Parents/Caregivers, Emergency Use Authorization (EUA) of COVID-19 Convalescent Plasma for Treatment of COVID-19 in Hospitalized Patients." The consent and accompanying documents are available on the Forms Portal.

Patients undergoing CCP transfusion should be monitored closely for transfusion reactions as per UCLA Health Transfusion Policy 1338. Any adverse reactions associated with CCP transfusion should be reported to the blood bank. For more information or questions, please contact Alyssa Ziman, MD at 310-267-8090 or call the Ronald Reagan UCLA Blood Bank at 310-267-8150.

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Table 3. Dosing of Specific Therapeutics

Agent	Dosing	Monitoring		
Remdesivir	200mg IV x1, followed by 100mg g24h for duration of	Self-limiting, reversible hepatotoxicity has been		
	hospitalization; 5 days recommended	observed, which resolved after therapy cessation.		Commented [SEA6]: Should we change this to "for 5 days or until hospital discharge (whichever comes first)," based
	Pediatric Dosing: For patients weighing 3.5 kg - <40 kg;			on how the clinical trials were conducted? Arguably if patient stable for discharge, they don't need more drug/we
	Loading dose: 5 mg/kg/dose IV x 1 dose (max 200 mg) Maintenance dose: 2.5 mg/kg/dose IV Q24H (max 100 mg); 5 days recommended			don't need to keep them here just for remaining doses. Perhaps we could also just say x3-5 days to cover both durations we would consider
	For patients weighing 40kg or higher: 200mg IV x1, followed by 100mg q24h for duration of hospitalization; 5 days recommended			Commented [KI7]: Change to for patients weighing 3 kg to <40 kg
		Transferier associated deviced to a second and	_	
Convalescent Plasma	2 units, if >85kg	(TACO), transfusion-associated circulatory overload (TACO), transfusion-associated acute lung injury (TRALI)		Commented [SEA8]: Changed to address patients that weigh exactly 85 kg, based on section above
Dexamethasone	6mg PO/IV daily for up to 10 days	Hyperglycemia, neuropsychiatric effects (insomnia,		
	Pediatric Dosing:	irritability), heartburn, impaired wound healing, fluid		
Baricitinib	4 mg PO daily for up to 14 days or hospital discharge (whichever	Superinfection, VTE, GI perforation, TB activation		
Danotanio	comes first)			
	eGFR 30-60 mL/min: 2 mg PO daily			
Tocilizumah	$\frac{1}{100} = \frac{1}{100} = \frac{1}$	GL perforation superinfection benatic injury TB	-	
		activation		Commented [SEA9]: Do we need to use AdjBW if dose caps?
Sarilumab	400 mg x 1 dose	GI perforation, superinfection, hepatic injury, TB activation		
Tofacitinib	10 mg PO twice daily for up to 14 days or hospital discharge	Thrombotic events, lymphopenia, liver enzyme		Commented [SEA10]: Should we make the language
	(whichever comes first)	elevations, superinfection, serious cardiac related		consistent between tofacit and baricit?
	eGFR<60 mi/min: 5 mg PO twice daily	events, GI perforation		

Drugs for which there is insufficient or no data:

Nitazoxanide, ivermectin, lopinavavir/ritonavir, favipiravir, colchicine, inhaled corticosteroids, fluvoxamine. Hydroxychloroquine is not recommended due to data that suggest no benefit.

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Table 4. Drugs in Pregnancy

Class	Agents	Data
Antivirals	Remdesivir	Data limited for remdesivir, likely safe
Corticosteroids	Hydrocortisone, Prednisone, Dexamethasone	Safe, for refractory shock per ICU indications Use of Dexamethasone should be discussed with MFM, but is currently recommended Dose may be adjusted for fetal benefit in case of impending delivery
Convalescent plasma	Convalescent plasma	Limited data, likely okay to use, not excluded from study
II-6 receptor blocker	Tocilizumab	Limited data, MFM consultation, monitoring of infant at birth



Section 3. Consultations to consider specifically for patients admitted due to COVID-19

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Pulmonary/ICU	Should be consulted for clinical deterioration		
Mental Health	Many patients in isolation may experience worsening of their underlying psychiatric illness		
and Psychiatric	 Urgent consult needed in patients expressing suicidal ideation, hallucination, psychosis, or agitation. 		
Care	Consult for other non-emergent issues: depression, anxiety		
	 Ensure at least PHQ-2 (if not PHQ-9, GAD-7) are administered within 3 days of admission and weekly thereafter Consider the phase account if provided in the phase of the phase of		
	Consider video/telephone consult, il needed		
Palliative care	 Early involvement for patients with significant frailty, elderly, difficulty with iADLs, ADLs to assess goals of care 		
	Prolonged ICU stay		
	Emotional, spiritual and symptomatic support at the end of life for family/patient Ethical decision marking		
	Eulical deusion-making Consider video/delaphone consult if needed		
Cardialagy	For SNF or Outpatient assistance Email <u>COVIDPalliativeCare@mednet.ucla.edu</u> or page the team at 89552		
Cardiology	For ICU patients, obtain 11E as needed		
	Monitor for CAD, cardionryopathy with labs as above		
Neurology	Scattered case reports and autopsy findings suggest that COVID-19 patients may uncommonly develop two neurologic complications that can exacerbate respiratory difficulty and cause inability to wean from a ventilator: A) Guillain-Barre syndrome – peripheral autoimmune disorder causing weakness/paralysis of all limbs and respiratory muscles; B) Bickerstaff's encephalitis – inflammation of the brainstem, including disruption of centers for respiratory drive.		
	To screen grossly for these conditions in patients with difficulty weaning, look for:		
	1) Weakness of all 4 limbs with reduced/absent reflexes		
	2) Severely impaired ability to move the eyes		
	screening and for management recommendations, please consult Neurology.		
Addiction	Assess substance use history		
medicine	 Consult in patients with history of opioid, methamphetamine or cocaine use disorders 		
	Consider video/telephone consult, if needed		
Chaplain,	Should not see patient in person		
rabbi, spiritual	May provide support for psychosocial, spiritual and existential suffering in patients with a life-limiting or life-threatening illness		
services			

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Section 4. Discharging patients home/to SNFs

Per LA County DPH, patients may end home isolation 5 days after the onset of symptoms, provided that symptoms are improving and fevers are resolved for at least 24 hours (without the use of fever-reducing medicines). Although not required, it is highly recommended that patients have a negative COVID-19 antigen test if they end isolation between days 6-10. Those who are severely immunocompromised should remain in isolation for at least 20 days, and duration of isolation should be discussed with ID consultation.

Patients should be advised to continue masking through day 10 when they are in public or when coming to clinic. This is especially true if patients continue to have some respiratory symptoms including cough.

These recommendations are based on data that suggest that even though PCRs may be positive for a prolonged period of time (>30d), viable virus is generally not seen in the nasopharynx or throat after 8 days and that the period of infectivity is the greatest in the 2-3 days before or after symptom onset.

For patients who live in congregate settings including skilled nursing facilities, additional precautions may be used. Patients should be kept on enhanced droplet isolation for at least 10 days after the onset of symptoms (20 days for residents with severely immunocompromising conditions) plus 24 hours without fevers and fever reducing medicines.

Please see isolation and quarantine guidelines: <u>http://publichealth.lacounty.gov/acd/ncorona2019/covidisolation/</u> http://publichealth.lacounty.gov/acd/ncorona2019/covidquarantine/ Please see guidance for transferring to SNFs: http://publichealth.lacounty.gov/acd/ncorona2019/healthfacilities/snf/prevention/

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