COVID-19 Pharmacological Treatment Options

Updated March 20:

This information is updated frequently during this evolving situation. Refer to Infonet often for the latest information and communications.

The UPMC System COVID-19 Therapeutics Committee has been created with representation from Infectious Disease, Infection Control, Critical Care, Hospital Medicine, Emergency Medicine, and Pharmacy professionals across UPMC. This team has been convened to review available literature regarding the safety and efficacy of prospective treatment regimens for COVID-19 patients.

Currently, there is no known effective treatment option for COVID-19 other than supportive care.

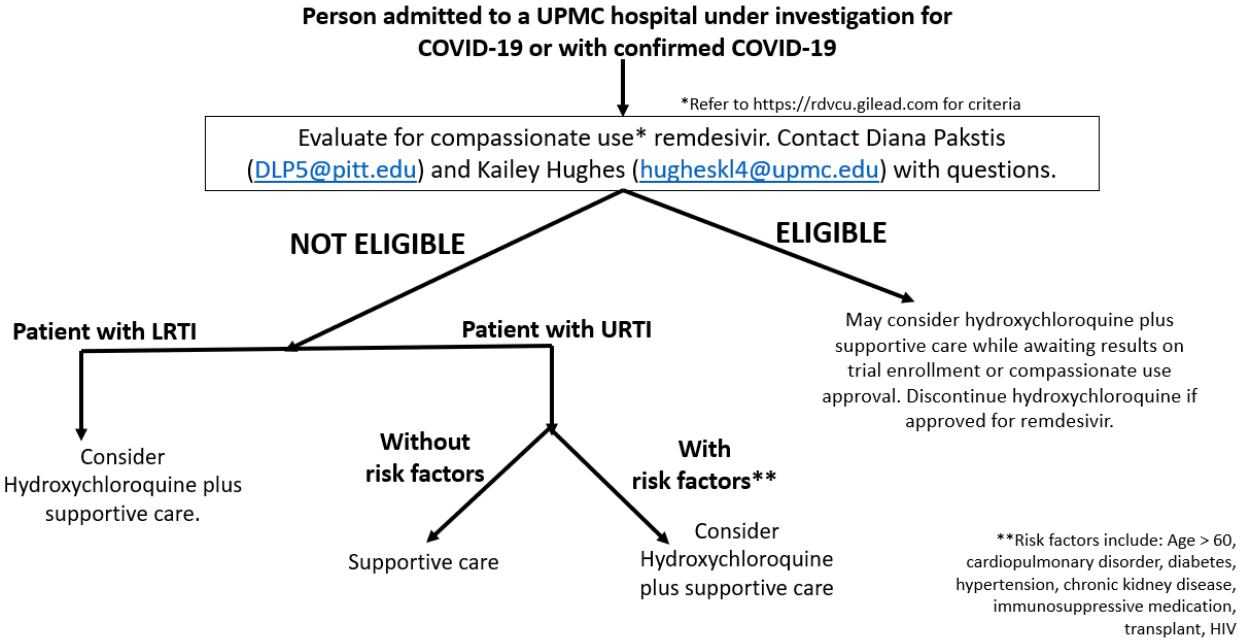
UPMC does NOT recommend:

- **Prophylaxis** against COVID-19.
- **Treatment for outpatients** except supportive care and symptom management.
- **A specific treatment option for inpatients** with COVID-19, but provides the following information to help guide UPMC providers considering antiviral treatment with key considerations regarding safe use based on currently available data.

No provider is required to prescribe antiviral agents for inpatients with COVID-19 given the absence of convincing data for efficacy and outcomes.

The goal of UPMC is to move toward treating all UPMC patients with COVID-19 in trials that allow for the accumulation of knowledge that will guide better management of this emerging pathogen. The institution is actively pursuing the creation of electronic health record driven studies in which to enroll patients to achieve that end. The consensus of the committee is that in the absence of data, all unapproved and unproven treatments should *only* be given in such a context.

Until such trials are available, if a prescriber decides it appropriate, UPMC will allow the use of hydroxychloroquine in the circumstances outlined in the algorithm below. Following the algorithm there are other recommendations concerning drugs that should not be used as well as comments concerning the use of NSAIDs and ACEI/ARBs.



LRTI = lower respiratory tract infection; URTI = upper respiratory tract infection

Hydroxychloroquine dosing and monitoring		
Hydroxychloroquine *Chloroquine is not available at UPMC hospitals*	400mg PO BID on day 1, then 600mg PO daily x 4 days Split dosing as 200mg PO TID if patient is experiencing GI symptoms. Administration with food may also decrease GI symptoms. Film-coated tablets may be crushed.	• Caution in patients with cardiac disease, may cause arrhythmias. Do not use if QTc > 500. • No dose adjustment in renal or hepatic impairment. • Drug may accumulate in fetal tissue including melanin structures of fetal eyes and is present in breast milk. • Most toxicities are associated with long term use. Patient may experience nausea, rash, hypoglycemia. • G6PD testing not required due to short duration of therapy

Therapies that currently have no routine role for the treatment of COVID-19	
Adjunctive corticosteroids	Use of corticosteroids for COVID-19 is controversial and existing data for use in other coronaviruses in heterogeneous and conflicting. The potential benefit of these agents to blunt the inflammatory cascade seen in severe disease needs to be carefully weighed against the concerns for secondary infections, adverse events, and other complications of corticosteroid therapy. **The Therapeutics Committee recommends that in the absence of data, corticosteroids should only be given in the context of a randomized, controlled trial.**
Anakinra	Interleukin-1 (IL-1) receptor antagonist hypothesized to quell cytokine storming. No data for use as adjunctive therapy for COVID-19 currently. No clinical trials are enrolling in China or the United States exploring this agent.
Azithromycin	Six patients treated with azithromycin and hydroxychloroquine in France experienced viral load reduction greater than hydroxychloroquine alone. These data do not support widespread use currently since clinical outcomes were not assessed and there is additive toxicity of azithromycin and hydroxychloroquine.
IVIG	IVIG remains on critical national shortage. The benefit in patients with COVID-19 is unclear. At this time, use should remain reserved to only UPMC System P&T approved indications.
Lopinavir/ritonavir	Demonstrated no benefit for patients with SARS-CoV-2 and is associated with significant drug-drug interactions and gastrointestinal toxicity.
Oseltamivir	Oseltamivir is inactive against SARS-CoV-2; the virus does not possess the drug target. Additionally, it is crucial to preserve oseltamivir use for patients with influenza infection.
Ribavirin +/- interferon	The risk of hematologic toxicity at high doses likely outweighs potential clinical benefit, and therefore ribavirin was not considered a viable candidate for further investigation by the World Health Organization research and development plan for SARS-CoV-2 given lack of in vitro efficacy, toxicity profile, and poor outcomes. Interferon may stimulate innate antiviral responses and is expected to have in vitro activity against 2019-nCoV but randomized trials in other coronaviruses demonstrated no clinical benefit. **Toxicities are substantial** including severe cytopenias, hepatoxicity (including fatality), neuropsychiatric events, and risk of developing fatal or life-threatening ischemia or infection, particularly when combined with ribavirin.
Tocilizumab	Humanized monoclonal antibody targeting interleukin-6 receptor (IL-6) recommended in Chinese COVID-19 guidelines for treatment of cytokine storming. Hyperinflammation and cytokine storming, including elevated IL-6, has been associated with increased mortality in patients with COVID-19. A pre-print (non-peer reviewed) case series of 21 patients treated with tocilizumab between February 5-14, 2020 in China reported marked success, including rapid resolution of fever and C-reactive protein, decreased oxygen requirements, and resolution of lung opacities on computerized tomography imaging. Ongoing trials in China for patients with COVID-19 pneumonia and elevated IL-6, but none registered in the United States. IL-6 testing is a send out lab at UPMC with a multiple day turnaround time. **UPMC supply of tocilizumab is very limited and currently reserved for use for conditions with proven benefit. The Therapeutics Committee will continue to assess evolving data for use of tocilizumab for patients with COVID-19.**

NSAIDS

On March 14, 2020, the French Health Minister stated NSAIDs could worsen clinical course of patients with COVID-19. There is currently no data to support an association between NSAIDs and worse outcomes in patients with COVID-19. The risks of NSAID therapy in patients with COVID-19 should, at this time, be viewed equally as patients without COVID-19 (e.g., gastrointestinal bleeding). On March 18, the World Health Organization stated they "do not recommend against the use of ibuprofen" in patients with COVID-19. Acetaminophen for fever is prudent.

ACE Inhibitors

SARS-CoV-2 uses ACE2 receptors for cell entry in the lungs. ACE inhibitors (e.g., lisinopril) may increase ACE2 expression. ACE2 is also protective against lung injury. There are no published data suggesting ACE inhibitors benefit or worsen conditions of patients with COVID-19. The European Society of Cardiology, Heart Failure Society of America, American College of Cardiology, and American Heart Association all state **patients should continue on their chronic medications, including ACE inhibitors.**

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