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COVID-19 Treatment Recommendations

Antivirals and Immunomodulators

There are currently no FDA approved treatments for COVID-19. Early supportive care with symptomatic treatment is the cornerstone of COVID-19 treatment.[1] Many treatment options with potential antiviral or immunomodulatory effects are currently under investigation but none have consistently reported strong data in support of their use and governing bodies only recommend their use in the context of a clinical trial. More information is provided on some of the agents under investigation for COVID-19 treatment in **Table 1** below.

Based on the current body of literature, **for ambulatory and inpatients with confirmed or suspected SARS-CoV-2, prophylactic or active treatment with investigational medications is NOT recommended,** outside of a clinical trial**.**

Corticosteroids

There is NO evidence to support the use of corticosteroids for the treatment of COVID-19, outside of a specific alternative indication such as septic shock, COPD exacerbation, or ARDS.[1,2] Systematic reviews in related viruses (MERS-CoV and SARS-CoV) have demonstrated no survival benefit and possible harm due to increased viral replication.

ACE-Is and ARBs

There is insufficient evidence to support starting or stopping ACE-Is or ARBs. Their use should continue per usual, unless there is another medical reason to discontinue them (e.g., hyperkalemia, AKI, hypotension).

NSAIDs

There is insufficient evidence to recommend discontinuation of NSAIDs in patients with COVID-19 symptoms. For symptomatic treatment of COVID-19 patients, acetaminophen can be used preferentially but it is not recommended at this time to discontinue NSAIDs in patients already on them.

Antibiotics

Routine use of empiric antibiotics for patients with COVID-19 pneumonia is not recommended unless there is another indication for antibiotics. Secondary bacterial infection is uncommon early in the COVID-19 course, even in the critically ill, and no associated risks for resistant pathogens like *Pseudomonas* or MRSA have been identified in these patients.[3,4] Standard CAP therapy should be used when warranted. Clinical and microbiologic data should be used to de-escalate and discontinue antibiotics. The shortest duration possible should be used to treat bacterial pneumonia. 5 days for CAP patients who defervesce within 72 hours and with no more than 1 sign of clinical instability, and 7 days for HAP/VAP, even due to *Pseudomonas* and MRSA. It should be noted that an extended duration of fevers is typical in COVID-19 patients.

Table 1: Select investigational agents for COVID-19 treatment – NOT recommended for use outside of a clinical trial		
Agent	**Adverse Effects**	**Comments**
Hydroxychloroquine[5-17] Dose: 400 mg PO q12h x 2 doses, then 200 mg PO q12h x 8 doses Duration: 5 days	GI intolerance, cytopenias, QT prolongation (increased risk when used with other QT prolonging agents like azithromycin), headaches, dizziness, glucose fluctuations. Most toxicities are associated with long-term use (e.g., retinopathy).	In vitro activity against SARS-CoV-2. Increases the pH at the surface of cell membranes inhibiting fusion of virus. Also causes inhibition of nucleic acid replication, glycosylation of viral proteins, virus assembly, new virus particle transport, and virus release. Several early small uncontrolled clinical reports purported benefits with the treatment of COVID-19. More recent studies have shown negative effects including one study in US veterans with increased mortality. FDA cautions against use of hydroxychloroquine for COVID-19 outside of the hospital or a clinical trial due to risk of heart rhythm problems. **Combination with azithromycin is NOT recommended** due to poor quality supporting evidence, several studies showing no benefit, potential for harm due to cardiac toxicity, and overuse of antibiotics.
Azithromycin[13-17] Dose: 500 mg IV/PO x 1 dose, then 250 mg IV/PO q24 x 4 doses Duration: 5 days	GI intolerance, QT prolongation, antibiotic resistance	No intrinsic activity against SARS-CoV-2. Small uncontrolled studies combining azithromycin with hydroxychloroquine do not provide convincing evidence for benefit in treatment of COVID-19. Several comparison studies since have shown no benefit to the combination, which also has the potential for significant cardiac toxicity. **The addition of azithromycin to hydroxychloroquine for the treatment of COVID-19 is NOT recommended.**
Remdesivir[7,18,19] Dose: 200 mg IV load, then 100 mg IV q24h Duration: 10 days	Reversible kidney toxicity due to cyclodextrane component, increased liver enzymes, abnormal PT & PTT, GI intolerance, headaches, hypotension during infusion. Prodrug and CYP3A4 substrate with potential for drug-drug interactions.	Nucleotide-analog inhibitor of RNA-dependent polymerases. Originally developed for treatment of Ebola but now being studied for use against SARS-CoV-2 due to potent in vitro activity. No controlled trials for the treatment of COVID-19 have been published yet. A study published on compassionate use showed potential clinical benefit, but a control group was not included. Remdesivir is NOT FDA approved and available for investigational use only from the manufacturer (Gilead) for limited compassionate use and expanded access. Compassionate use requests currently only available for patients who are pregnant or < 18 years old. Doctors can request expanded access for eligible patients from Gilead by visiting: https://clinicaltrials.gov/ct2/show/NCT04323761.
Lopinavir/Ritonavir[20-22] Dose: 400/100 mg PO q12h Duration: 5-10 days	Adverse effects are common and can lead to early discontinuation. GI intolerances, hepatitis, LFT abnormalities, pancreatitis	In vitro activity against SARS-CoV-2. Viral protease inhibitor. A randomized open-label study of lopinavir/ritonavir use in moderately ill hospitalized patients demonstrated no benefit in primary or secondary outcomes. Significant drug-drug interactions. Adverse effects are common and not well tolerated.
Tocilizumab[23-25] Dose: 400 mg IV x 1 dose, may be repeated x 1 in 12 hours if needed	Injection-site reactions, neutropenia, LFT abnormalities, opportunistic infections	Recombinant humanized monoclonal antibody that inhibits IL-6, potentially combatting cytokine release syndrome in critically ill patients. IL-6 levels have been elevated in COVID-19 patients requiring mechanical ventilation. Preliminary data have suggested potential for benefit in severely ill COVID-19 patients, but neutropenia can be long lasting so there is a risk for opportunistic infections. Limited supply and an expensive agent.

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