COVID-19 Pharmacologic Inpatient Treatment Guidelines

This document provides a brief overview of available agents to be used in the inpatient setting, with recommendations for their use as compiled by the MVAHCS ID section. It will be updated as new information becomes available. There are therapy options for patient's hospitalized for COVID-19 and options available for patients with COVID-19 who are hospitalized for reasons other than COVID-19

1. **Inpatient Therapy Options: Patients hospitalized FOR COVID-19 – see NIH guidance**
   Hospitalized Adults: Therapeutic Management | COVID-19 Treatment Guidelines (nih.gov)

Proven Therapies– orderable by any inpatient team for patients hospitalized FOR COVID-19		
Drug	Consider for:	Contraindications/Adverse Effects
DEXAMETHASONE PO/IV ****Can be ordered by any physician**** Dose: 6 mg IV/PO Qday for 10 days	○ Confirmed COVID-19 **AND** ○ Hospitalized **AND** ○ Severe or critical COVID-19 (supplemental oxygen, high-flow oxygen, or noninvasive or invasive ventilation)	○ Mild/moderate COVID ○ Sepsis
REMDESIVIR IV **** Can be ordered by any physician via CDSS**** **FDA approved** Dose: ≥ 40 kg: loading dose of 200 mg IV Qday on day 1, followed by 100 mg IV qday for 4 additional doses or until hospital discharge	○ Confirmed COVID-19 **AND** ○ Hospitalized **AND** ○ Severe COVID-19 (supplemental oxygen, high-flow oxygen, or noninvasive ventilation) ○ Less benefit in mild/moderate COVID-19 (no oxygen needs) but may be considered if high risk of disease progression. May be harmful for critical COVID (mechanical ventilation) Prior to administration: • Baseline eGFR • Baseline hepatic function • Baseline INR Obtain daily while on remdesivir: • LFTs (AST, ALT, ALP, bili, albumin, total protein, INR), Chem-7	ABSOLUTE CONTRAINDICATIONS: • Known hypersensitivity to remdesivir or ingredients • ALT ≥ 10x ULN RELATIVE CONTRAINDICATIONS: • Renal dysfunction (eGFR < 30 mL/min) ** If potential benefit outweighs potential risk, may use remdesivir. Cyclodextrin vehicle may accumulate with renal insufficiency, causing neuropathy and nephrotoxicity. Cyclodextrin is dialyzable. • Pregnancy (balance risk:benefit to mother and fetus) • Hepatic impairment Known adverse events: • Infusion-related reactions • Hepatic toxicity

		○ Discontinue if ALT ≥ 10x ULN or with symptomatic liver dysfunction ○ Discontinue if ALT elevation plus liver inflammation (increased conjugated bili, ALP, or INR). • Rash • Thrombocytopenia
Beneficial Therapies – available under Emergency Use Authorization (EUA)		
Drug	Consider for:	Considerations/Exclusion Criteria
BARICITINIB PO Available under EUA. Dose: 4 mg PO Qday for 14 days or until hospital discharge	○ Confirmed COVID-19 **AND** ○ Hospitalized **AND** ○ Severe COVID on high-flow oxygen or noninvasive ventilation OR severe COVID on supplemental oxygen **AND**	CONTRAINDICATIONS: ESRD, dialysis, or acute kidney injury Known active tuberculosis CAUTION: Other severe infection other than COVID Severe hepatic impairment Pregnancy (limited data) DOSE ADJUSTMENT for renal function (eGFR<60) or hepatic impairment Dose adjust for drug interactions • Before giving, must discuss info in the FDA's EUA "Fact Sheets" for clinicians and patients/surrogates. Must document this discussion in the chart
TOCILIZUMAB (IL- 6 receptor blocker) ****Orderable via CDSS under EUA**** <u>COVID 19 regimen</u> 800mg IV x 1 if weight <u>≥</u> 90 kg 600 mg IV x 1 if weight <u>≥</u>65 kg and < 90kg 400 mg IV x 1 if weight <u>≥</u>40 kg and <65 kg	○ Confirmed COVID-19 **AND** ○ Hospitalized **AND** ○ Clinical evidence of progressive COVID-19 (supplemental oxygen, high-flow oxygen, or noninvasive or invasive ventilation)	○ Outpatients ○ Current documented or suspected bacterial or fungal infection ○ Active tuberculosis ○ ALT/AST> 10x ULN

If ≤ 40 kg; use 8mg/kg dosing Could consider 2nd dose – uncertain benefit		

2. Therapy options for outpatients or patient's hospitalized WITH COVID -19 (admission reason is not COVID related)

Beneficial Therapies – available under Emergency Use Authorization (EUA) for patients who are hospitalized but **not due to COVID-19** – listed in order of preference		
PAXLOVID (Nirmatrelvir + Ritonovir) **** for use only in outpatients, or patients hospitalized but not due to COVID-19**** **Orderable via CDSS** Available under EUA	○ Confirmed COVID-19 AND ○ Mild to moderate COVID-19 AND ○ Higher risk to progression to severe COVID-19 (see full list on CDC webpage) ○ Within 5 days of symptom onset	○ Hospitalized due to COVID-19 ○ Require oxygen therapy due to COVID-19 ○ Require an increase in baseline oxygen flow rate due to COVID-19 in those on chronic oxygen therapy due to underlying comorbidity ○ Note the many drug -drug interactions; many can be managed with temporary dose adjustment - discuss with pharmacy and prescriber
REMDESIVIR IV **Orderable via CDSS- only available for inpatients not hospitalized for COVID** Outpatient dosing: 200 mg on day 1 100 mg on days 2 and 3 **FDA approved**	○ Confirmed COVID-19 AND ○ Mild to moderate COVID-19 AND ○ Higher risk to progression to severe COVID-19 (see full list on CDC webpage) ○ Within 7 days of symptom onset	○ Known hypersensitivity to remdesivir or ingredients ○ ALT ≥ 10x ULN
Molnupiravir ****Only consider if none of above options are available or appropriate**** Available under EUA	○ Confirmed COVID-19 AND ○ Mild to moderate COVID-19 AND ○ Higher risk to progression to severe COVID-19 (see full list on CDC webpage) ○ Within 5 days of symptom onset ○ None of above options are available or appropriate	○ Hospitalized due to COVID-19 ○ Require oxygen therapy or increase in oxygen therapy due to COVID-19 ○ Contraception recommended in patient's with childbearing potential or partners with childbearing potential ○ Other options available

Therapies Not Recommended: benefit unlikely or slight, and potentially outweighed by risks	
Medication	**Rationale for Recommendation**
Hydroxychloroquine	Available evidence is insufficient to recommend this
Azithromycin	Available evidence is insufficient to recommend this in combination with HCQ.
Darunavir / cobicistat	No laboratory or clinical data demonstrate potency against SARS-CoV-2
Interferon alpha	Interferon alpha preparations have been studied (often in combination with ribavirin) for other coronaviruses, including SARS-CoV-1 and MERS, without clinical success. Side effects are likely to outweigh the clinical benefit.
Interferon beta	Triple regimen of interferon beta (if symptoms < 1 week) + lopinavir/ritonavir + ribavirin possibly shortened illness duration in mildly ill inpatients, but nearly half of recipients developed diarrhea.
Influenza agents	Coronaviruses do not utilize neuraminidase for replication. No activity is expected.
Lopinavir / ritonavir	Negative RCT, negative open-label trial RCT. Possible benefit for mild disease when combined with ribavirin + interferon beta (see above), but diarrhea.
Ribavirin	Ribavirin has been studied (often in combination with interferon) in other coronaviruses including SARS-CoV-1 and MERS without clinical success. Side effects such as anemia are likely to outweigh the potential benefit. Possible benefit for mild disease when combined with lopinavir/ritonavir + interferon beta (see above), but diarrhea.
Convalescent plasma	Negative RCT and lacks clear evidence of overall mortality reduction or improved clinical status; no way to tell high-titer units (may be helpful) from low-titer units (unhelpful)