Providence St. Joseph Health Infectious Diseases Clinical Decision Team and Antimicrobial Stewardship Committee

Guidance for SARS-CoV-2 (COVID-19) Positive in Non-pregnant, Hospitalized Adult Patients

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Disclaimer: THE BELOW INFORMATION APPLIES TO PATIENTS REQUIRING ADMISSION TO AN ACUTE CARE FACILITY. OUTSIDE OF REMDESIVIR, NO AGENT HAS BEEN APPROVED BY THE FDA FOR THE TREATMENT OF COVID-19. ALL AGENTS HAVE POTENTIAL SIDE EFFECTS. ASSESSMENT OF BENEFIT VERSUS RISK MUST BE MADE PRIOR TO USE AND ON A CASE-BY-CASE BASIS.

Therapeutic Agent	Dose and Duration	Inclusion Criteria	Exclusion Criteria	National Guideline Recommendations	Comment
Remdesivir	200mg IV loading dose followed 100mg IV daily x 4 days • Durations should be limited to 5 days. • If a patient is otherwise ready for discharge prior to completion of the course, remdesivir can be discontinued • In non-immunosuppressed patients, consider discontinuing remdesivir in patients off supplemental oxygen and afebrile (T <38°C) for 24 hours and otherwise ready for discharge	• Confirmed SARs-CoV-2 • Hospitalized patients • Nonintubated patients requiring supplemental oxygen to maintain SpO2 > 93% *Supplemental oxygen is recommended for patients with SpO2 ≤ 92% **The current literature does not support the use of remdesivir in patients (1) receiving mechanical ventilation at the time of RDV initiation and/or (2) whose symptom onset exceeds 10 days ***Low flow oxygen is defined as requiring ≤ 6 L/min	• AST / ALT > 10 x ULN • CrCl < 30 ml/min {eGFR may be an acceptable alternative for specific patient populations (i.e. age > 70 years)} • Patient who are not hypoxemic or not requiring supplemental oxygen* • Pediatric patients <12 years old or weighing 3.5kg to less than 40kg. • Durations exceeding 5 days • Mechanically ventilated at the time of RDV initiation*	• IDSA • Hospitalized without supplemental oxygen: Recommend against using RDV • Hospitalized with hypoxemia or oxygen requirement: Recommend use • NIH • Hospitalized without supplemental oxygen: Insufficient data to recommend for or against • Hospitalized and requiring supplemental oxygen: RDV alone (BIIa) or RDV plus DEX (BIII) or DEX alone (BI) • Hospitalized and requiring oxygen delivery through a high-flow device or noninvasive ventilation: DEX alone (AI) or RDV plus DEX (BIII) • Invasive mechanical ventilation or ECMO: Not recommended	• FDA approved for hospitalized patients > 12 years old • *RDV may be appropriate treatment for patients not on oxygen or hypoxemic (e.g., a person who is at a particularly high risk for clinical deterioration) or mechanical ventilation. Treatment decision should be made on a case by case basis after discussion with ID/AMS. • In the event of drug shortages, clinically patients should be prioritized in the following order: Supplemental oxygen/low flow nasal cannula (≤6L/min), High flow nasal cannula/noninvasive ventilation. Patients with symptom onset of <10 days should be prioritized • Refer to Ethic Leadership Council guidance on remdesivir allocation. • Emergency use authorization for hospitalized pediatric patients < 12 years old or weighing 3.5-40kg. • Fact Sheet for healthcare providers. • Informed consent for the EUA must be documented using the smartphrase .REMDEPEDEUA. • Parents and caregivers must receive the following fact sheet.

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Dexamethasone	6mg IV / PO daily x 10 days or until hospital discharge	• Requiring supplemental oxygen, mechanical ventilation, or extracorporeal membrane oxygenation (ECMO) • Pneumonia on imaging is not required	• Patients not receiving supplemental oxygen	• IDSA • Hospitalized without supplemental oxygen: Recommend against use • Hospitalized with an oxygen requirement: Recommend use • NIH • Hospitalized without supplemental oxygen: Recommend against use • Hospitalized and requiring supplemental oxygen—RDV alone (BIIa) or RDV plus DEX (BIII) or DEX alone (BI) • Hospitalized and requiring oxygen delivery through a high-flow device or noninvasive ventilation—DEX alone (AI) or RDV plus DEX (BIII) • Invasive mechanical ventilation or ECMO: DEX alone (AI)	• May substitute prednisone 40 mg oral or IV solumedrol 30mg if dexamethasone is not available
Tocilizumab	One time dose: Weight < 30Kg: 12mg/kg Weight > 30kg: 8mg/kg (maximum dose of 800mg) *Second dose approved via EUA if clinical signs/symptoms worsen or do not improve within 8 hours after the first dose. However,	• Confirmed SARS-CoV-2 • Receiving dexamethasone plus other standard individualized treatment • Radiographic evidence of pulmonary infiltrate • Receiving invasive or noninvasive mechanical ventilation or high flow O_2 ○ May consider in patients not yet on high flow oxygen but demonstrating clear progressive need for oxygen	• Co-existing active severe bacterial and fungal infection • ALT/AST > 10 x ULN • ANC < 1,000 /mm^3 • Plt < 50,000/mm^3 • Use in severely immunocompromised patients should be considered on a case-by-case basis	• IDSA • Hospitalized with progressive severe or critical COVID-19 with elevated markers of inflammation: Recommend • NIH • Patients within 24 hrs of admission to the ICU and who required invasive or noninvasive mechanical ventilation or high-flow oxygen (>0.4 FiO2/30 L/min of oxygen flow): insufficient data to	• Consider restricting to pulmonology, critical care, and/or infectious diseases. Ministries may designate other representative(s) at their discretion. • Use is not restricted based on baseline CRP. However, studies suggest that tocilizumab may be more beneficial in patients with CRP > 7.5mg/dL • Available under FDA emergency use authorization for patients ≥ 2 years old • Fact sheet for healthcare providers • Patient and caregivers must receive the following fact sheet. • Informed consent must be documented using the smartphrase .TOCIEUA.

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	AMS/ID CDT does not endorse the routine use of second dose	therapy (>6 L/min) likely requiring high flow • Demonstrating disease progression or increasing severity of illness > 48 hours after the initiation of standard therapy • For select patients who present with severe illness requiring persistent high flow or intubation, starting tocilizumab sooner than 48 hours after the start of standard therapy could be considered on a case-by-case basis		recommend either for or against use. • Patients who do not require ICU-level care or who are admitted to the ICU but do not meet the above criteria: Not recommended.	• Use with caution in patients who may be at increased risk of GI perforation or demyelinating disorders
Baricitinib	4mg PO daily x 14 days or until hospital discharge	• Confirmed SARS-CoV-2 • Hospitalized • Nonintubated patients requiring noninvasive ventilation or high-flow oxygen* • Receiving dexamethasone alone or dexamethasone plus remdesivir • Demonstrating disease progression or increasing severity of illness *FDA EUA includes patients on mechanical ventilation or ECMO. However, data in this patient population is	• Patient who are on dialysis or patients with eGFR < 15mL/min/1.73m2 • Known active tuberculosis • Absolute lymphocyte count (ALC) < 200 cells/µL • Absolute neutrophil count (ANC) < 500 cell/µL • Known or newly diagnosed thrombosis • Use with caution in patients with an increased risk of thrombosis. Thrombosis, including deep vein thrombosis	• IDSA • Recommend combination therapy with RDV in patients with hypoxia or receiving supplemental oxygen and with a contraindication to corticosteroids • Recommend treatment with baricitinib plus remdesivir plus corticosteroid only in the context of a clinical trial • NIH • Recommends either baricitinib or tocilizumab in combination with dexamethasone or dexamethasone plus remdesivir for patient on	• Consider restricting to pulmonology, critical care, and/or infectious diseases. Ministries may designate other representative(s) at their discretion • Available under FDA emergency use authorization • Fact sheet for healthcare providers • Patients and caregivers must receive the following fact sheet • Prophylaxis for venous thromboembolism (VTE) is recommended unless contraindicated • Informed consent must be documented using the smartphrase .BARICITEUA.

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		limited and thus this group is not included in current NIH recommendations. Providers may consider use on a case-by-case basis if alternative therapy such as, tocilizumab, is unavailable. If started prior to MV or ECMO, can continue. @Patients with hypoxia or nonintubated patients requiring supplemental oxygen whom have a contraindication to corticosteroids may receive bariticinib in place of corticosteroids	(DVT), pulmonary embolis (PE), and arterial thrombosis have been observed. Promptly evaluate new-onset symptoms of DVT, PE, or arterial thrombosis.	high-flow oxygen or noninvasive ventilation with evidence of progression or increased biomarkers • Recommend use in nonintubated patients who require oxygen supplementation and cannot receive a corticosteroid	
Casirivimab/imdevimab (PROPHYLAXIS)	600mg casirivimab plus 600mg imdevimab IV/SC once* *For individuals in whom repeat dosing is determined to be appropriate for ongoing exposure to SARS-CoV-2 for >4 weeks and who are not expected to mount an adequate immune response, subsequent repeat dosing of 300mg casirivimab and 300mg imdevimab IV/SC every 4 weeks	• Adult or pediatric patients (12 years of age or older weighing at least 40kg) • High risk for progression to severe COVID-19 (see treatment section below for criteria) • Patients not fully vaccinated* OR Expected not to mount an adequate immune response to complete SARS-CoV-2 vaccination. Criteria AND • Exposed to an individual infected with SARS-CoV-2 consistent with CDC close contact criteria OR at high risk of exposure to an individual infected with SARS-CoV-2 in the same institutional		• IDSA: No recommendation • NIH: Recommends post exposure prophylaxis for patients who meet the EUA criteria	• Available under FDA emergency use authorization • Fact sheet for healthcare providers • Patients and caregivers must receive the following fact sheet • Informed consent must be documented using the smartphrase .CASIMDEVPPYEUA. • Clinically monitor patients during administration and observe patients for at least 1 hours after the infusion is complete

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		setting (eg. Nursing homes, prison, etc) *Fully vaccinated = 2 weeks after the second vaccine dose in 2-dose series (e.g Pfizer or Moderna) or 2 weeks after a single-dose vaccine (e.g J&J)			
Casirivimab/imdevimab (TREATMENT)	600mg casirivimab plus 600mg imdevimab IV once *Subcutaneous administration can be considered in situations where IV administration is not feasible or would delay treatment	Adult ambulatory patients with mild to moderate COVID-19 with positive SARS-CoV-2 viral testing AND who are at high risk for progressing to severe COVID-19 and/or hospitalization (see below). *Treatment should be administered as soon as possible after a positive test **AND** within 10 days of symptom onset. **Administering as soon as possible to symptom onset may maximize the potential benefits of this agent. The following medical conditions or other factors may place patients at higher risk for progression to severe COVID-19: • Older age (ie. age ≥65) • Obesity or being overweight (ie. BMI >25 kg/m^2) • Pregnancy	• 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 an underlying non-COVID-19 related comorbidity *May consider use in patients with mild to moderate COVID-19 who are hospitalized for a reason other than COVID-19 but meet other EUA criteria.	• IDSA • Recommend casirivimab/imdevimab in patients with mild to moderate COVID-19 at high risk for progression to severe disease. • NIH • Recommend casirivimab/imdevimab in high risk outpatients as defined by the EUA • Consider for patients with mild to moderate COVID-19 who are hospitalized for a reason other than COVID-19 but meet other EUA criteria.	• Available under FDA emergency use authorization • Fact sheet for healthcare providers • Patients and caregivers must receive the following fact sheet • Informed consent must be documented using the smartphrase .CASIMDEVEUA. • Clinically monitor patients during administration and observe patients for at least 1 hours after the infusion is complete
Bamlanivimab/etesevimab	700mg bamlanivimab plus 1,400mg etesevimab IV once			• IDSA • Recommend bamlanivimab/etesevimab in patients with mild to moderate COVID-19 at high risk for progression to severe disease. • NIH • Recommend against use of bamlanivimab/etesevimab	• Distribution is restricted in certain areas with elevated prevalence of Beta and Gamma variants. Updated distribution can be found here. As of 6/25/21, shipment is paused nationwide. • Available under FDA emergency use authorization • Fact sheet for healthcare providers • Patients and caregivers must receive the following fact sheet

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		• Chronic kidney disease • Diabetes • Immunosuppressive disease or immunosuppressive treatment • Cardiovascular disease (including congenital heart disease) or hypertension • Chronic lung diseases • Sickle cell disease • Neurodevelopmental disorders or other conditions that confer medical complexity (ie. genetic or metabolic syndromes and severe congenital anomalies) • Having a medical-related technological dependence • Other medical conditions or factors (ie., race or ethnicity) may also place individual patients at high risk for progression to severe COVID-19 and authorization of monoclonal antibodies under the EUA is not limited to the medical conditions or factors listed above. PSJH data showed that Hispanic patients were at a higher risk of morbidity. •*CDC variant tracker* • *As of 6/25/21, shipment of bamlanivimab/*		in high-risk outpatients as defined by the EUA • Recommend against use in patients with mild to moderate COVID-19 who are hospitalized for a reason other than COVID-19 but meet other EUA criteria.	• Informed consent must be documented using the smartphrase .BAMETEUA. • Clinically monitor patients during administration and observe patients for at least 1 hours after the infusion is complete
Sotrovimab	500mg IV once			• IDSA • No specific recommendation for sotrovimab • NIH • Recommend sotrovimab in high-risk outpatients as defined by the EUA •Consider for patients with mild to moderate COVID-19 who are hospitalized for a reason other than COVID-19 but meet other EUA criteria.	• Available under FDA emergency use authorization • Fact sheet for healthcare providers • Patients and caregivers must receive the following fact sheet • Informed consent must be documented using the smartphrase .SOTROVEUA • Clinically monitor patients during administration and observe patients for at least 1 hours after the infusion is complete

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		etesevimab *is paused nationwide. Updated distribution can be found here.*			
Convalescent Plasma		• Confirmed SARS-CoV-2		• IDSA– • Recommends against using convalescent plasma • NIH— • Patients without impaired immunity: recommends against use • Patients with impaired immunity: insufficient data to recommend for or against the use of high-titer convalescent plasma	• As of 02/04/21, only high titer convalescent plasma is approved under FDA emergency use authorization • Fact sheet for healthcare providers • Patients and caregivers must receive the following fact sheet • Refer to ID CDT / AMS statement on use of convalescent plasma. • Informed consent must be documented using the smartphrase .CPEUA.
Colchicine	• NIH: Recommend against use of colchicine for the treatment of hospitalized patients • ID CDT/ AMS does not recommend use				
Fluvoxamine	• NIH: insufficient data to recommend either for or against the use of fluvoxamine • ID CDT / AMS does not recommend use				
Sarilumab	• NIH: insufficient data to recommend either for or against the use of sarilumab for hospitalized patients with COVID-19 who are within 24 hours of admission to the ICU and who require invasive mechanical ventilation, noninvasive ventilation, or high-flow oxygen (>0.4 FiO_2/30 L/min of oxygen flow). • ID CDT / AMS does not recommend use				
Ivermectin	• NIH: insufficient data to recommend either for or against the use of ivermectin. • IDSA: recommend against using ivermectin for hospitalized or non hospitalized patients outside of the context of a clinical trial. • ID CDT / AMS does not recommend use				
Hydroxychloroquine (HCQ), Chloroquine	• IDSA and NIH do not recommend use of hydroxychloroquine or chloroquine • IDSA and NIH do not recommend use of hydroxychloroquine or chloroquine plus azithromycin *Use of HCQ in combination with remdesivir is not recommended • ID CDT / AMS does not recommend use				
Lopinavir/ritonavir (LPV/r)	• IDSA and NIH do not recommend routine use of LPV/r • ID CDT / AMS does not recommend use				
Available Clinical Trials	• Contact local principal investigator or study team for guidance regarding enrollment. • Refer to Ethics Leadership Council Guidance on Accepting transfers of patients from non-PSJH facilities to PSJH facilities for the sole purpose of enrolling in Covid-19 study of therapeutic agents.				