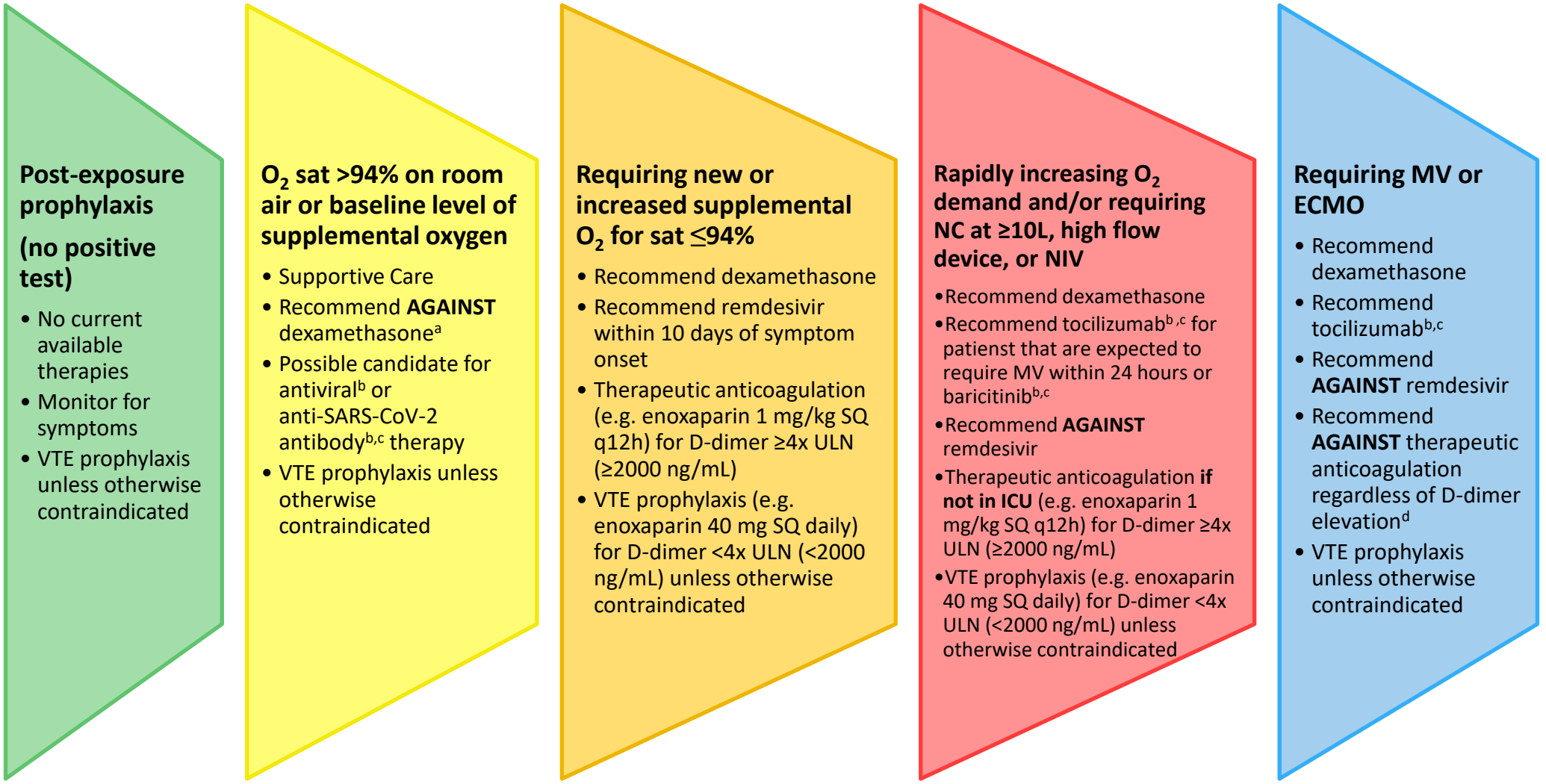
CATHOLIC HEALTH COVID-19 INPATIENT THERAPEUTICS BEST PRACTICE GUIDELINE



See tables below for dosing information and additional treatment decision criteria

[a]corticosteroids that are prescribed for an underlying condition should be continued, [b]based on availability, [c]requires Infectious Diseases approval
[d]unless other non-COVID-19 indication for therapeutic anticoagulation, for ECMO give heparin as usual per protocol with ACT monitoring
VTE= venous thromboembolism, SQ= subcutaneous, ULN= upper limit of normal, NC= nasal cannula, NIV= non-invasive ventilation (e.g. BIPAP), MV=mechanical ventilation, ECMO= extracorporeal membrane oxygenation

Table 1. Drug Dosing and Treatment Decision Criteria

Drug	Dosing Information	Comments/Considerations
Remdesivir *FDA-approved*	**For patients requiring new or increased supplemental O_2 for sat ≤94%** **5-day** regimen: 200 mg IV X1 day 1 then 100 mg daily X 4 more days	**May be used IF all criteria met:** • <10 days from symptom onset • **NOT** requiring BIPAP, High Flow Nasal Cannula (≥10L) or Invasive Ventilation • eGFR>30 mL/min/1.73 m^2 • No significant sustained Bradycardia • No significant LFT abnormalities *Patient does NOT need to complete 5 days of therapy if ready for discharge before that time*
	For patients with O_2 sat >94% on room air or baseline level of supplemental oxygen **3-day** regimen: 200 mg IV X1 day 1 then 100 mg daily X 2 more days **efficacy data on the 3 day regimen was in unvaccinated individuals only	See Figure 1 for guidance on therapy preference in non-hospitalized patients or patients hospitalized for a reason other than COVID-19 IF **symptoms ≤7 days** AND high-risk patient for disease progression **(TABLE 2)** Should NOT be given with other PO anti-SARS-CoV-2 antivirals
Dexamethasone	6mg IV/PO Daily up to 10 days	If there is concern for ARDS with failure to improve on 6mg daily dosing AND supporting data suggesting ARDS (e.g. PaO_2/FiO_2 <200), higher dosing may be utilized, up to 10 days: Dexamethasone 20mg IV daily X5 days then 10mg IV daily X5 days

Table 1 (continued). Drug Dosing and Treatment Decision Criteria

Drug	Dosing Information	Comments/Considerations
Baricitinib *FDA EUA* Requires ID approval Therapy dependent on availability	4 mg PO daily for 14 days or until hospital discharge (whichever comes first) Dose adjustments for eGFR: • eGFR 30 to <60 mL/min/1.73 m^2: Baricitinib 2 mg PO once daily • eGFR 15 to <30 mL/min/1.73 m^2: Baricitinib 1 mg PO once daily • eGFR <15 mL/min/1.73 m^2: Baricitinib is not recommended	**Consider Baricitinib if all of the following are present:** 1. Symptoms Present <14 days 2. Marked Elevation in Inflammatory markers (e.g. elevated CRP, D-dimer, LDH, or ferritin) ***AND*** 3. **None** of the following present: • Known Tuberculosis or suspected latent TB infection • On immunosuppressives at baseline • Active Hepatitis B • Active bacterial, fungal or parasitic coinfection • eGFR <15 mL/min/1.73 m^2 • Absolute lymphocyte count (ALC) <200 cells/µL • Absolute neutrophil count (ANC) <500 cells/µL • ALT and/or AST is >5 times upper limit of normal • Cirrhosis *Caution is advised if history of significant hypercoagulable state preceding COVID-19 diagnosis*
Tocilizumab *FDA EUA* Requires ID approval Therapy dependent on availability	8 mg/kg (actual body weight) IV x1, maximum dose= 800 mg Tociluzimab considered for patients that are expected to require mechanical ventilation within 24h or admitted to ICU in past 24h due to respiratory failure	**Consider Tocilizumab if all of the following are present:** 1. Symptoms Present <14 days 2. Marked Elevation in Inflammatory markers (e.g. elevated CRP, D-dimer, LDH, or ferritin) ***AND*** 3. **None** of the following present: • Known Tb or significant risk factor for LTBI • On significant immunosuppressives at baseline • Active Hepatitis B • Active bacterial, fungal or parasitic coinfection • Platelets < 50,000/ µL • AST and ALT >3 times the upper limit of normal • In ICU >24h due to COVID-19

Table 1 (continued). Drug Dosing and Treatment Decision Criteria

Drug	Dosing Information	Comments/Considerations
Heparin **(LMWH or UFH)**	**<u>Patient NOT in the ICU</u>** **D-dimer < 4X the ULN (<2000 ng/mL)** Standard VTE prophylaxis: enoxaparin 40 mg SQ daily or UFH 5,000 units SQ q8-12h	
	D-dimer ≥ 4x the ULN (≥2000 ng/mL) Consider therapeutic-dose anticoagulation in this population: enoxaparin 1 mg/kg SQ q12h **OR** unfractionated heparin drip	• Administer for 14 days or until hospital discharge, unless there is a diagnosis of VTE or another indication for therapeutic anticoagulation • No studies in COVID-19 support the use of anticoagulation administered at a dose between prophylactic and therapeutic doses (e.g. enoxaparin 1 mg/kg SQ daily or 0.5 mg/kg SQ q12h), therefore this strategy is not recommended • Use should be weighed against other factors including bleeding risk and patient's severity of illness
	<u>Patient in ICU, regardless of D-dimer elevation</u> Standard VTE prophylaxis, unless other non-COVID-19 indication for therapeutic anticoagulation enoxaparin 40 mg SQ daily or UFH 5,000 units SQ q8-12h	If patient started on therapeutic anticoagulation before transfer to the ICU, switch to a prophylactic dose of anticoagulation, unless there is a non-COVID-19 indication

Table 1 (continued). Drug Dosing and Treatment Decision Criteria

Drug	Dosing Information	Comments/Considerations
Nirmatrelvir/ ritonavir (Paxlovid) *FDA EUA*	300 mg nirmatrelvir + 100 mg ritonavir PO q12h X5 days Dose adjustment for eGFR: • eGFR 30 to <60 mL/min: nirmatrelvir 150 mg with ritonavir 100 mg twice daily • eGFR <30 mL: avoid use Severe Hepatic Impairment (Child-Pugh Class C): • Not recommended **NOTE: nirmatrelvir and ritonavir are prescribed and given as separate tablets that are packaged together and are NOT a single tablet combination formulation**	See Figure 1 for guidance on therapy preference in non-hospitalized patients or patients hospitalized for a reason other than COVID-19 Should meet the following criteria: • ***Symptoms ≤5 days*** • *mild to moderate illness (no hypoxia)* • *high risk for progression to severe disease* ***(TABLE 2)*** • *no major drug interactions** • *eGFR of >30 mL/min* *Because ritonavir-boosted nirmatrelvir is the only highly effective oral antiviral for the treatment of COVID-19, many (but not all) drug interactions can be safely managed and **should not preclude** the use of this medication. See the following website to determine potential interactions and advice regarding concomitant use of Paxlovid: https://www.covid19-druginteractions.org/checker

Table 1 (continued). Drug Dosing and Treatment Decision Criteria

Drug	Dosing Information	Comments/Considerations
Molnupiravir (Lagevrio) *FDA EUA*	800 mg PO q12h X 5 days • No renal/hepatic dose adjustments	See Figure 1 for guidance on therapy preference in non-hospitalized patients or patients hospitalized for a reason other than COVID-19 Should meet the following criteria: • ***Symptoms ≤5 days*** • *mild to moderate illness (no hypoxia)* • *high risk for progression to severe disease* ***(TABLE 2)*** • *Not pregnant* • *Unable to use other recommended alternative therapies for high-risk individuals* ***Important consideration for sexually active individuals:*** Patients of childbearing potential should be counseled about abstaining from sex or using reliable contraception for the duration of therapy and for up to 4 days after receiving molnupiravir. Reproductive toxicity has been reported in animal studies of molnupiravir, and molnupiravir may be mutagenic during pregnancy. The FDA EUA states that men of reproductive potential who are sexually active with individuals of childbearing potential should be counseled to abstain from sex or use a reliable method of contraception for the duration of treatment **and for at least 3 months after the last dose of molnupiravir**.

Table 1 (continued). Drug Dosing and Treatment Decision Criteria

Drug	Dosing Information	Comments/Considerations
Bebtelovimab *FDA EUA*	175 mg IV x 1 dose • No renal/hepatic dose adjustments	See Figure 1 for guidance on therapy preference in non-hospitalized patients or patients hospitalized for a reason other than COVID-19 Should meet the following criteria: • ***Symptoms ≤7 days*** • *mild to moderate illness (no hypoxia)* • *high risk for progression to severe disease* ***(TABLE 2)*** • *Unable to use other recommended alternative therapies for high-risk individuals*
Other previously available anti-SARS-CoV-2 antibody products are not currently recommended based on poor in-vitro activity against predominant circulating virus strains: **Bamlanivimab/Etesevimab (Omicron BA.1)** **Carisivimab/Imdevimab (Omicron BA.1)** **Sotrovimab (Omicron BA.2)**		

Table 2. Risk factors conveying high-risk for progression to severe COVID-19

<table>
<tr><th>High Risk Conditions</th><th>Conditions Suggestive of High Risk</th></tr>
<tr><td rowspan="4">

Cancer
Cerebrovascular disease
Chronic kidney disease
Chronic lung diseases limited to:

Interstitial lung disease, Pulmonary embolism, Pulmonary hypertension, Bronchiectasis, COPD (chronic obstructive pulmonary disease)

Chronic liver diseases limited to:

Cirrhosis, Non-alcoholic fatty liver disease, Alcoholic liver disease, Autoimmune hepatitis

Cystic fibrosis
Diabetes mellitus, type 1 and type 2
Disabilities

Attention-Deficit/Hyperactivity Disorder (ADHD), Cerebral Palsy, Congenital Malformations (Birth Defects), Limitations with self-care or activities of daily living, Intellectual and Developmental Disabilities, Learning Disabilities, Spinal Cord Injuries

Heart conditions (such as heart failure, coronary artery disease, or cardiomyopathies)
HIV (human immunodeficiency virus)
Mental health disorders limited to:

Mood disorders, including depression, Schizophrenia spectrum disorders

Neurologic conditions limited to dementia
Obesity (BMI ≥30 kg/m^2)
Primary Immunodeficiencies
Pregnancy and recent pregnancy
Physical inactivity
Smoking, current and former
Solid organ or hematopoietic cell transplantation
Tuberculosis
Use of corticosteroids or other immunosuppressive medications

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Children with certain underlying conditions
Overweight (BMI>25 kg/m2, but <30 kg/m2)
Sickle cell disease
Substance use disorders
Thalassemia

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<tr><th>Mixed Evidence on Risk</th></tr>
<tr><td>

Alpha 1 antitrypsin deficiency
Asthma
Bronchopulmonary dysplasia
Hepatitis B
Hepatitis C
Hypertension

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<tr><td>For more information on medical conditions associated with higher risk for severe COVID-19, go to the CDC webpage dedicated to this topic:

https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-care/underlyingconditions.html (Control+click)</td></tr>
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Figure 1. Therapy preference in non-hospitalized patients or those admitted for reasons other than COVID-19

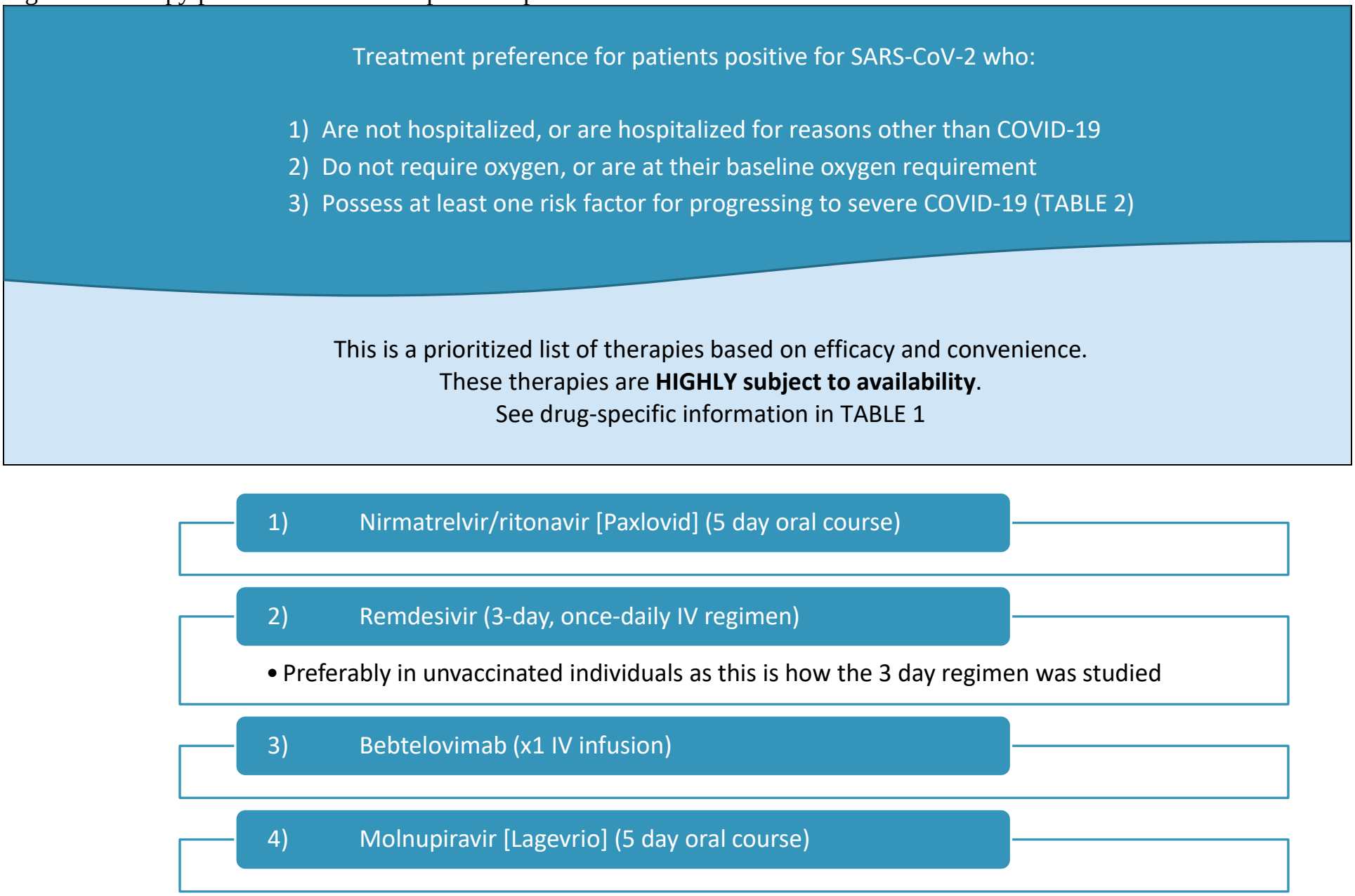

Table 3. Agents NOT recommended for the treatment or prevention of COVID-19

Treatment	Reason Not Recommended	Notes	Potential Safety Issues
Routine use of Antibiotics on Admission	Initial use of antibiotics in patients with COVID-19 should be avoided outside of septic shock or clinical suspicion for concurrent bacterial infection (bacterial pneumonia or other source). Procalcitonin may be a useful tool to rule out subsequent development of bacterial infection in cases with lack of improvement or clinical deterioration.	It is estimated that bacterial pneumonia co-infection is uncommon at presentation in patients with COVID-19 (3.5%)[15]. Secondary bacterial occurs in about 14% of hospitalized patients, but develops several days after admission in most instances. Secondary pneumonia is often characterized by worsening symptoms, increased sputum, focal, more dense infiltrates, new fevers and rising white cell counts. It typically occurs later in the course of disease and is most often observed in patients on mechanical ventilators.	Inappropriate use of antibiotics increases the risk of C. difficile, antibiotic associated toxicities (e.g. acute kidney injury), and acquisition of resistant organisms (e.g. MRSA).
Ivermectin	Insufficient evidence to suggest benefit. Recent prospective randomized trials failed to show a benefit in preventing progression to severe illness[8-10]	A high percentage of earlier pre-published and published studies to date that reported a possible benefit had incomplete information and significant methodological limitations[11]. Multiple studies on Ivermectin submitted to preprint sites and journals were later retracted due to significant methodological issues, and in some instances, evidence of data manipulation.[12-14] Several additional prospective clinical trials are underway	• Adverse effects may include dizziness, pruritis, nausea, or diarrhea. • Neurological adverse effects have been reported with the use of ivermectin for the treatment of onchocerciasis and other parasitic diseases, but it is not clear whether these adverse effects were caused by ivermectin or the underlying conditions. • Ivermectin is a minor cytochrome P 3A4 substrate and a p-glycoprotein substrate. • The FDA issued a warning in April 2020 that ivermectin intended for use in animals **should not be used** to treat COVID-19 in humans. • Teratogenic in animal studies; avoid in pregnancy

Selected References:

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6. Villar J, Ferrando C, Martinez D, et al. Dexamethasone treatment for the acute respiratory distress syndrome: a multicentre, randomised controlled trial. Lancet Respir Med 2020;8:267-76.

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9. Lopez-Medina E, Lopez P, Hurtado IC, et al. Effect of Ivermectin on Time to Resolution of Symptoms Among Adults With Mild COVID-19: A Randomized Clinical Trial. JAMA 2021;325:1426-35.

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13. Samaha AA, Mouawia H, Fawaz M, et al. Retraction: Samaha et al. Effects of a Single Dose of Ivermectin on Viral and Clinical Outcomes in Asymptomatic SARS-CoV-2 Infected Subjects: A Pilot Clinical Trial in Lebanon. Viruses 2021, 13, 989. Viruses 2021;13.

14. Marcus AO, Ivan. Retraction Watch: Retracted coranavirus (COVID-19) papers. 2022.

15. Langford BJ, So M, Raybardhan S, et al. Bacterial co-infection and secondary infection in patients with COVID-19: a living rapid review and meta-analysis. Clin Microbiol Infect 2020;26:1622-9.

16. Gottlieb RL, Vaca CE et al; GS-US-540-9012 (PINETREE) Investigators. Early Remdesivir to Prevent Progression to Severe Covid-19 in Outpatients. N Engl J Med. 2022 Jan 27;386(4):305-315. doi: 10.1056/NEJMoa2116846. Epub 2021 Dec 22. PMID: 34937145; PMCID: PMC8757570.