Outpatient Treatment Options for Mild to Moderate COVID-19

Intended Audience: Physicians, Pharmacists, and Allied health providers

Last Updated: 5/9/2022

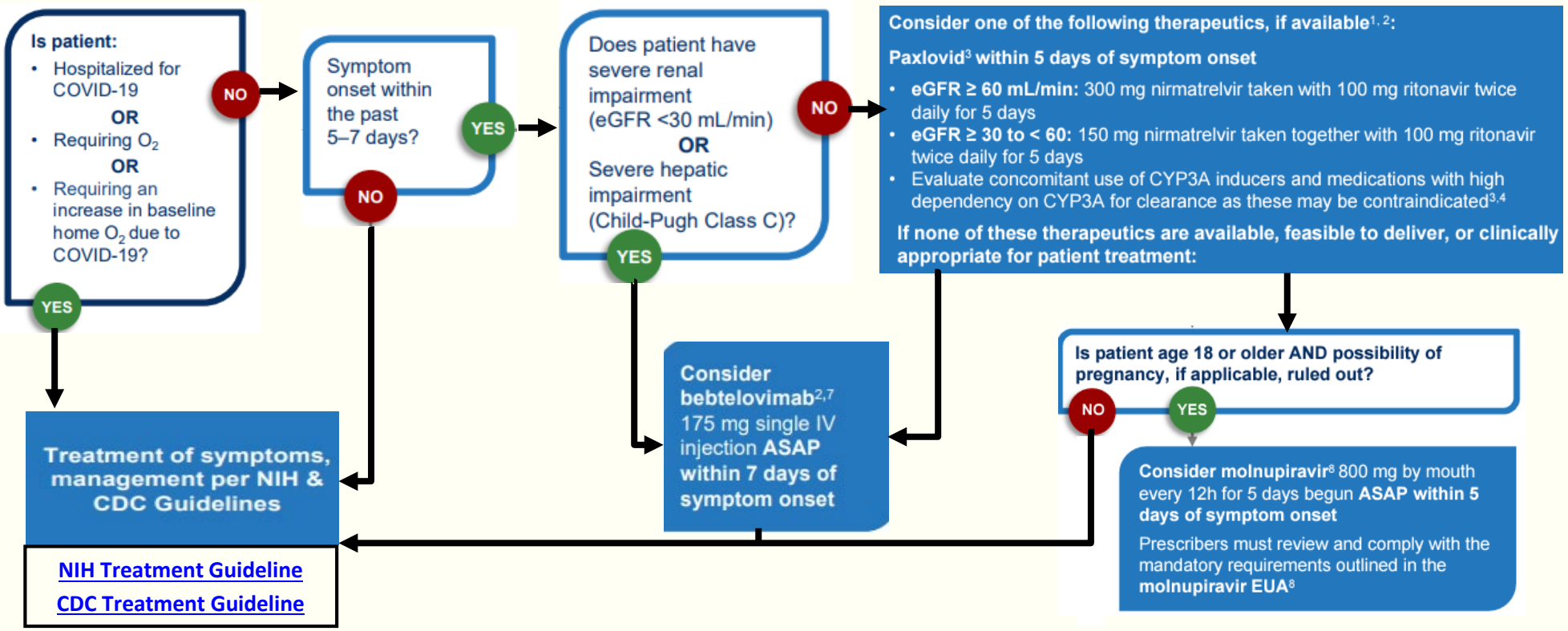
Background:

The FDA has issued an Emergency Use Authorization (EUA) for three additional agents used for the treatment of mild to moderate COVID-19 infection. These agents include two oral antiviral agents, Paxlovid and Molnupiravir, as well as an IV monoclonal antibody treatment, Bebtelovimab. These agents offer protection against currently circulating variants of SARS-CoV-2, including Omicron.

When considering treatment, it's important to assess and prioritize patients based on their risk of progressing to severe COVID-19. Consider reviewing the NIH Statement on Therapies for High Risk, Non-Hospitalized Patients with Mild to Moderate COVID-19 and CDC guidance on medical conditions associated with higher risk of severe COVID-19.

General Management of Outpatients with COVID-19

- Antiviral treatments are available by prescription only and should be initiated as soon as possible after diagnosis of COVID-19, and within 5 days of symptom onset.
- Monoclonal antibodies (Bebtelovimab) are available by physician order at Sarasota Memorial Hospital. The infusion must be administered as soon as possible after diagnosis of COVID-19, and within 7 days of symptom onset.
- Guidelines currently **recommend against** the use of antibacterial therapy (e.g., azithromycin, doxycycline) **AND** the use of Dexamethasone or other systemic glucocorticoids for the outpatient treatment of COVID-19 in the absence of another indication. Large clinical trials have shown no benefit in this population.



Comparison of FDA Authorized Outpatient Treatments:

	Paxlovid (Nirmatrelvir/Ritonavir) **Preferred**	Lagevrio (Molnupiravir)	Bebtelovimab
Mechanism of Action	Viral protease inhibitor; stops viral replication	Nucleoside analog; inhibits viral replication by viral mutagenesis	Monoclonal antibodies against spike protein; blocks viral entry
Prescribing Window	Within 5 days on symptom onset **Requires a prescription and usually obtained from a local pharmacy**		Within 7 days of symptom onset *Requires an order and obtained from hospital/clinic*
Treatment Efficacy[4]	88% reduction in hospitalizations/ deaths; NNT of ~ 18 in unvaccinated patients with at least one risk factor	30% reduction in hospitalizations/ deaths: NNT of ~35 in unvaccinated patients with at least one risk factor	*In vitro* activity against circulating Omicron subvariants, but no clinical efficacy data in patients who are at high risk of progressing to severe COVID-19
Age/Weight Requirements	12 years and older and at least 40 kg	18 years and older	12 years and older and at least 40 kg
Limitations of Use	Not for: • Patients requiring hospitalization due to severe or critical COVID-19 • Pre- or post-exposure prophylaxis or prevention of COVID-19	Not for: • Patients less than 18 years old • Initiation in patients who are hospitalized due to COVID-19 • Pre- or post-exposure prophylaxis or prevention of COVID-19	Not for patients who: • Are hospitalized due to COVID-19 • Require oxygen therapy, respiratory support, or increase in baseline oxygen requirements due to COVID-19
Dose	300 mg nirmatrelvir (two 150 mg tablets) PLUS 100 mg ritonavir every 12 hours **Dose must be adjusted for renal dysfunction**	800 mg molnupiravir (four 200 mg capsules) every 12 hours **Total of 8 capsules daily**	175 mg single IV push over at least 30 seconds **Requires one hour observation period**
Duration	5 days	5 days	Single dose
Renal Dose Adjustment	eGFR: 30-59: 150 mg nirmatrelvir (one tablet) plus 100 mg ritonavir BID eGFR < 30: not recommended	None	None
Hepatic Dose Adjustment	Not recommended in patients with severe hepatic impairment	None	Not specified
Pregnancy and Lactation	No dose adjustment needed	Not recommended in pregnancy; Breastfeeding not recommended during treatment or for 4 days after final dose (pump and dump)	No dose adjustment needed
Drug Interactions	CYP3A4 inducers and substrates (see below for list and resources)	None	Unlikely
Adverse Reactions	Dysgeusia, diarrhea, hypertension, myalgia	Diarrhea, nausea, dizziness	Infusion-related reactions, pyrexia, chills, dizziness, dyspnea, pruritus, rash
Websites	Paxlovid Website	Molnupiravir Website	Bebtelovimab Website

Drugs Interactions with Paxlovid:

Paxlovid has several drug interactions mediated by interaction with CYP3A4, including tacrolimus, Brilinta, Eliquis, and Xarelto. These interactions may require temporary discontinuation or medication dose adjustments and should be carefully evaluated prior to prescribing Paxlovid. See below for drug interaction screening resources.

- IDSA - Management of Drug Interactions With Nirmatrelvir/Ritonavir (Paxlovid): Resource for Clinicians
- The University of Liverpool COVID-19 Drug Interaction Checker is a great resource for evaluating drug interactions

Drugs contraindicated with concomitant Paxlovid use (not a comprehensive list):

- Alfuzosin
- Analgesics: meperidine, piroxicam
- Ranolazine
- Antiarrhythmics: amiodarone, dronedarone, flecainide, propafenone, quinidine
- Colchicine
- Anticonvulsants: carbamazepine, phenobarbital, phenytoin
- St John's Wort
- Antipsychotics: lurasidone (Latuda), clozapine
- Ergot derivatives
- Statins: lovastatin, simvastatin
- Sildenafil when being used for pulmonary hypertension
- Sedative/hypnotics: triazolam, oral midazolam
- Anticancer drugs: apalutamide
- Rifampin

Where to Find:

Oral COVID-19 medications are now widely available in the community via local pharmacies and health clinics. These agents are NOT authorized to be initiated in patients hospitalized with severe or critical COVID-19, but can be continued if admitted during course of therapy and prescriber feels continuation is warranted.

Monoclonal antibodies (e.g., bebtelovimab) must be ordered by a provider and obtained from a hospital or infusion location. Use this form to determine if your patient is eligible for treatment at Sarasota Memorial. Visit www.smh.com/covid19 for more COVID information.

HHS Medication Locator Website – Use this tool to find local pharmacies and Test-To-Treat locations near you or your patients.

Florida Department of Health Locator Website – Use this tool to find various treatment and prophylaxis sites, including monoclonal antibody treatments.

Please note that this information is from HHS and the Florida Department of Health and **does not guarantee availability** of the medications. It is highly encouraged to call the pharmacy to confirm availability before prescribing either of these agents.

References:

1. ASPR COVID-19 Outpatient Therapeutics Clinical Decision Aid – Updated April 2022
2. CDC - Underlying Medical Conditions Associated with Higher Risk for Severe COVID-19: Information for Healthcare Professionals
3. Molnupiravir [EUA Fact Sheet]. Merck; 2021
4. Paxlovid [EUA Fact Sheet]. Pfizer; 2021
5. Bebtelovimab [EUA Fact Sheet]. Lilly; 2022
6. For more details on clinical trial results, see Section 18 of each respective product's Fact Sheet for Health Care Providers.