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PUBLIC HEALTH ADVISORY

To:	All Health Care
From:	Dr. Isaac Benowitz, Maine CDC State Epidemiologist
Subject:	**Update on COVID-19 Therapeutics**
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Update on COVID-19 Therapeutics

This health alert provides updates on (1) the use of monoclonal antibody therapies and (2) the availability of oral antivirals and infusion therapies for outpatients with COVID-19. This alert also contains information on how healthcare providers and patients can access oral antivirals and infusion therapies, which must be started in the first few days after symptom onset. Finally, this alert provides information on a long-acting monoclonal antibody therapy for pre-exposure prophylaxis in immunocompromised patients.

In short, given the increasing prevalence of the SARS-CoV-2 Omicron variant in the State, Maine CDC recommends healthcare providers suspend use of two monoclonal antibody therapies, bamlanivimab/etesevimab ("bam-ete") and casirivimab/imdevimab (REGEN-COV). A third monoclonal antibody therapy, sotrovimab, remains effective against the Omicron variant and should continue to be offered to patients meeting criteria.

With respect to oral antiviral therapies, Paxlovid and molnupiravir, Maine CDC is working with two pharmacy chains, Walmart and Hannaford, to make these therapies available across the State. More information will follow soon describing how to determine which patients should receive these therapies in the setting of limited availabilities.

I. Recommendation to Suspend Use of Certain Monoclonal Antibody Therapies

As of January 7, 2022, the U.S. CDC estimates that the Omicron variant accounts for roughly 95% of all U.S. COVID-19 cases. In the New England region, Omicron is estimated to account for roughly 82% of all new COVID-19 cases. Point estimates from laboratories across Maine suggest the Omicron variant accounts for at least 70%, and perhaps up to 90%, of COVID-19 cases statewide. Modeling data based

on the spread of previous SARS-CoV-2 variants in Maine estimate that Omicron accounts for the majority of new COVID-19 cases in Maine. Analysis of monoclonal antibody therapies indicates that bam/ete and REGEN-COV are not effective against the Omicron variant and should not be used once the Omicron variant is predominant in a region.

Given the Omicron prevalence data noted above, Maine CDC recommends that, effective immediately, providers suspend use of bam-ete and REGEN-COV for the treatment COVID-19. Instead, healthcare providers should use sotrovimab when monoclonal antibody therapy is indicated. Maine CDC will update this recommendation if epidemiological conditions change.

II. Four Therapeutic Options for Outpatients with Mild/Moderate COVID-19 Illness

Several therapies are now available in the United States for the treatment of outpatients with mild/moderate COVID-19 illness who are at high risk for progression to severe COVID-19 disease. Two are oral antiviral therapies (Paxlovid and molnupiravir) and two are therapies available by infusion (remdesivir and sotrovimab).

These therapies are available in Maine in very limited supplies. Paxlovid, molnupiravir, and sotrovimab are only available under FDA Emergency Use Authorization (EUA) and should be prescribed only to outpatients with mild/moderate COVID-19 illness who meet other eligibility criteria as outlined in the respective EUA documents. Remdesivir is FDA-approved for hospitalized patients, and recently published literature suggests efficacy for the treatment of mild-moderate COVID-19 in outpatient settings.

Table 1 and Figure 1, attached, outline the currently available options for outpatients with mild/moderate COVID-19 illness and provide a flowchart that may be helpful to determine patient eligibility for these therapies.

Maine CDC is considering options to prioritize these therapies for patients who meet additional criteria to ensure that treatment is available to patients at the highest risk of severe COVID-19 related outcomes. Further information will be provided once available.

III. Pharmacies Dispensing Oral Antivirals in Maine

Paxlovid and molnupiravir are now available at selected Walmart and Hannaford stores across Maine. Maine CDC is working with these pharmacy chains to make these therapies available at locations that maximize access for patients across the State. For updated information on stores receiving these therapies and contact information for these locations, go to:

- *Walmart:* http://walmart.com/covidmedication
- *Hannaford:* https://www.hannaford.com/covid19antivirals

Supplies of these oral antiviral therapies are expected to increase over coming weeks, but the extent to which they will increase is unknown. Additionally, two Maine federally qualified health centers (Penobscot Community Health Center and HealthReach) will receive limited supplies of these oral antiviral therapies directly from the federal government, with supplies intended for patients with an established primary care relationship to these health centers.

IV. Medical Facilities Providing Infusions of Sotrovimab and Remdesivir

Sotrovimab and remdesivir are available to outpatients only via infusion. Maine CDC has partnered with over 40 locations across the state to provide monoclonal antibody therapy, and many of these locations will continue to provide sotrovimab. Maine CDC is working with these and other locations to determine where remdesivir will be available, and will communicate this information as it becomes available.

Locations offering monoclonal antibody infusion of sotrovimab:
https://www.maine.gov/dhhs/mecdc/infectious-disease/epi/airborne/coronavirus/mAb_ME%20Providers.pdf

V. Preparing to Treat Mild/Moderate COVID-19

All four treatment options described above must be started early in the course of illness. The oral antiviral therapies must be started in the first five days of illness, posing a hurdle to treat patients with mild/moderate illness. Remdesivir should be started in the first 7 days, and sotrovimab must be started in the first 10 days. To ensure that high-risk patients in Maine can access these therapies quickly, clinicians should ensure patient readiness to access these therapies if needed. Clinicians may also find it useful to consult a clinical decision-making tool for use of COVID-19 therapies recently developed by the federal Health and Human Services Office of the Assistant Secretary for Preparedness and Response (Figure 1, attached).

Clinicians should identify which of their patients would meet eligibility criteria for these outpatient therapies were they to develop mild/moderate COVID-19. Clinicians should consider communicating proactively with these patients to ensure that these patients have been vaccinated and have received a booster dose of vaccine if eligible, and to raise awareness of the existence of these therapies and steps patients should take quickly if they develop symptoms of COVID-19. Outpatient offices and health centers should consider how to ensure that patients who develop symptoms of COVID-19 and would be eligible for any of these therapies can be seen urgently for evaluation and prescription, if indicated. Also, since the therapies described above are not used for other conditions, health care provider groups could consider identifying one or more clinicians to maintain expertise in risks/benefits and patient management.

Patients, particularly those at risk for severe COVID-19 illness, should have a plan for how to quickly be tested for COVID-19 and evaluated clinically if they develop symptoms of COVID-19. A provider will need to evaluate the patient prior to determining if an oral antiviral or monoclonal antibody infusion is an appropriate treatment option and whether other care is needed. Testing could occur at an outpatient medical office or pharmacy, or via a rapid test kit, including kits obtained ahead of time for this possibility.

VI. Long-acting Monoclonal Antibody Therapy for Immunocompromised Patients

Astra-Zeneca's Evusheld is a long-acting monoclonal antibody therapy for use as pre-exposure prophylaxis against severe COVID-19 in high-risk, immunocompromised patients. Initial supplies in Maine, which are very limited, have been allocated to five clinical centers that routinely care for such patients, including cancer and transplant patients. These clinical centers have begun outreach to their established patients and can accept referrals of outside patients. Maine CDC is working with

stakeholders to develop a tiered approach to providing Evusheld, starting with the patients at highest risk, based on underlying medical conditions.

The following document describes patients who are currently eligible for Evusheld therapy and will be updated as other tiers are finalized: *Prioritization of Evusheld treatment at five clinical centers (https://www.maine.gov/tools/whatsnew/attach.php?id=6442309&an=1)*

This document also includes points of contact for the clinical centers where Evusheld is available. Any clinician caring for patients who meet current eligibility criteria, as described in this document, should contact one of the five clinical centers listed to refer patients for treatment. Evusheld will be available to patients who fit additional tiers once patients in higher tiers have received treatment. As supplies of Evusheld increase, this therapy may be made available at additional clinical centers in the State.

VII. Resources

NIH: The COVID-19 Treatment Guidelines Panel's Statement on Therapies for High-Risk, Nonhospitalized Patients With Mild to Moderate COVID-19: https://www.covid19treatmentguidelines.nih.gov/therapies/statement-on-therapies-for-high-risk-nonhospitalized-patients/

Sotrovimab
- EUA Fact Sheet for Healthcare Providers: https://www.fda.gov/media/149534/download
- EAU Fact Sheet for Patients: https://www.fda.gov/media/149533/download
- NIH Treatment guidelines: https://www.covid19treatmentguidelines.nih.gov/therapies/anti-sars-cov-2-antibody-products/anti-sars-cov-2-monoclonal-antibodies/

Remdesivir
- NIH outpatient treatment guidelines: https://www.idsociety.org/globalassets/idsa/practice-guidelines/covid-19/treatment/idsa-covid-19-gl-tx-and-mgmt---remdesivir-2021-12-24.pdf
- IDSA outpatient treatment: https://www.idsociety.org/globalassets/idsa/practice-guidelines/covid-19/treatment/idsa-covid-19-gl-tx-and-mgmt---remdesivir-2021-12-24.pdf
- NEJM study: https://www.nejm.org/doi/full/10.1056/NEJMoa2116846
- Prescribing info from the company: https://www.vekluryhcp.com

Paxlovid
- EAU Fact Sheet for Providers: https://www.fda.gov/media/155050/download
- EAU Fact Sheet for Patients: https://www.fda.gov/media/155051/download

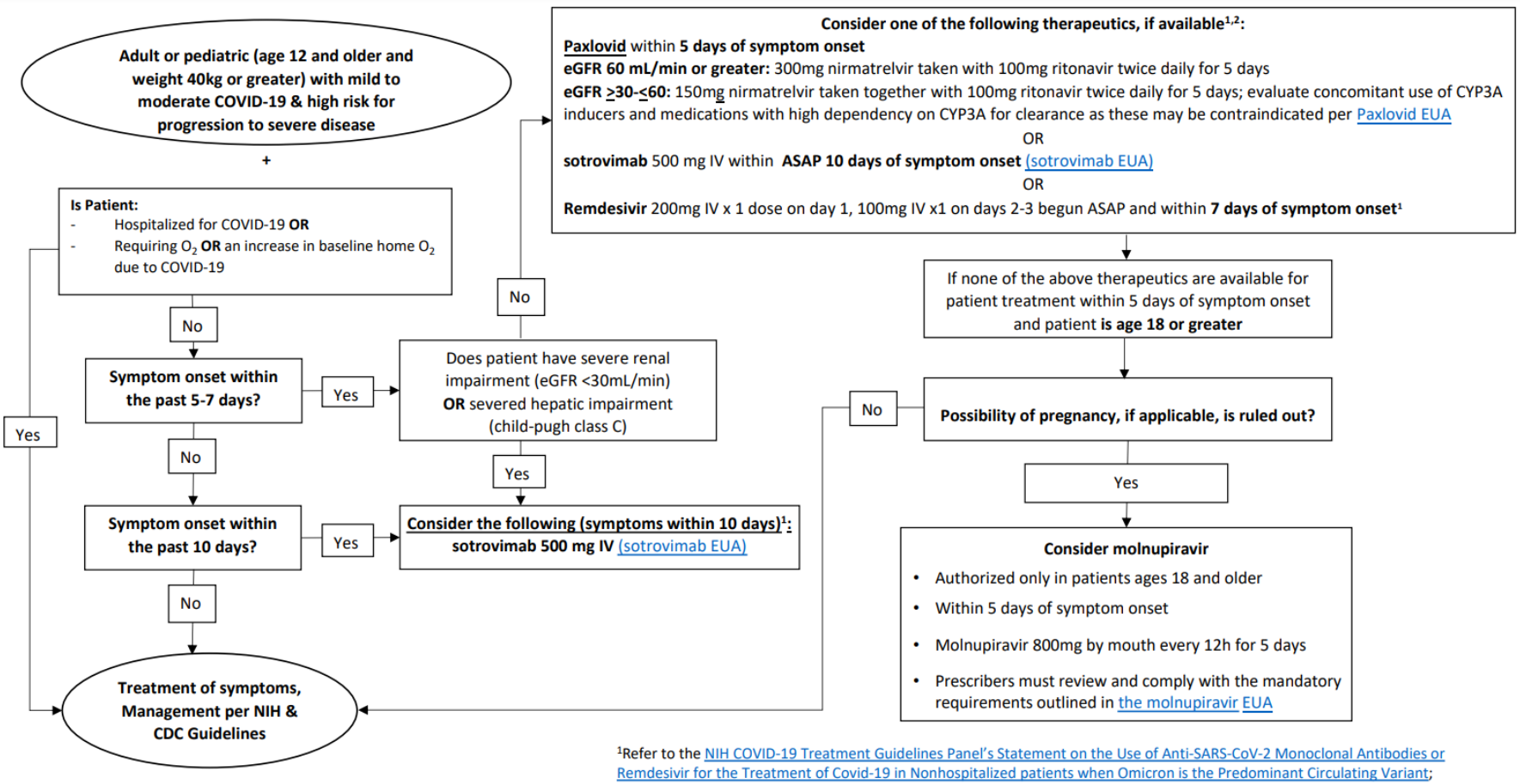
Molnupiravir
- FDA EUA Fact Sheet for Providers: https://www.fda.gov/media/155054/download
- FDA Fact Sheet for Patients: https://www.fda.gov/media/155055/download

Evusheld
- FDA EUA Fact Sheet for Providers: https://www.fda.gov/media/154701/download
- FDA Fact Sheet for Patients: https://www.fda.gov/media/154702/download

Table 1. Four Therapeutic Options for Outpatients with Mild/Moderate COVID-19 Illness

Drug name	**Remdesivir** (Veklury)	**Sotrovimab**	**Paxlovid** (ritonavir-boosted nirmatrelvir)	**Molnupiravir**
Company	Gilead	GlaxoSmithKline	Pfizer	Merck
Type of Medicine	Nucleoside analog	Monoclonal antibody	Protease inhibitor	Nucleoside analog
Relative Reductions in Hospitalizations	87%	85%	88%	30%
Start within # of Days after Symptom Onset	7	10	5	5
Route	IV	IV	Oral (with or without food)	Oral (with or without food)
Ages FDA Approval or Authorization For	Only approved for hospitalized patients. Outpatient treatment based on information from the literature.	FDA EUA for 12+ years and 40+ kg	FDA EUA for 12+ years and 40+ kg	FDA EUA for 18+ years of age
Eligible population	Outpatients with mild/moderate COVID-19 at high risk of progression to severe disease	Outpatients with mild/moderate COVID-19 at high risk for progression to severe disease	Outpatients with mild/moderate COVID-19 at high risk for progression to severe disease	Outpatients with mild/moderate COVID-19 at high risk for progression to severe disease, for whom alternative FDA-authorized COVID-19 treatment options are not accessible or clinically appropriate
Dosage	200 mg (day 1) 100 mg (day 2) 100 mg (day 3)	500 mg (single dose)	300 mg nirmatrelvir (2 x 150 mg tablets) with 100 mg ritonavir (1 x 100 mg tablet): all three taken together twice daily for 5 days	800 mg (4 x 200 mg capsules) given every 12 hours for 5 days
Some Specific Contraindications and Precautions (See Fact Sheets for full list)	Can reduce renal and liver functions		Contraindications/precautions include CYP3A dependent medication. Special dosing for moderate renal impairment; is not recommended for severe renal or hepatic impairment.	Advise those of childbearing age to use effective contraception
Pregnancy/ lactation	NIH: "Remdesivir should not be withheld from pregnant patients if it is otherwise indicated"	Authorized in pregnancy	See EUA Fact Sheet for info	Not recommended during pregnancy. See EUA Fact Sheet.

Figure 1. Therapeutics Decision Aid for Outpatients with Mild/Moderate COVID-19 Illness



Available online at: https://www.phe.gov/emergency/events/COVID19/therapeutics/Documents/COVID-Therapeutics-Decision-Aid.pdf