COVID-19 OUTPATIENT THERAPY

Guidance for outpatient therapies for patients with mild to moderate COVID-19

Michigan.gov/COVIDTherapy

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Purpose: Provide a clinically focused overview of outpatient therapies for mild to moderate COVID-19 in patients at risk for hospitalization or death - including times when the demand for these therapies meets or exceeds available supply. Guidelines may be adjusted should another surge cause an increased demand for therapeutics.

Background: Since November 2020, options for outpatient therapies for patients with mild to moderate COVID-19 have become increasingly available. These include monoclonal antibody (mAb) therapy and, more recently, oral antiviral therapy. Collectively, these medications have prevented thousands of hospitalizations and deaths in Michigan. Until recently, these medications have often been in limited supply, necessitating prioritizing eligibility to those at higher risk. As current COVID-19 activity declines and with increasing medication supply, there is no longer a need for limiting eligibility beyond the requirements established by the Food and Drug Administration (FDA). In the event of future COVID-19 surges and/or reductions in supply, prioritization may need to be reestablished.

It is important that all clinicians caring for COVID-19 patients be aware of the availability of these important life-saving medications and consider their use when clinically indicated.

Throughout this pandemic, the number of patients presenting for care has caused a surge at hospitals, urgent care, and primary care providers. To help communicate with the public, MDHHS has developed an *Ongoing Response to the COVID-19 cycle* recognizing the ability to flex mitigations measures and therapeutics based on the status of COVID in a community, region, and the state. The COVID-19 cycle is broken into three key phases:

- Response – local and state public health implement rapid response to a surge. The public may be advised to increase masking, testing, social distancing, and use of outpatient therapeutics.
- Recovery- this is post surge. No immediate resurgence predicted. Local and state public health will monitor conditions that could lead to future surges. Clinicians should continue to identify patients who may benefit from outpatient therapies.
- Readiness- A surge in cases is expected, with implications on severity of illness and hospital capacity. Local and state public health work to ensure enough supplies of tests, masks and medications are available. Increased communications to the public regarding possible new risks. Increased communications with clinicians should modification of eligibility criteria for COVID therapeutics be necessary.

Risk for Hospitalization or Death: The FDA has indicated in their emergency use authorizations that these medications are intended for those who are at increased risk of hospitalization or death who are not hospitalized when treatment is started. Those who are immunocompromised or not up to date on the COVID-19 vaccine are particularly at risk and those with any of the following conditions identified in the FDA EUAs:

- Older age (for example ≥65 years of age)
- Obesity or being overweight (e.g., BMI >25 kg/m^2), or BMI ≥85th percentile pediatrics
- Pregnancy
- Chronic kidney disease
- Diabetes
- Immunosuppressive disease or immunosuppressive treatment
- Cardiovascular disease (including congenital heart disease) or hypertension
- Chronic lung diseases (e.g., COPD, moderate to severe asthma, etc.)
- Sickle cell disease
- Neurodevelopmental disorders (e.g., cerebral palsy) or other complexity conditions
- Medical-related technological dependence (e.g., tracheostomy, gastrostomy)
- Other conditions identified by the CDC for the person at risk for disease severity

Available Outpatient Therapeutics: Currently, the following medications are readily available for use in eligible patients (per EUA) with mild to moderate COVID-19. Facilities administering medications by an intravenous route may be limited in their capacity to provide therapy and may need to establish criteria to assure higher risk patients are treated first.

- Find oral medications
- Find sites administering monoclonal antibody therapy

The information below and in the accompanying appendix is intended to be a brief overview of the medications and not a substitute for information in the applicable EUA. These medications are listed in their order of preference based on efficacy and convenience of use (consistent with NIH guidelines).

Paxlovid (nirmatrelvir/ritonavir)

- Mechanism: antiviral (protease inhibitor)
- Given orally twice daily for 5 days
- Started within 5 days of symptom onset
- Age ≥12 YO and weight ≥40 kg
- Evaluate for drug-to-drug interactions

Remdesivir

- Mechanism: antiviral (RNA polymerase inhibitor)
- Given by intravenous infusion daily for 3 days
- Started within 7 days of symptom onset
- Can be used for children weighing >3kg as an alternative to monoclonal antibody therapy

Bebtelovimab[1]

- Mechanism: neutralizing monoclonal antibody
- Given by intravenous infusion once
- Started within 7 days of symptom onset
- Age ≥12 YO and weight ≥40 kg
- Used when other treatment options are not accessible or clinically appropriate.

Molnupiravir

- Mechanism: antiviral (mutagenic)
- Given orally twice daily for 5 days
- Started within 5 days of symptom onset
- Age ≥18 YO
- Contraindicated in pregnancy
- Used when other treatment options are not accessible or clinically appropriate

EUA Provider Factsheet Links

Paxlovid: Fact Sheet for Healthcare Providers: Emergency Use Authorization for Paxlovid
Remdesivir: Veklury (remdesivir) Fact Sheet for Healthcare Providers
Bebtelovimab: Fact Sheet for Healthcare Providers: Emergency Use Authorization for Bebtelovimab
Molnupiravir: Fact Sheet for Healthcare Providers: Emergency Use Authorization for Molnupiravir

The PINETREE study on the use of outpatient remdesivir: Study to Evaluate the Efficacy and Safety of Remdesivir (GS-5734™) Treatment of Coronavirus Disease 2019 (COVID-19) in an Outpatient Setting

Additional Information

Additional information about these medications can be obtained through the MDHHS therapeutics website at Michigan.gov/COVIDTherapy - select "For Health Care Providers". Questions may be submitted by email to mdhhs-covid-therapies@michigan.gov.

[1] Bebtelovimab is active in vitro against all circulating Omicron subvariants, but there are no clinical efficacy data from placebo-controlled trials that evaluated the use of bebtelovimab in patients who are at high risk of progressing to severe COVID-19. Therefore, bebtelovimab should be used only when the preferred treatment options are not available, feasible to use, or clinically appropriate.

Appendix A

COVID-19 OUTPATIENT THERAPY: Guidance for outpatient management of patients with mild to moderate COVID-19.				
	Paxlovid (ritonavir-boosted nirmatrelvir)	**Remdesivir**	**Bebtelovimab**	**Molnupiravir***
Core Criteria	• Mild to moderate COVID-19. • Test positive for the virus causing COVID-19 including PCR and antigen testing. Self-attestation of positive home test results permitted. • At high risk for disease progression and hospitalization or death (see below).			
FDA Fact Sheet	Paxlovid Fact Sheet	Remdesivir Fact Sheet	Bebtelovimab Fact Sheet	Molnupiravir Fact Sheet
Age/weight	≥12 YO / 40 kg	≥28 Days old and ≥3kg	≥12 YO / 40 kg	≥ 18 YO / N/A
Days from symptom onset	5 days	7 days	7 days	5 days
Duration of therapy	5 days	Daily x3 days	Once	5 days
Route of administration	Oral	Intravenous	Intravenous	Oral
First line/Alternative	First line	First line	Alternative	Alternative
Risk Factors	• Older age (for example ≥65 years of age) • Obesity or being overweight (for example, adults with BMI >25 kg/m2, or if 12 to 17 years of age, have BMI ≥85th percentile for their age and gender based on CDC growth charts) • Pregnancy • Chronic kidney disease • Diabetes • Immunosuppressive disease or immunosuppressive treatment • Cardiovascular disease (including congenital heart disease) or hypertension • Chronic lung diseases (for example, chronic obstructive pulmonary disease, asthma [moderate-to-severe], interstitial lung disease, cystic fibrosis and pulmonary hypertension) • Sickle cell disease • Neurodevelopmental disorders (for example, cerebral palsy) or other conditions that confer medical complexity (for example, genetic or metabolic syndromes and severe congenital anomalies) • Having a medical-related technological dependence (for example, tracheostomy, gastrostomy, or positive pressure ventilation [not related to COVID 19]) Other medical conditions or factors (for example, race or ethnicity) may also place individual patients at high risk for progression to severe COVID-19, and authorization of sotrovimab under the EUA is not limited to the medical conditions or factors listed above. For additional information on medical conditions and factors associated with increased risk for progression to severe COVID-19, see the CDC web page: People with Certain Medical Conditions. Healthcare providers should consider the benefit-risk for an individual patient.			
Prioritization	N/A	Higher-risk patients may be scheduled before lower risk patients.	Higher-risk patients may be scheduled before lower risk patients.	N/A
Vaccination Status	N/A	Those not up to date should be treated first	Those not up to date should be treated first	N/A
Drug Interactions	Paxlovid drug interaction guides: MI Medicine Tool and Liverpool COVID-19 Interactions (covid19-druginteractions.org)			