

Information Sheet

DATE

January 26, 2022

SUBJECT

Update Regarding COVID-19 Therapeutics



BACKGROUND

There have been several recent updates involving the coronavirus disease 2019 (COVID-19) therapeutic supply purchased by the federal government and allocated by the state. There were also recent updates on the outpatient use of remdesivir, which is commercially available and not currently offered as a part of the state-led allocation.

INFORMATION

OMICRON VARIANT AND THE MONOCLONAL ANTIBODY THERAPEUTICS

Centers for Disease Control and Prevention ([CDC data](#)) released last week confirms that Omicron is the overwhelmingly dominant variant of concern (VOC) in the United States at a prevalence of greater than 97.8% in all regions and nationally greater than 99%. Private sector data points to Omicron's dominance as well. For example, Walgreens [estimates](#) that every state is above 95% Omicron. As of January 25, there have been 715 cases in Montana infected with the Omicron variant, detected in most of Montana's local and tribal health jurisdictions. Last week, 38/38 (100%) specimens that were collected and sequenced were Omicron. To date, in the month of January, 622/678 (92%) specimens in Montana that were collected and sequenced were Omicron

On January 24, 2022, the Food and Drug Administration (FDA) updated the Emergency Use Authorization (EUA) fact sheets for [bamlanivimab and etesevimab](#) and [casirivimab and imdevimab](#). FDA now states these two treatments are **not currently authorized** for use anywhere in the U.S., due to the prevalence of Omicron. The [National Institutes of Health \(NIH\) updated its clinical guidelines](#) to recommend against the use of bamlanivimab plus etesevimab and casirivimab plus imdevimab (REGEN-COV) at this time. HHS/ASPR advises sites to keep their existing supplies on hand and await further guidance on inventory management. Please see the [FDA press announcement](#) for additional information.

As a result of the extremely high prevalence of Omicron and recent guidance from FDA and NIH, HHS/ASPR will not include bamlanivimab plus etesevimab and casirivimab plus imdevimab (REGEN-COV) in the COVID-19 therapeutics allocations at this time.

OTHER COVID-19 THERAPEUTICS

There are several other available options for outpatient treatment of mild to moderate COVID-19 in individuals at risk for progression to severe disease, as described below.

SOTROVIMAB

The FDA updated the Health Care Provider Fact Sheets for [sotrovimab](#) with specific information regarding expected activity against the Omicron variant (B.1.1.529/BA.1). These data show that sotrovimab **appears to retain** activity against the Omicron variant.

[Sotrovimab](#) is available for the treatment of mild-to-moderate coronavirus disease 2019 (COVID-19) in adults and pediatric patients (12 years of age and older weighing at least 40 kg) with positive results of direct SARS-

CoV-2 viral testing, and who are at high risk for progression to severe COVID-19, including hospitalization or death.

The following medical conditions or other factors may place adults and pediatric patients (age 12-17 years and weighing at least 40 kg) at higher risk for severe COVID-19:

- Older age (≥ 65 years of age)
- Obesity or being overweight (adults with BMI > 25 kg/m, or if age 12-17, have BMI ≥ 85 th 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 place individual patients at high risk for severe COVID-19. ***Authorization of monoclonal antibody therapy under the EUA is not limited to the medical conditions or factors listed above.*** For more information on medical conditions and factors associated with increased risk, see [the CDC's website](#). Healthcare providers should consider the benefit-risk ratio for individual patients. A full description of the clinical indications is included in the Emergency Use Authorization for the available product, [sotrovimab](#).

Monoclonal antibody treatments are not authorized for use in patients who are hospitalized due to COVID-19, in those who require oxygen therapy due to COVID-19, or in those who require an increase in baseline oxygen flow rate due to COVID-19 (e.g., for those on chronic oxygen therapy due to an underlying non-COVID-19 related comorbidity).

There is a limited supply of sotrovimab available for request, when necessary.

ORAL ANTIVIRAL MEDICATIONS

Two oral COVID-19 antiviral medications for non-hospitalized patients at high risk for progression to severe COVID-19 recently received Emergency Use Authorization (EUA) from the U.S. Food and Drug Administration (FDA). DPHHS is working with the Federal Retail Pharmacy Program to distribute these therapeutics across the state and expects to receive allocations of these products every two weeks. DPHHS will have some flexibility in offering to specific pharmacy sites as well as not all Montana counties have access to one of the federal partners. The oral antivirals described below may only be prescribed for an individual patient by physicians, advanced practice registered nurses, and physician assistants that are licensed or authorized under state law to prescribe drugs in the therapeutic class to which the oral antivirals belong (i.e., anti-infectives). Both oral antivirals must be initiated within 5 days of symptom onset. A test-to-treat model is an ideal strategy for the oral antiviral products, given the short window between symptom onset and treatment required by the EUA. Both EUAs direct readers to the Centers for Disease Control and Prevention [People with Certain Medical Conditions](#) for information on medical conditions and factors associated with increased risk for progression to severe COVID-19 and state the healthcare providers should consider the benefit-risk for an individual patient.

Once the oral antiviral products arrive in the state, site information will be available on the DPHHS [COVID-19 Therapeutics](#) webpage.

PAXLOVID

Paxlovid (Pfizer product) received [EUA](#) on December 22, 2021. Paxlovid is comprised of nirmatrelvir, a SARS-CoV-2 main protease inhibitor, co-packaged with ritonavir, an HIV-1 protease inhibitor and CYP3A inhibitor. Ritonavir, which has no activity against SARS-CoV-2 on its own, is included to inhibit the CYP3A-mediated metabolism of nirmatrelvir and consequently increase nirmatrelvir plasma concentrations to levels anticipated to inhibit SARS-CoV-2 replication.

Paxlovid received EUA for the treatment of mild-to-moderate coronavirus disease 2019 (COVID-19) in adults and pediatric patients (12 years of age and older weighing at least 40 kg) with positive results of direct severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) viral testing, and who are at high risk for progression to severe COVID-19, including hospitalization or death.

The EUA Fact Sheet for Healthcare Providers includes important information on potential drug interactions, drug resistance, and special dosing considerations for individuals with moderate renal impairment. Healthcare providers should carefully review the EUA and National Institutes of Health (NIH) statement below prior to prescribing this medication.

- [Paxlovid Fact Sheet for Healthcare Providers](#)
- [Paxlovid Patients and Caregivers](#)
- NIH: [The COVID-19 Treatment Guidelines Panel's Statement on Potential Drug-Drug Interactions Between Ritonavir-Boosted Nirmatrelvir \(Paxlovid\) and Concomitant Medications](#)

MOLNUPIRAVIR

Molnupiravir (Merck product) received [EUA](#) on December 23, 2021. Molnupiravir is a nucleoside analogue that inhibits SARS-CoV-2 replication by viral mutagenesis.

Molnupiravir may only be used for the treatment of mild-to-moderate COVID-19 in adults:

- With positive results of direct SARS-CoV-2 viral testing, **and**
- Who are at high-risk for progression to severe COVID-19, including hospitalization or death, **and**
- For whom alternative COVID-19 treatment options authorized by FDA are not accessible or clinically appropriate.

The EUA Fact Sheet for Healthcare Providers includes important information on the use of this product in individuals of reproductive age with childbearing potential. Molnupiravir is not recommended for use during pregnancy. Molnupiravir is not authorized for use in patients less than 18 years of age because it may affect bone and cartilage growth. Healthcare providers should carefully review the EUA prior to prescribing this medication.

- [Molnupiravir Fact Sheet for Healthcare Providers](#)
- [Molnupiravir Fact Sheet for Patients and Caregivers](#)
- [FDA Molnupiravir Checklist Tool for Prescribers](#)

REMDESIVIR

The U.S. Food and Drug Administration (FDA) has issued an Emergency Use Authorization (EUA) to permit the emergency use of VEKLURY (remdesivir) for the treatment of coronavirus disease 2019 (COVID-19) in pediatric patients weighing 3.5 kg to less than 40 kg or pediatric patients less than 12 years of age

weighing at least 3.5 kg, with positive results of direct severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) viral testing, who are:

- Hospitalized, or
- Not hospitalized and have mild-to-moderate COVID-19, and are at high risk for progression to severe COVID-19, including hospitalization or death. Refer to [CDC website](#) for additional details.

Remdesivir resources:

- [Remdesivir Fact Sheet for Healthcare Providers](#)
- [Remdesivir Fact Sheet for Parents and Caregivers](#)

MONOCLONAL ANTIBODY FOR PRE-EXPOSURE PROPHYLAXIS

EVUSHELD

[Evusheld](#) (AZD7442) is tixagevimab and cilgavimab, which are neutralizing IgG1 monoclonal antibodies that bind to distinct, non-overlapping epitopes within the receptor binding domain of the spike protein of SARS-CoV2. Evusheld is authorized for the pre-exposure prophylaxis of adults and certain pediatric individuals with immune compromised systems and thus are not expected to mount an adequate immune response following vaccination, or for whom vaccination is not indicated due to health conditions or a history of severe allergic reactions. The EUA states ***Evusheld (AZD7442) is not a substitute for vaccination.***

The FDA issued an EUA for the emergency use of the unapproved product EVUSHELD (tixagevimab co-packaged with cilgavimab) for the pre-exposure prophylaxis of COVID-19 in adults and pediatric individuals (12 years of age and older weighing at least 40 kg):

- Who are not currently infected with SARS-CoV-2 and who have not had a known recent exposure to an individual infected with SARS-CoV-2; **and**
 - o Who have moderate to severe immune compromise due to a medical condition or receipt of immunosuppressive medications or treatments and may not mount an adequate immune response to COVID-19 vaccination; **or**
 - o For whom vaccination with any available COVID-19 vaccine, according to the approved or authorized schedule, is not recommended due to a history of severe adverse reaction (e.g., severe allergic reaction) to a COVID-19 vaccine(s) and/or COVID-19 vaccine component(s).

This product has been distributed to facilities caring for potentially eligible populations, per the EUA. Facilities may develop prioritization strategies for equitable allocation of this product. Healthcare providers should carefully review the EUA prior to prescribing this medication. Sites offering Evusheld are available on the [HHS Therapeutics Distribution Locator for Provider Use](#).

RECOMMENDATIONS

HEALTHCARE PROVIDERS

1. Review the CDC guidance for [People with Certain Medical Conditions](#) and the FDA EUA Fact Sheets for Healthcare Providers for appropriate patient selection for treatment or pre-exposure prophylaxis.
 - a. [Sotrovimab Fact Sheet for Healthcare Providers](#)
 - b. [Paxlovid Fact Sheet for Healthcare Providers](#)
 - c. [Molnupiravir Fact Sheet for Healthcare Providers](#)
 - d. [Remdesivir Fact Sheet for Healthcare Providers](#) (commercially available)
 - e. [Evusheld Fact Sheet for Healthcare Providers](#)

2. Develop a test-to-treat strategy for high risk individuals who test positive for COVID-19, given the short window between symptom onset and treatment required by the EUAs (e.g., within 5 days of symptoms onset for the oral antiviral products).
3. Review the [HHS Therapeutics Distribution Locator for Provider Use](#) which provides sites of the oral antiviral and Evusheld administration.
4. Review the National Institutes of Health Statements on the use of COVID-19 therapeutics in the setting of product scarcity.
 - a. December 23, 2021: [COVID-19 Treatment Guidelines Panel's Interim Statement on Patient Prioritization for Outpatient Anti-SARS-CoV-2 Therapies or Preventive Strategies When There Are Logistical or Supply Constraints](#)
 - b. December 30, 2021: [The COVID-19 Treatment Guidelines Panel's Statement on Therapies for High-Risk, Nonhospitalized Patients With Mild to Moderate COVID-19](#)
5. Review the Infectious Diseases Society of America updates on Evusheld, the oral antiviral agents, and remdesivir.
 - a. [Oral Antiviral Agents for COVID-19](#)
 - b. [Neutralizing Antibodies for Pre-exposure and Post-exposure Prophylaxis](#)
 - c. [Remdesivir](#) (commercially available)
6. Counsel patients on safe prescription pick up practices for the oral antiviral therapeutics to minimize COVID-19 exposure for pharmacy personnel and the general public.
7. Reinforce the central importance of receiving [COVID-19 vaccination](#) and a booster dose, when eligible. Given recent influenza activity in the state, advise patients on the opportunity for concurrent influenza vaccination.

PUBLIC HEALTH AGENCIES

1. Develop a test-to-treat referral approach for high risk individuals who test positive for COVID-19, given the short window between symptom onset and treatment required by the EUAs (e.g., within 5 days of symptoms onset for the oral antiviral products), in addition to a need for a healthcare provider order for all of these treatments. Advise individuals who test positive early about treatment options and the need for medical consultation prior to receipt of these treatment.
2. Review the DPHHS [COVID-19 Therapeutics](#) webpage for administration site locations.
3. Reinforce the central importance of receiving [COVID-19 vaccination](#) and a booster dose, when eligible.

FACILITIES OFFERING COVID-19 THERAPEUTICS

1. Reporting requirements for inventories and utilization:
 - a. Weekly reporting is required for sotrovimab.
 - i. Long-term care/skilled nursing facilities report to National Healthcare Safety Network (NHSN).
 - ii. Hospitals and hospital pharmacies report to HHSProtect, TeleTracking, Health Departments
 - iii. Non-hospital facilities report to HHS TeleTracking
 - b. Daily reporting is required for Evusheld, Paxlovid, and molnupiravir through HPoP. Please find additional information on facility-level reporting [here](#).

Facilities interested in requesting a portion of the state allocation should contact Dr. Maggie Cook-Shimanek at Margaret.Cook-Shimanek@mt.gov.

Referenced Links

1. Molnupiravir Fact Sheet for Healthcare Providers - <https://www.fda.gov/media/155054/download>
2. Molnupiravir Fact Sheet for Patients and Caregivers - <https://www.fda.gov/media/155055/download>
3. Paxlovid Fact Sheet for Healthcare Providers - <https://www.fda.gov/media/155050/download>
4. Paxlovid Patients and Caregivers - <https://www.fda.gov/media/155051/download>

5. Evusheld Fact Sheet for Healthcare Providers - <https://www.fda.gov/media/154701/download>
6. Bamlanivimab and etesevimab Fact Sheet for Healthcare Providers administered together - <https://www.fda.gov/media/145802/download>
7. Casirivimab and imdevimab Fact Sheet for Healthcare Providers (REGEN-COV) - <https://www.fda.gov/media/145611/download>
8. Sotrovimab Fact Sheet for Healthcare Providers - <https://www.fda.gov/media/149534/download>
9. Centers for Disease Control and Prevention (CDC) website: <https://www.cdc.gov/coronavirus/2019-ncov/needextra-precautions/people-with-medical-conditions.html>
10. NIH COVID-19 Treatment Guidelines Panel's Statement: <https://www.covid19treatmentguidelines.nih.gov/therapies/statement-on-anti-sars-cov-2-mabs-and-rdv-and-omicron/>
11. NIH COVID-19 Treatment Guidelines Panel's Interim Statement on Patient Prioritization for Outpatient Anti-SARS-CoV-2 Therapies or Preventive Strategies When There Are Logistical or Supply Constraints: <https://www.covid19treatmentguidelines.nih.gov/therapies/statement-on-patient-prioritization-for-outpatient-therapies/>
12. DPHHS Weekly Montana COVID-19 Epi Profile - <https://dphhs.mt.gov/publichealth/cdepi/diseases/coronavirusmt/demographics>
13. FDA Molnupiravir Checklist Tool for Prescribers - <https://www.fda.gov/media/155118/download>