

Montana Health Alert Network

DPHHS HAN

UPDATE

Cover Sheet

DATE

December 30, 2021

SUBJECT

Recent Updates Regarding COVID-19 Therapeutics

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DPHHS HAN

Information Sheet



DATE

December 30, 2021

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. Two oral antiviral products and a monoclonal antibody product for pre-exposure prophylaxis are newly available in the state-led allocation and there are updates regarding the existing state-allocated therapeutics, *bamlanivimab* and *etesevimab*, *casirivimab* and *imdevimab*, and *sotrovimab*, as below.

As with past potentially scarce state-led resource allocations (e.g., *remdesivir*), it is expected that facilities will view the products discussed below as a shared community resource, reserved for judicious use in high risk populations. If demand outpaces supply for a particular product, allocations will be determined through a method developed by DPHHS in consultation with healthcare ethicists.

INFORMATION

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. Montana received a federal allocation of 180 patient courses of this medication. *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 prior to prescribing this medication.

- [Paxlovid Fact Sheet for Healthcare Providers](#)
- [Paxlovid Patients and Caregivers](#)

Molnupiravir

Molnupiravir (Merck product) received [EUA](#) on December 23, 2021. Montana received a federal allocation of 800 patient courses of this medication. *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](#)

Omicron Variant and *Bamlanivimab* and *Etesevimab*, *Casirivimab* and *Imdevimab*, and *Sotrovimab*

The FDA updated the Health Care Provider Fact Sheets for [bamlanivimab and etesevimab](#) administered together, [casirivimab and imdevimab](#) (REGEN-COV), and [sotrovimab](#) with specific information regarding expected activity against the Omicron variant (B.1.1.529/BA.1). These data show that it is *unlikely* that *bamlanivimab* and *etesevimab* administered together or REGEN-COV will retain activity against this variant. Based on similar cell culture data currently available, *sotrovimab* *appears to retain* activity against the Omicron variant.

The U.S. Health and Human Services (HHS) acknowledges the Omicron situation may vary in different geographic regions of the country and for different health care facilities. There may be circumstances, such as lower frequency of Omicron in a region and limited supply of alternative treatment options, in which the use of for *bamlanivimab* and *etesevimab* administered together and *casirivimab* and *imdevimab* is clinically appropriate. HHS encourages health departments and healthcare providers to assess local data and review the National Institutes of Health guidelines to help inform treatment decisions.

Additional information, including thresholds for continued use based on omicron prevalence, is available in the [COVID-19 Treatment Guidelines Panel's Statement on the Use of Anti-SARS-CoV-2 Monoclonal Antibodies or Remdesivir for](#)

[the Treatment of COVID-19 in Nonhospitalized Patients When Omicron Is the Predominant Circulating Variant](#). The [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](#) offers guidance on patient prioritization for receipt of treatment. Sites with monoclonal antibody therapeutics are currently available on the DPHHS [COVID-19 Therapeutics](#) webpage.

There is a limited supply of *sotrovimab*, *casirivimab* and *imdevimab*, and *bamlanivimab* and *etesevimab* available for order in the Amerisource distributor portal, when necessary.

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***
 - 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***
 - 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).

The initial allocation of 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* will soon be available on the DPHHS [COVID-19 Therapeutics](#) webpage.

RECOMMENDATIONS

Healthcare Providers

1. Review the CDC guidance for [People with Certain Medical Conditions](#) and the new and/or updated FDA EUA Fact Sheets for Healthcare Providers for appropriate patient selection for treatment.
 - a. [Molnupiravir Fact Sheet for Healthcare Providers](#)
 - b. [Paxlovid Fact Sheet for Healthcare Providers](#)
 - c. [Evusheld Fact Sheet for Healthcare Providers](#)
 - d. [Bamlanivimab and etesevimab Fact Sheet for Healthcare Providers](#) administered together
 - e. [Casirivimab and imdevimab Fact Sheet for Healthcare Providers](#) (REGEN-COV)
 - f. [Sotrovimab 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. Consider [local Omicron variant prevalence](#) in the selection of outpatient therapeutics.
4. Review the National Institutes of Health Statements on the use of COVID-19 therapeutics in the setting of product scarcity and circulating omicron variant.
 - a. [COVID-19 Treatment Guidelines Panel's Statement on the Use of Anti-SARS-CoV-2 Monoclonal Antibodies or Remdesivir for the Treatment of COVID-19 in Nonhospitalized Patients When Omicron Is the Predominant Circulating Variant](#)
 - b. [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](#)
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](#)
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.

Public Health Agencies

1. Monitor and report on local Omicron variant prevalence.
2. 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.
3. Review the DPHHS [COVID-19 Therapeutics](#) webpage for administration site locations.

Facilities Offering COVID-19 Therapeutics

1. Reporting requirements for inventories and utilization:
2. Weekly reporting is required for *bamlanivimab* and *etesevimab*, *casirivimab* and *imdevimab*.
3. Long-term care/skilled nursing facilities report to National Healthcare Safety Network (NHSN).
4. Hospitals and hospital pharmacies report to HHSProtect, TeleTracking, Health Departments
5. Non-hospital facilities report to HHS TeleTracking
6. Daily reporting is required for *Evusheld*, *Paxlovid*, and *molnupiravir* through HPoP.

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>