

DATE:	01/15/2022
TO:	Health Alert Network
FROM:	Keara Klinepeter, Acting Secretary of Health
SUBJECT:	Therapeutics to Prevent and Treat COVID-19
DISTRIBUTION:	Statewide
LOCATION:	n/a
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COUNTY:	n/a
MUNICIPALITY:	n/a
ZIP CODE:	n/a

This transmission is a “Health Advisory” which provides important information for a specific incident or situation; may not require immediate action.

HOSPITALS: PLEASE SHARE WITH ALL MEDICAL, PEDIATRIC, NURSING AND LABORATORY STAFF IN YOUR HOSPITAL; **EMS COUNCILS:** PLEASE DISTRIBUTE AS APPROPRIATE; **FQHCs:** PLEASE DISTRIBUTE AS APPROPRIATE **LOCAL HEALTH JURISDICTIONS:** PLEASE DISTRIBUTE AS APPROPRIATE; **PROFESSIONAL ORGANIZATIONS:** PLEASE DISTRIBUTE TO YOUR MEMBERSHIP; **LONG-TERM CARE FACILITIES:** PLEASE SHARE WITH ALL MEDICAL, INFECTION CONTROL, AND NURSING STAFF IN YOUR FACILITY

- The SARS-CoV-2 Omicron variant has quickly become the dominant variant of concern in the United States and is present in all 50 states, including Pennsylvania.
- Vaccination (especially after receipt of a booster dose) is expected to protect against severe illness, hospitalizations, and deaths from infection with the Omicron variant.
- Therapeutics are also available for preventing and treating COVID-19 in specific at-risk populations.
- Providers may continue to consider treatment options previously detailed in [HAN 575](#) and [HAN 613](#).
 - The FDA has issued Emergency Use Authorizations (EUAs) for anti-SARS-CoV-2 monoclonal antibodies, combination therapies bamlanivimab plus etesevimab and casirivimab plus imdevimab (REGEN-COV), and monotherapy sotrovimab for use in non-hospitalized patients.
 - The federal government’s current supply of sotrovimab is *extremely limited*. Continued use of bamlanivimab plus etesevimab and casirivimab plus imdevimab (REGEN-COV) monoclonal antibody products is recommended while reserving sotrovimab for treatment of eligible outpatients at *highest* risk.
- Treatment options also include intravenous (IV) antiviral agent, remdesivir, for hospitalized patients and two oral antiviral agents, Paxlovid and molnupiravir for non-hospitalized patients.
- Pre-exposure prevention of COVID-19 with EVUSHELD is available for certain at-risk individuals.
- Post-exposure prophylaxis for COVID-19 with casirivimab plus imdevimab (REGEN-COV) or bamlanivimab plus etesevimab is available for certain at-risk individuals.
- Details on how to obtain the agents listed above can be found at the [PA DOH website](#).
- If you have questions about this guidance, please call your local health department or **1-877-PA-HEALTH (1-877-724-3258)**.

A. Background

Pennsylvania Department of Health (DOH) provides this guidance based on available information about COVID-19 and is subject to change.

In Pennsylvania, COVID-19 cases and COVID-19-related hospitalizations continue to occur. DOH aims to provide healthcare providers (in both inpatient and outpatient settings) an outline of the current options available for treatment of COVID-19. This advisory is supplemental to [HAN 575](#) and [HAN 613](#) and includes additional information about oral antiviral agents. Insurance coverage for treatment remains [mandated by federal law](#). Healthcare providers are encouraged to utilize the treatment options, when clinically appropriate, with the goal of reducing hospital admissions and/or duration of hospitalizations, and the overall COVID-19 burden in the community.

The SARS-CoV-2 [Omicron](#) variant has quickly become the dominant variant of concern in the United States and is present in all 50 states. Eligible individuals should get all [vaccines and booster shots](#) as the best preventive measure available against severe disease, hospitalizations, and death due to COVID-19. Vaccination is expected to protect against severe illness, hospitalizations, and deaths from infection with the Omicron variant. Some studies have found lower effectiveness of the primary series of vaccines against infection and demonstrated the importance of booster doses.¹⁻³

Therapeutics are also available for preventing and treating COVID-19 in specific at-risk populations. These therapeutics differ in efficacy, route of administration, risk profile, and whether they are [authorized](#) by the U.S Food and Drug Administration (FDA) for adults only or adults and certain pediatric populations. Some therapeutics are in short supply, but availability is expected to increase in the coming months. This advisory serves to familiarize healthcare providers with available therapeutics, with how and when to prescribe and [prioritize](#) them, and with how to recognize contraindications.

At this time, differentiating cases of Omicron variant from other variants (e.g. Delta) requires [specialized testing](#) (e.g., ThermoFisher Taqpath assay) or testing that may take several days for results (e.g., genomic sequencing). Additionally, cases of infection with Omicron variant appear clinically similar to cases of infection with other variants. Treatment options for COVID-19, as detailed in [HAN 575](#), include three monoclonal antibody treatment regimens; thus far, one of these treatments, sotrovimab, has proven effective against Omicron, while the other two monoclonal antibody treatment options have shown decreased effectiveness against Omicron. However, due to the limitations in both early detection of Omicron variant and in supply of sotrovimab, it is challenging to determine which patients should receive sotrovimab.

COVID-19 therapeutics also include two oral antivirals, Paxlovid and molnupiravir (both of which have recently been issued EUAs for use as treatment against COVID-19), and options for pre-exposure prevention and post-exposure prophylaxis of COVID-19, all of which are detailed below.

B. Anti-SARS-CoV-2 Monoclonal Antibody Treatment

The FDA has issued Emergency Use Authorizations (EUAs) for certain anti-SARS-CoV-2 monoclonal antibodies, combination therapies [bamlanivimab plus etesevimab](#) and [casirivimab plus imdevimab](#), and monotherapy sotrovimab. The EUAs allow for use of the agents in patients who meet the following criteria:

- Non-hospitalized patients
- Age 12 or older, and weighing 40 kg or more [casirivimab plus imdevimab, and sotrovimab]
 - bamlanivimab plus etesevimab: *all ages*, including neonates
- Laboratory confirmed SARS-CoV-2 infection (PCR test)
- Mild-to-moderate COVID-19 disease who are at high risk of progressing to severe disease and/or hospitalization (see below)
- It is recommended that these drugs be administered as soon as possible after a positive SARS-CoV-2 test result, and within 10 days of symptom onset.

Unless there is another indication for use of these agents or use is part of a clinical trial, it is not recommended for patients hospitalized because of COVID-19 to receive the above monoclonal antibody treatments.

1. [Sotrovimab](#)

Early in vitro data suggests sotrovimab retains activity against the Omicron variant.

The federal government's current supply of sotrovimab is *extremely limited*. Continued use of bamlanivimab plus etesevimab and casirivimab plus imdevimab (REGEN-COV) monoclonal antibody products is recommended while reserving sotrovimab for treatment of eligible outpatients at *highest risk* who are either:

- Diagnosed with a [test](#) that may identify a potential case of the Omicron variant; or
- Are present in local settings where reported prevalence of Omicron is greater than 20%; AND
- Meet criteria for administration of sotrovimab (listed above)
 - Are at high risk of progression to severe disease and/or hospitalization
 - These patients include:
 - Older age (≥65 years of age)
 - Obesity or being overweight (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])

Healthcare providers should consider the benefit-risk for an individual patient, with the above in mind.

Sotrovimab is not a substitute for COVID-19 vaccination **and is not authorized for use as pre-exposure prophylaxis to prevent COVID-19.**

C. [Antiviral Agents](#)

[Remdesivir:](#)

- A nucleoside analog approved by the FDA for the treatment of hospitalized patients with COVID-19.
- A recent randomized placebo-controlled outpatient study evaluated three daily intravenous (IV) infusions of remdesivir given within seven days of symptom onset.
 - This study found that the reduction in hospitalization rates was similar to that achieved by using anti-SARS-CoV-2 monoclonal antibody-based therapy.⁴
- Remdesivir is expected to be effective against the Omicron variant based on in vitro data; however, in vivo data are currently limited.⁵
- Outpatient use of remdesivir requires support of IV infusion centers with appropriate skilled staffing.

Oral antiviral agents:

Paxlovid (ritonavir-boosted nirmatrelvir):

- Available under EUA by the FDA for treating COVID-19 in an outpatient setting for those with mild-to-moderate disease who are at high risk of progressing to severe disease and/or hospitalization (see Section C. above).
- Age 12 or older, and weighing 40 kg or more
- Administration: twice daily for five days
 - Ideally within five days of symptom onset for optimal efficacy
- Currently in very limited supply and use should be prioritized for higher risk populations
- Expected to be active against all circulating variants of concern, including Omicron.⁵
- Due to the potential for severe drug-drug interactions with ritonavir, a medication used for HIV treatment, it is recommended that healthcare providers not experienced in prescribing Paxlovid become acquainted with the possible drug-drug interactions. Healthcare providers could also contact a local clinical pharmacist or an infectious disease specialist for guidance.

Molnupiravir:

- Available under EUA by the FDA for treating COVID-19 in an outpatient setting for those with mild-to-moderate disease who are at high risk of progressing to severe disease and/or hospitalization (see Section C. above).
- Age ≥ 18 years old
- Administration: twice daily for five days
 - Ideally within five days of symptom onset for optimal efficacy.
- Molnupiravir should only be used when other options are not available, due to its lower efficacy (see below).
- Expected to be active against all circulating variants of concern, including Omicron.⁵
- Not recommended for use in:
 - Pregnant patients (because of potential mutagenicity)
 - Patients who are breastfeeding or pediatric patients
 - Due to limited data within these populations and concerns for potential bone growth toxicity in the young.

From their individual clinical trials, compared to placebo, severe outcomes (hospitalization or death) were reduced by 88% for Paxlovid compared to 30% for molnupiravir.⁶

There are considerable differences in efficacy, risk profiles, and use restrictions between the two oral antivirals. Healthcare providers should familiarize themselves with these distinctions in order to make informed clinical decisions and engage in risk-benefit discussions with patients.

D. Pre-Exposure Prophylaxis for High-Risk Groups

EVUSHELD:

- Tixagevimab plus cilgavimab (co-packaged and administered together)
 - Long-acting anti-SARS-CoV-2 monoclonal antibodies
- Issued an EUA by the FDA for use as pre-exposure prophylaxis against COVID-19
 - The only product available for this indication
 - Not indicated for treatment of patients with COVID-19
- Expected to be effective against the Omicron variant
- Intended for the following individuals:
 - Are not currently infected with COVID-19 and have no known recent exposures to a person infected with COVID-19, AND
 - Are moderately to severely immunocompromised, AND are not expected to have an effective response to vaccination, OR
 - for whom the COVID-19 vaccination is contraindicated/not recommended.

E. Post-Exposure Prophylaxis

Casirivimab plus imdevimab ([REGEN-COV](#))

- Age >12 and weighing > 40 kg
- See [HAN 588](#) for additional details.

Bamlanivimab plus etesevimab

- All ages, including neonates

Both agents above have EUAs that cover use of the agents for both post-exposure prophylaxis and treatment of COVID-19.

Eligible individuals include those who:

- Are at high risk for progression to severe COVID-19, AND
- Are not fully vaccinated OR are not expected to mount an adequate response to vaccination (e.g., immunocompromised individuals), AND
- Have been exposed to a SARS-CoV-2 infected individual OR are at high risk of exposure to an infected individual because of infection occurring in the same congregate setting (such as in nursing homes or prisons).

The issuance of an EUA does not constitute FDA approval.

Details on how to obtain the therapeutic agents listed above can be found at the [PA DOH website](#).

F. Additional Information:

For the most up-to-date information on COVID-19 monoclonal antibody treatment changes:

The U.S. Dept of Health & Human Services, Office of the Assistant Secretary for Preparedness and Response maintains a webpage for Public Health Emergency and Preparedness which maintains the most up-to-date information on COVID-19 monoclonal antibody treatment changes, including issuance/reversals of EUAs, and/or pauses in distribution of monoclonal antibodies.

(<https://www.phe.gov/emergency/events/COVID19/therapeutics/Pages/default.aspx>)

Clinicians with questions about approved treatments and those with EUAs issued by the FDA may refer to the reference NIH web page: Therapeutic Management | COVID-19 Treatment Guidelines

(<https://www.covid19treatmentguidelines.nih.gov/therapeutic-management/>).

Individuals interested in receiving further PA-HANs are encouraged to register at

<https://www.health.pa.gov/topics/prep/PA-HAN/Pages/HAN.aspx>.

References

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2. Ferguson N, Ghani A, Cori A, et al. Report 49: Growth, population distribution and immune escape of Omicron in England. Imperial College London (2021-12-20). doi: <https://doi.org/10.25561/93038> (direct link: <https://spiral.imperial.ac.uk/handle/10044/1/93038>).
3. Discovery Health. Real world analysis of Omicron outbreak in South Africa including vaccine effectiveness. Accessed 2021-12-23 at <https://www.discovery.co.za/corporate/news-room> (direct link: https://resources.mynewsdesk.com/image/upload/fl_attachment/lw9szzdtqfvwitkfbcoq).
4. Gottlieb, Robert L et al. Early Remdesivir to Prevent Progression to Severe Covid-19 in Outpatients. The New England Journal of Medicine (2021): <https://www.nejm.org/doi/full/10.1056/NEJMoa2116846>
5. Vangeel L, De Jonghe S, Maes P, et al. Remdesivir, Molnupiravir and Nirmatrelvir remain active against SARS-CoV-2 Omicron and other variants of concern. bioRxiv 2021. doi: <https://doi.org/10.1101/2021.12.27.474275>.

6. Bernal, A, Gomes da Silva, M, Musungaie, D, et al. Molnupiravir for Oral Treatment of Covid-19 in Nonhospitalized Patients. The New England Journal of Medicine (2021). doi: 10.1056/NEJMoa2116044.

If you have questions about this guidance, please call your local health department or **1-877-PA-HEALTH (1-877-724-3258)**.

Categories of Health Alert messages:

Health Alert: conveys the highest level of importance; warrants immediate action or attention.

Health Advisory: provides important information for a specific incident or situation; may not require immediate action.

Health Update: provides updated information regarding an incident or situation; unlikely to require immediate action.

This information is current as of January 15, 2022 but may be modified in the future. We will continue to post updated information regarding the most common questions about this subject.