Nebraska Department of Health and Human Services

HEALTH ALERT NETWORK Update

NEBRASKA
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DEPT. OF HEALTH AND HUMAN SERVICES

TO: Healthcare Providers, Infection Control, Hospitals, Labs, and Public Health

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RE: Omicron predominant in Nebraska & therapeutics updates

DATE: January 4, 2022

Since the first identification of the Omicron variant of SARS-CoV-2 in Nebraska on December 2nd, 2021, Omicron has spread across the state and now accounts for 52% of specimens collected and sequenced within the past two weeks. Jurisdictional variation exists but given its rapid growth, it is likely Omicron will soon become predominant even in regions with lower proportions of Omicron identifications currently. The spike protein mutations characteristic of Omicron allow it to evade neutralization by bamlanivimab-etesevimab or casirivimab-imdevimab (Regeneron), which are now considered ineffective for patients infected with the Omicron variant. Sotrovimab remains effective but is in short supply nationally and statewide. Given the rapidly diminishing clinical utility of bamlanivimab-etesevimab and casirivimab-imdevimab, the limited supply of sotrovimab, and the limited supply of antiviral therapies (i.e., molnupiravir, nirmatrelvir-ritonavir [Paxlovid]), prioritization of therapeutics will be required as we await improvement in the supply chain.

The NIH have developed criteria for identifying and prioritizing those expected to benefit the most from receiving the limited supply of COVID-19 therapeutics currently available (https://www.covid19treatmentguidelines.nih.gov/therapies/statement-on-patient-prioritization-for-outpatient-therapies/). Please consider these tiers when assessing which patients should receive allocated therapeutics in the setting of scarce resources (in decreasing order of priority):

- Tier 1 - Immunocompromised individuals not expected to mount an adequate immune response to COVID-19 vaccination or SARS-CoV-2 infection due to their underlying conditions, regardless of vaccine status OR unvaccinated individuals at the highest risk of severe disease (anyone aged ≥75 years or anyone aged ≥65 years with additional risk factors)
- Tier 2 - Unvaccinated individuals at risk of severe disease not included in Tier 1 (anyone aged ≥65 years or anyone aged <65 years with clinical risk factors)
- Tier 3 - Vaccinated individuals at high risk of severe disease (anyone aged ≥75 years or anyone aged ≥65 years with clinical risk factors), including vaccinated individuals who have not received a COVID-19 vaccine booster
- Tier 4 - Vaccinated individuals at risk of severe disease (anyone aged ≥65 years or anyone aged <65 with clinical risk factors), including vaccinated individuals who have not received a COVID-19 vaccine booster

In the setting of Omicron predominance and limited therapeutic options for treatment of mild-to-moderate outpatient COVID-19 in high-risk individuals, it is recommended to apply the NIH treatment algorithm (https://files.covid19treatmentguidelines.nih.gov/guidelines/covid19treatmentguidelines.pdf) in determining when to use each therapeutic (in decreasing order of preference):

- Nirmatrelvir 300 mg with ritonavir 100 mg (Paxlovid) orally twice daily for 5 days
- Sotrovimab 500 mg, administered as a single intravenous (IV) infusion
- Remdesivir 200 mg IV on Day 1, followed by remdesivir 100 mg IV on Days 2 and 3
- Molnupiravir 800 mg orally twice daily for 5 days

Patient-specific factors should also be considered when determining which therapeutic might be most appropriate in a specific clinical situation:

- Unable to access infusion site or receive infusions - consider an oral antiviral
- Onset of symptoms more than 5 days prior - consider sotrovimab (must be started within 10 days) or remdesivir (started within 7 days)
- Pregnancy/breastfeeding - molnupiravir NOT recommended
- Patients 12-17 years old - molnupiravir NOT recommended
- Patients <12 years old - consider remdesivir
- Drug-drug interactions with ritonavir (refer to: https://www.covid19treatmentguidelines.nih.gov/therapies/statement-on-paxlovid-drug-drug-interactions/, and/or consult with a pharmacist)
    - Significant drug-drug interaction - nirmatrelvir-ritonavir NOT recommended
    - Moderate drug-drug interaction - adjust interacting medication regimen as appropriate, in consultation with pharmacist and prescriber of the interacting medication
- Patients with moderate renal impairment - dose adjustment for nirmatrelvir-ritonavir (NOT recommended with CrCL<30 mL/min)

This is an official
CDC HEALTH ADVISORY

Distributed via the CDC Health Alert Network
Friday, December 31, 2021, 5:00 PM ET
CDCHAN-00461

Using Therapeutics to Prevent and Treat COVID-19

Summary
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. The Centers for Disease Control and Prevention (CDC) recommends that 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. 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 Health Alert Network (HAN) Health Advisory serves to familiarize healthcare providers with available therapeutics, understand how and when to prescribe and prioritize them, and recognize contraindications.

Background
On November 24, 2021, a new variant of SARS-CoV-2, B.1.1.529 (Omicron), was reported to the World Health Organization (WHO). On December 1, 2021, the first case of COVID-19 attributed to Omicron was reported in the United States. CDC has been working with state, tribal, local, and territorial public health officials to monitor the spread of the Omicron variant in the United States and has identified a rapid increase in infections consistent with what has been observed in other countries. Current CDC recommendations for vaccines and booster shots are 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). The United States Government is continuously working with private and public partners to bring new therapeutic options for use against SARS-CoV-2 variants of concern, including the Omicron variant.

Monoclonal Antibodies
The Omicron variant, with its numerous mutations in the spike protein, is not neutralized by bamlanivimab and etesevimab or casirivimab and imdevimab, the most frequently prescribed monoclonal antibody-based COVID-19 treatments (4-5). Despite some reduction in neutralization concentrations, sotrovimab remains effective against all variants of concern, including Omicron (6). However, sotrovimab is currently in limited supply, and its use should be prioritized for nonhospitalized patients with risk factors for progression to severe COVID-19, including individuals who are unvaccinated, have not received all vaccines and booster shots as recommended by CDC, individuals with clinical risk factors, older age (for example ≥65 years of age), and individuals not expected to mount an adequate immune response. Sotrovimab can be used in these high-risk individuals when Paxlovid (described below) is not indicated due to potential severe drug-drug interactions or if Paxlovid is not available.

Antivirals
- Remdesivir is a nucleoside analog approved by FDA for the treatment of hospitalized patients with COVID-19. A recent randomized placebo-controlled outpatient study evaluated three daily intravenous (IV) infusion 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 (7). Remdesivir is expected to be effective against the Omicron variant based on in vitro data; however, in vivo data are currently limited (8). Outpatient use of remdesivir requires support of IV infusion centers with appropriate skilled staffing.

- Two oral antivirals, Paxlovid (ritonavir-boosted nirmatrelvir) and molnupiravir, are now available under Emergency Use Authorization by FDA for treating COVID-19 in outpatients with mild to moderate disease. Each drug is administered twice daily for five days. There are considerable differences in efficacy, risk profiles, and use restrictions between the two oral antivirals. From their individual clinical trials, compared to placebo, severe outcomes (hospitalization or death) were reduced by 88% for Paxlovid compared to 30% for molnupiravir (9). Healthcare providers need to be familiar with these distinctions to make clinical decisions and inform patients. In addition, initiating treatment with these oral antivirals must begin within five days of symptom onset to maintain product efficacy. Paxlovid is currently in very limited supply and use should be prioritized for higher risk populations. Due to the potential for severe drug-drug interactions with ritonavir, a medication used for HIV treatment, CDC strongly suggests that healthcare providers not experienced in prescribing Paxlovid refer to the NIH Statement on Paxlovid Drug-Drug Interactions | COVID-19 Treatment Guidelines. Healthcare providers could also contact a local clinical pharmacist or an infectious disease specialist for advice. Like Paxlovid, molnupiravir is expected to be active against all circulating variants of concern, including Omicron (8). Molnupiravir should only be used when other options are not available, due to its lower efficacy. Molnupiravir use is not recommended in pregnancy because of potential mutagenicity. Molnupiravir is also not recommended in patients who are breastfeeding or pediatric patients due to limited data within these populations and concerns for potential bone growth toxicity in the young.

Pre-exposure therapeutics for high-risk groups

AstraZeneca's EVUSHELD, which includes two long-acting anti-SARS-CoV-2 monoclonal antibodies, is the only Emergency Use Authorization pre-exposure prophylaxis product available. EVUSHELD is expected to be effective against the Omicron variant; however, treatment effectiveness should be monitored. EVUSHELD is intended for the highest risk immunocompromised patients who are not expected to have an effective response to vaccination. EVUSHELD is indicated for pre-exposure prophylaxis only and not for treatment of patients with COVID-19.

Recommendations for Healthcare Providers

- As with all therapeutics, the best use of therapeutics includes an appropriate clinical assessment and an up-to-date and informed risk-benefit discussion to address any questions or concerns from patients.
- Obtain further information on clinical use of products through NIH's COVID-19 Treatment Guidelines, the Assistant Secretary for Preparedness and Response Public Health Emergency COVID-19 Therapeutics site, and through professional societies such as IDSA's Guidelines on the Management of Patients with COVID-19.
- Check with state and local health departments on key sites that have been identified for distribution of therapeutics, including cancer treatment centers and oncology providers.
- If the Delta variant still represents a significant proportion of infections in a region and other options are not available or are contraindicated, eligible patients can be offered bamlanivimab and etesevimab or casirivimab and imdevimab, with the understanding that these treatments would be ineffective against the Omicron variant. This concern can be mitigated if virus-specific diagnostic testing in a given patient indicates infection with the Omicron variant is unlikely.
- Prioritize high risk patients, particularly if therapeutics are in short supply, using NIH COVID-19 Treatment Guidelines when supply constraints exist. This document presents a tiered approach to prioritization.
- Continue to encourage COVID-19 vaccination, including booster vaccination.

Recommendations for Public Health Departments and Public Health Jurisdictions

- State and local health departments should be aware of locations of available therapeutics within their jurisdictions.
- Health departments should communicate ongoing and up-to-date information on therapeutics for COVID-19 and their availability to healthcare providers within their jurisdiction until product locators become readily available.

For More Information

- Omicron Variant: What You Need to Know | CDC
- Interim Clinical Considerations for Use of COVID-19 Vaccines | CDC
- CDC COVID Data Tracker
- COVID-19 Treatment Guidelines: What's New
- COVID-19 Treatment Guidelines: Antiviral Therapy
- NIH Statement on Therapies for High-Risk, Nonhospitalized Patients | COVID-19 Treatment Guidelines
- NIH Statement on Paxlovid Drug-Drug Interactions | COVID-19 Treatment Guidelines
- 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
- Side by Side Overview of Outpatient Therapies Authorized for Treatment of Mild-Moderate COVID-19

References

1. Andrews N, Stowe J, Kirseborm F, et al. Effectiveness of COVID-19 vaccines against the Omicron (B.1.1529) variant of concern. medRxiv 2021. doi: https://doi.org/10.1101/2021.12.14.21267615
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. Aggarwal A, Ospina Stella A, Walker G, et al. SARS-CoV-2 Omicron: evasion of potent humoral responses and resistance to clinical immunotherapeutics relative to viral variants of concern. medRxiv 2021. doi**:** https://doi.org/10.1101/2021.12.14.21267772
5. Planas D, Saunders N, Maes P, et al. Considerable escape of SARS-CoV-2 variant Omicron to antibody neutralization. bioRxiv 2021. doi: https://doi.org/10.1101/2021.12.14.472630
6. Cathcart A, Havenar-Daughton C, Lempp F, et a. The dual function monoclonal antibodies VIR-7831 and VIR-7832 demonstrate potent in vitro and in vivo activity against SARS-CoV-2. bioRxiv 2021. doi: https://doi.org/10.1101/2021.03.09.434607
7. 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
8. 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
9. 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

The Centers for Disease Control and Prevention (CDC) protects people's health and safety by preventing and controlling diseases and injuries; enhances health decisions by providing credible information on critical health issues; and promotes healthy living through strong partnerships with local, national, and international organizations.

Categories of Health Alert Network messages:

Health Alert	Requires immediate action or attention, highest level of importance
Health Advisory	May not require immediate action; provides important information for a specific incident or situation
Health Update	Unlikely to require immediate action; provides updated information regarding an incident or situation
HAN Info Service	Does not require immediate action; provides general public health information

##This message was distributed to state and local health officers, state and local epidemiologists, state and local laboratory directors, public information officers, HAN coordinators, and clinician organizations##