The following message was sent to you through the Alaska Public Health Alert Network (AK PHAN). Please share this information with others who may be interested.

The Alaska Section of Epidemiology (SOE) is forwarding this U.S. Centers for Disease Control and Prevention (CDC) Health Update to Alaska health care professionals for their attention.

As Omicron takes over as the predominant variant, providers should be aware that Omicron is resistant to REGEN-COV as well as benlanivimab+etesevimab. Sotrovimab should be considered the preferred COVID-19 monoclonal antibody in Alaska as it retains activity against Omicron. Facilities should hold onto their supply of the other monoclonals but prioritize sotrovimab. It is available across Alaska but is a much more limited resource due to the supply chain.

NIH has updated their recommendations for scarce COVUD-19 treatment resources: https://www.covid19treatmentguidelines.nih.gov/therapies/statement-on-patient-prioritization-for-outpatient-therapies

CDC provides this summary of evidence for high risk conditions: https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-care/underlyingconditions.html

This is an official

CDC HEALTH ADVISORY

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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 recommend 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

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