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EPI-NEWS

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IN THIS ISSUE: CDC HAN – IMPORTANT UPDATES ON COVID-19 THERAPEUTICS

CDC HEALTH ALERT NETWORK (HAN)

Important Updates on COVID-19 Therapeutics for Treatment and Prevention

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Summary

The Centers for Disease Control and Prevention (CDC) is issuing this Health Alert Network (HAN) Health Update to supplement the CDC HAN Health Advisories issued on April 25, 2022 and May 24, 2022 to emphasize to healthcare providers, public health departments, and the public that the majority of Omicron sublineages circulating in the United States have reduced susceptibility to the monoclonal antibody, bebtelovimab and the monoclonal antibody combination, cilgavimab and tixagevimab (Evusheld™).

Because of this reduced susceptibility, on November 30, 2022, the Food and Drug Administration (FDA) announced https://www.fda.gov/drugs/drug-safety-and-availability/fda-announces-bebtelovimab-not-currently-authorized-any-us-region that the use of bebtelovimab is not currently authorized for use for patients with COVID-19. The monoclonal antibody combination, cilgavimab and tixagevimab (EvusheldTM), currently recommended for pre-exposure prophylaxis, remains authorized for persons with moderate to severe immunosuppression and for those 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 to a COVID-19 vaccine(s) and/or COVID-19 vaccine component(s). However, providers should be aware and communicate to patients that its effectiveness may be increasingly limited against circulating Omicron sublineages.

Antiviral therapeutics https://www.covid19treatmentguidelines.nih.gov/tables/therapeutic-management-of-nonhospitalized-adults/ for the treatment https://www.covid19treatmentguidelines.nih.gov/management/clinical-management-of-adults/nonhospitalized-adults--therapeutic-management/ of COVID-19, ritonavir-boosted nirmatrelvir (Paxlovid™) https://www.covid19treatmentguidelines.nih.gov/therapies/antivirals-including-antibody-products/ritonavir-boosted-nirmatrelvir--paxlovid-/paxlovid-drug-drug-interactions/, remdesivir (Veklury®) https://www.covid19treatmentguidelines.nih.gov/therapies/antivirals-including-antibody-products/remdesivir/, and molnupiravir (Lagevrio™) https://www.covid19treatmentguidelines.nih.gov/therapies/antivirals-including-antibody-products/molnupiravir/, retain activity against currently circulating Omicron sublineages. These medications can prevent severe disease, hospitalization, and death and are widely available but have been underused.

This HAN Health Update provides health care professionals, public health officials, and the public with guidance on improving use of therapeutics for treatment of COVID-19 and strategies to prevent serious outcomes of COVID-19.

Background

CDC genomic surveillance https://covid.cdc.gov/covid-data-tracker/#variant-proportions estimates that the combined proportion of COVID-19 cases caused by the Omicron BQ.1 and BQ.1.1 lineages has reached 76% nationally and is above 50% in each HHS region.[1] Both of these sublineages contain a mutation (K444T) in the spike protein that confers resistance to the monoclonal antibody bebtelovimab[2], which was previously authorized as one of the second-line therapies to treat COVID-19. Given the current high prevalence of variants resistant to bebtelovimab, FDA announced on November 30, 2022, that the use of bebtelovimab is not currently authorized for patients with COVID-19 in the United States.[3] FDA will continue to monitor the frequency of circulating variants and may provide future updates as appropriate.

Early outpatient treatment of mild-to-moderate COVID-19 with a recommended first-line therapy, ritonavir boosted nirmatrelvir (Paxlovid™) or remdesivir (Veklury®), or the second-line therapy, molnupiravir

(Lagevrio™) have been shown to prevent hospitalizations and deaths.[4,5,6] Ritonavir-boosted nirmatrelvir (Paxlovid™) may also reduce the risk for post-COVID-19 conditions.[7] **Fortunately, all three of these antiviral medications are expected to retain activity against the currently circulating variants and are currently widely available for all eligible persons** https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-care/underlyingconditions.html. However, only a minority of eligible patients and fewer patients from populations disproportionately affected by COVID-19 have received them.[8,9] Oral antivirals can be accessed with a provider prescription at pharmacies nationwide and at Test to Treat locations https://aspr.hhs.gov/TestToTreat/Pages/default.aspx. People with mild to moderate symptoms of COVID-19 who (1) are aged 50 years and older, or (2) have an underlying condition, or (3) have moderate to severe immunosuppression, are at risk for severe COVID-19 outcomes and are eligible for treatment. Regardless of their vaccination status, all of these groups of people should be tested for SARS-CoV-2 as soon as possible after symptom onset and receive treatment within 5 to 7 days of symptom onset with one of several treatment options.

In a recent CDC study https://www.cdc.gov/mmwr/volumes/71/wr/mm7148e2.htm, most people eligible for ritonavir-boosted nirmatrelvir for treatment of COVID-19 in every age group, including those aged older than 65 years, did not receive a prescription for this medication.[8] Racial and ethnic disparities in outpatient treatment with all treatment options have been identified.[9] The recent CDC study examined hospitalization rates among U.S. adults eligible for COVID19 treatment with ritonavir-boosted nirmatrelvir who were diagnosed with COVID-19 during April through August 2022.[8] People who were prescribed ritonavir-boosted nirmatrelvir within 5 days of diagnosis had a 51% lower hospitalization rate within the 30 days following diagnosis than those who were not prescribed this medication. People who were previously infected with SARS-CoV-2 and those who had received 3 or more COVID-19 vaccinations also benefited from ritonavir-boosted nirmatrelvir.[8] Other studies have also reported a 45%-89% reduction in emergency department visits, hospitalizations, and deaths due to COVID-19 among patients prescribed ritonavir-boosted nirmatrelvir.[10-15] The recent increases in the case and hospitalization rates highlight the importance of preventing severe illness through the use of prevention measures and therapeutics.

Considerations in the management of concomitant medications https://www.covid19treatmentguidelines.nih.gov/therapies/concomitant-medications/ with ritonavir-boosted nirmatrelvir, such that a temporary pause or reduction in dose is necessary, can be found in the NIH COVID-19 treatment guidelines https://www.covid19treatmentguidelines.nih.gov/therapies/antivirals-including-antibody-products/summary-recommendations/; additional resources include the Liverpool COVID-19 Drug Interactions website https://covid19-druginteractions.org/checker, the Ontario COVID-19 Science Advisory Table https://covid19-sciencetable.ca/sciencebrief/nirmatrelvir-ritonavir-paxlovid-what-prescribers-and-pharmacists-need-to-know-3-0/, the ritonavir-boosted nirmatrelvir FDA EUA fact sheet and checklist. For patients with contraindications to ritonavir-boosted nirmatrelvir, and for whom remdesivir is not feasible, clinicians should consider treatment with molnupiravir. No drug-drug interactions have been identified for molnupiravir. Antibacterial therapy and corticosteroids are not recommended for the primary treatment of COVID-19 in the absence of another indication.

Additional data show that the prevalence of Omicron sublineages that are resistant to cilgavimab plus tixagevimab (EvusheldTM) in laboratory assays[16] is rapidly increasing and has reached 82% nationally. Currently, this combination is the only agent FDA currently authorized for SARS-CoV-2 pre-exposure prophylaxis (PrEP) in people who are not expected to mount an adequate immune response to COVID-19 vaccination or those with contraindications for COVID-19 vaccines. Therefore, the NIH COVID-19 Guidelines Panel continues to recommend the use of cilgavimab plus tixagevimab as PrEP for eligible individuals. This recommendation may change if the prevalence of resistant sublineages increases. This combination may be offered to these patients (adults and adolescents [aged ≥12 years and weighing ≥40 kg]) who do not have SARS-CoV-2 infection. Providers and patients should be aware of the potential for reduced effectiveness and emphasize the need for additional prevention measures. CDC recommends that these groups, their household members, and close contacts stay up to date with vaccinations, including getting the bivalent booster when eligible.

Prevention measures for all people at risk for severe illness, particularly people with moderate to severe

immunosuppression, should be encouraged to protect people from infections. Prevention measures include wearing high quality and well-fitting masks, keeping distance between themselves and others, improving ventilation, and developing a care plan, in consultation with their physician. The care plan https://www.cdc.gov/coronavirus/2019-ncov/downloads/332440-A_FS_COVID_Plan_FINAL.pdf should include prompt testing at onset of COVID-19 symptoms and rapid access to antivirals if SARSCoV-2 infection is detected. CDC recommends people aged 6 months and older who are eligible receive one updated (bivalent) vaccine if it has been at least two months since they received their most recent COVID-19 dose (either primary series or original monovalent booster).

General Recommendations for Clinicians and Public Health Practitioners

- Stay up-to-date on the appropriate use and authorization of clinically-indicated therapeutics, drug interactions, and the circulating SARS-CoV-2 variants through:
  - o National Institutes of Health COVID-19 Treatment Guidelines https://www.covid19treatmentguidelines.nih.gov/
  - o Treatment and prevention options through FDA Emergency Use Authorization https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization#coviddrugs
  - o Currently circulating variants at CDC Data Tracker https://covid.cdc.gov/covid-data-tracker/#datatracker-home
- As healthcare providers consider a treatment plan for each of their eligible patients, they should review the patient's renal and hepatic function and all the patient's other medications.
  - o There are considerable differences in characteristics, eligibility criteria, preferred therapy, administration, risk profiles, and use restrictions between the three antivirals, ritonavirboosted nirmatrelvir (Paxlovid™, multiple drug-drug interactions), remdesivir (Veklury® possible drug-drug interactions), and molnupiravir (Lagevrio™, no known drug-drug interactions).
  - o Healthcare providers need to be familiar with these distinctions to make clinical decisions and inform patients.
- Educate patients about the importance of early testing if COVID-19 symptoms develop, particularly if they have moderate or severe immunosuppression.
- Because symptoms are similar, consider influenza testing for patients at high risk for severe influenza.
  - o CDC has testing guidance for clinicians when SARS-CoV-2 and influenza viruses are cocirculating. Because SARS-CoV-2 and influenza virus co-infection can occur, a positive influenza test result without SARS-CoV-2 testing does not exclude COVID-19, and a positive SARS-CoV-2 test result without influenza testing does not exclude influenza.
  - o Guidance for antiviral treatment for influenza does not vary with SARS-CoV-2 coinfection.
- Educate patients at higher risk for severe COVID-19 that they are eligible for COVID-19 treatment if they develop mild or moderate COVID-19.
- Consider and prescribe COVID-19 treatment for patients at higher risk for severe COVID-19.
  - o Treatment initiation with these antivirals must begin within 5 to 7 days of symptom onset, depending on the therapy.
  - o Consider the use of convalescent plasma for in- or outpatient treatment for immunocompromised persons when other options are not possible.
- Obtain information on availability and access to outpatient COVID-19 treatments, including pharmacies where antivirals for COVID-19 are distributed and Test to Treat locations; call the support line at 1-800-232-0233 (TTY 888-720-7489), or contact the health department in your jurisdiction.
- To prevent serious outcomes of COVID-19, including severe disease, hospitalization, and death
  - o Educate patients about prevention measures (including masks, ventilation) and the benefits of treatments.
  - o Concern about recurrence of symptoms after treatment should not prevent treatment for those at risk for severe disease, hospitalization, and death.
  - o Recommend that people aged 6 months and older who are eligible receive one updated (bivalent) vaccine if it has been at least two months since they received their most recent COVID-19 dose (either primary series or original monovalent booster).

Recommendations for the Public

- If you have mild or moderate symptoms of COVID-19 AND you are aged 50 years or older, OR have a condition placing you at increased risk of getting very sick from COVID-19, get tested as soon as possible, following CDC guidance on testing for COVID-19.
- If you are 65 years old or older or have a condition placing you at risk for severe influenza, also consider getting an influenza test.
- Find out how to get treatment. One of the preferred COVID-19 treatments involves just 5 days of a prescribed oral medication.
- Because antivirals work best early in the course of illness, start treatment within 5 to 7 days of symptom onset.
- **Contact a healthcare provider right away after a positive home COVID-19 test to discuss treatment options**, even if your symptoms are mild, and especially if you are immunocompromised.

• Take your prescription to one of 40,000 locations, or visit a Test to Treat location, and, if eligible, receive a prescription from a provider at that location or call 1-800-232-0233 (TTY 1-888-720- 7489) to find a testing location that can provide treatment if you test positive.
• Stay up to date with COVID-19 vaccination and getting an influenza vaccination; they are still the best ways to prevent severe outcomes of COVID-19 and influenza, including severe disease, hospitalization, and death. CDC recommends that people aged 6 months and older who are eligible receive one updated (bivalent) SARS-CoV-2 booster if it has been at least 2 months since they received their most recent dose (either primary series or original monovalent booster).
• Protect yourself, family, and friends, particularly if you have moderate to severe immunosuppression, with prevention measures against infection. These include wearing high quality and well-fitting masks, keeping distance between themselves and others, improving ventilation, staying home when sick, and developing a care plan.

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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.

DEPARTMENT OF HEALTH AND HUMAN SERVICES

HAN Message Types

- **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.
- **Info Service:** Provides general information that is not necessarily considered to be of an emergent nature.