

Nebraska Department of Health and Human Services

Health Alert Network

Update

December 7, 2022

COVID-19 therapeutics updates & shortages of oseltamivir, amoxicillin, & amoxicillin-clavulanate

COVID-19 monoclonal antibodies (mAbs)

- On November 30, 2022, the **FDA paused authorization of the mAb bebtelovimab** for treatment of COVID-19, citing it is not expected to neutralize the dominant BQ.1 and BQ 1.1 subvariants of Omicron. It is not medically appropriate at this time, to treat patients with COVID-19 with bebtelovimab in the US. [FDA Announces Bebtelovimab is Not Currently Authorized in Any US Region | FDA](#)
- The subvariants BA.4.6, BA.2.75.2, BA.5.2.6, BF.7, BQ.1, and BQ.1.1 are *likely* to be resistant to tixagevimab plus cilgavimab (Evusheld). [National](#) and [local](#) rates of subvariants will be closely monitored as it is likely Evusheld approval may be revoked by the FDA. The current recommendation is to advise patients regarding possibility of breakthrough infections when Evusheld is used and advise them to seek timely medical attention if symptoms occur.

COVID-19 oral antivirals

- Paxlovid (nirmatrelvir/ritonavir) and Lagevrio (molnupiravir) continue to be available under Emergency Use Authorization by FDA for treating COVID-19 in outpatients with mild to moderate disease. Both agents are expected to retain effectiveness against currently emerging SARS-CoV-2 variants (including XBB, BQ.1, and BQ.1.1).
- **Despite the difficulties navigating Paxlovid drug interactions and renal adjustments, effectiveness in preventing severe outcomes is substantial and thus Paxlovid should be prioritized.** From their individual clinical trials, compared to placebo, severe outcomes (hospitalization or death) were reduced by 88% for Paxlovid (nirmatrelvir/ritonavir) compared to 30% for Lagevrio (molnupiravir). Due to lower efficacy in clinical trials, molnupiravir is considered an alternative agent and should be used **ONLY** when preferred therapies are unavailable, not feasible to use, or clinically inappropriate.
- Each drug is administered twice daily for five days and must be initiated within five days of symptom onset to maintain efficacy. For Paxlovid, moderate renal disease (GFR <60 ml/min) requires a dose adjustment; severe renal disease (GFR <30 ml/min) is a contraindication. Few medications are absolute contraindications for Paxlovid (nirmatrelvir/ritonavir) administration, others require dose adjustment or holding: [Liverpool COVID-19 Interactions \(covid19-druginteractions.org\)](#). Pharmacist consultation can facilitate management of drug-drug interactions with concomitant medications and renal dose adjustments.
- Pharmacies in Nebraska with available COVID therapeutics can be found at: [COVID-19 Therapeutics Locator](#)
- Long-term care facilities (LTCF) in Nebraska can request oral antivirals through Nebraska [Antimicrobial Stewardship Assessment and Promotion Program](#) (ASAP). Pharmacists at ASAP also assist LTCF clinicians with management of drug interactions and dose adjustments, as needed.
- Pharmacies can request **nirmatrelvir/ritonavir, molnupiravir and tixagevimab/cilgavimab by emailing dhhs.therapeutics@nebraska.gov**. The email should include name of the site and physical address along with primary contact name, email address and phone number.

Remdesivir

- Remdesivir is recommended as a preferred treatment for COVID-19 if Paxlovid is not appropriate for mild to moderate disease due to drug-drug interactions, renal impairment, or NPO status. Because remdesivir requires intravenous infusions for 3 consecutive days, there might be logistical constraints to administering remdesivir in many settings. It can be administered in hospitals, long-term care facilities, home health care, and infusion centers.

COVID-19 bivalent vaccine boosters

- SARS-CoV-2 bivalent mRNA booster doses (for use in patients 5 years of age and older) [offer protection](#) against both the ancestral SARS-CoV-2 virus and newer Omicron subvariants and is more effective than monovalent mRNA COVID-19 vaccines against symptomatic infection during the period of SARS-CoV-2 Omicron variant predominance. Emerging evidence suggests that COVID-19 vaccination provides some protection against [multisystem inflammatory syndrome \(MIS-C\) in children](#) and against post-COVID-19 conditions, and that vaccination among persons with post-COVID-19 conditions might help reduce symptoms. [Long COVID Risk and Pre-COVID Vaccination](#). A bivalent booster dose is [recommended](#) to be administered at least 2 months after completion of the primary series (for people who have not received any booster doses), or at least 2 months after the last monovalent booster.

Influenza oral antivirals for Influenza

- **Pharmacies across the country are experiencing a nationwide shortage of oseltamivir (Tamiflu), the primary antiviral agent used for the treatment of influenza.** [ASHP Drug Shortage Detail: Oseltamivir](#)
- Consider treating all influenza positive hospitalized patients with priority given to those <5 days from symptom onset. [IDSA Guidelines for Management of Seasonal Influenza](#)
- Consider treating only high-risk symptomatic outpatients with a positive test. Treatment must be started <48 hours from symptom onset for: >65 years or <5 years of age (especially <2 years of age); <18 years old receiving chronic aspirin or salicylate containing medications; pregnant or postpartum (within 2 weeks after end of pregnancy) women; Chronic pulmonary, cardiovascular, renal, hepatic, hematologic, neuro/neurodevelopmental, metabolic disorders (including diabetes); Immunocompromised or Residents of nursing homes or long-term care facilities; BMI >40; American Indians/Alaska Natives
- Medication supply for post-exposure chemoprophylaxis will likely be unavailable due to drug shortage. Consider prioritizing influenza treatment over chemoprophylaxis until the shortage is resolved.
- Baloxavir (Xofluza), inhaled zanamivir and intravenous peramivir are [some of the alternative antivirals](#) approved for influenza treatment depending upon approved age groups, clinical scenario and contraindications.

Influenza vaccination

- Influenza vaccines [have been updated](#) for the current season and should offer protection against the predominant influenza A(H3N2) viruses to date. Anyone who has not received an influenza vaccine this season should get vaccinated now. [CDC recommends](#) influenza vaccination with a licensed age-appropriate influenza vaccine for all people 6 months and older. Influenza and COVID-19 vaccines [can be administered at the same visit](#). Vaccination is the best way to reduce the chance of illness, hospitalization, and death.

Amoxicillin & amoxicillin/clavulanate shortage updates

- Pharmacies across the country are experiencing a nationwide shortage of amoxicillin and amoxicillin-clavulanate. [Drug Shortage Detail: Amoxicillin](#) [Drug Shortage Detail: Amoxicillin and Clavulanate](#)
- Prescribers are encouraged to familiarize themselves with alternative treatment options for indications that commonly use amoxicillin as first line treatment, including otitis media, community-acquired pneumonia, acute bacterial sinusitis, Group A *Streptococcus* pharyngitis, dental prophylaxis, and post-splenectomy prophylaxis.
- Publicly available guidance & protocols on alternatives: [Nebraska Children's Hospital & Medical Center](#), [Nebraska Medicine](#), and [American Academy of Pediatrics](#)

Jenna Preusker, PharmD
HAI/AR Pharmacist
402-552-3093

Dr. M. Salman Ashraf
HAI/AR Medical Director
402-219-3115

Dr. Gary Anthone
CMO Public Health
402-471-8566

Dr. Matthew Donahue
State Epidemiologist
402-471-2937