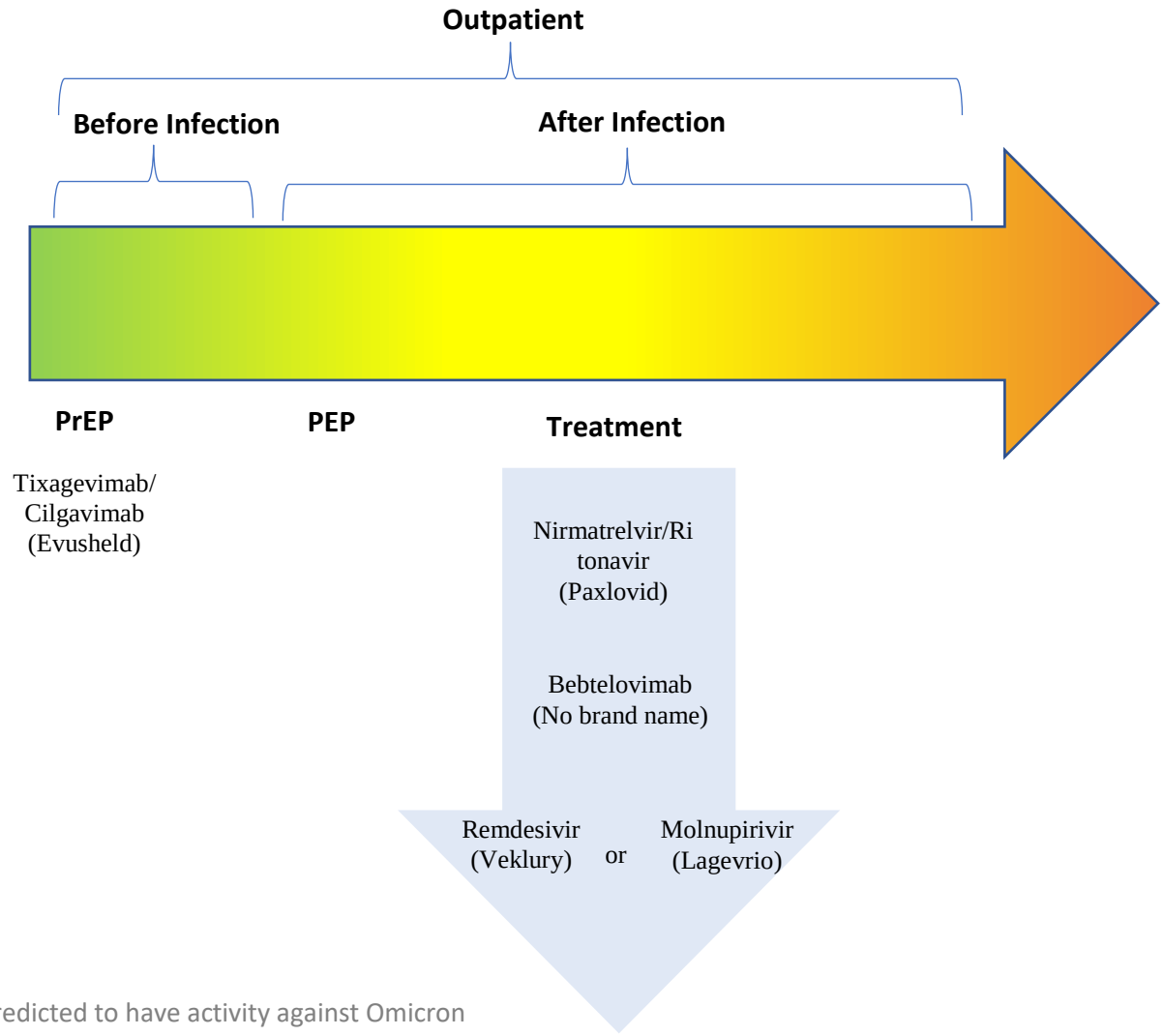
Treatment and Prevention of COVID-19 – What Healthcare Providers Need to Know Now

April 15, 2022

The FDA has authorized several medications to prevent and treat COVID-19. These are welcome advances, but it can be hard to keep straight what is available, for which people, and how these are impacted as new variants arise.

Below is a summary of our options right now for both preventing and treating COVID-19, considering availability of agents, their clinical trial efficacy, predicted activity against circulating SARS-CoV-2 variants, as well as the criteria for their use.



*Not predicted to have activity against Omicron

Treatment selection in order of preference. Base use on availability, ability to administer as soon as possible after symptom onset, EUA restrictions, and patient characteristics.

Agents to PREVENT COVID-19

Pre-Exposure Prophylaxis (PrEP)

Why: PrEP is administered to those without known or suspected COVID-19 who are unlikely to respond to vaccination or have a medical contraindication to vaccination to prevent them from becoming infected or developing severe disease, if they do.

What: **Tixagevimab/Cilgavimab (Evusheld)**, a combination monoclonal antibody, is the only agent authorized for COVID-19 PrEP. It is administered intramuscularly as two separate gluteal injections.

Due to a decrease in the neutralizing activity of tixagevimab/cilgavimab against the Omicron sub-variants the initial dose was increased from 150 mg of each component to 300 mg of each component. Patients who who have already received the previously authorized initial dose (150 mg of tixagevimab and 150 mg of cilgavimab) **should receive an additional dose as soon as possible, with the dose based on the following criteria:**

- If the patient received their initial dose ≤ 3 months ago, the patient should receive a dose of 150 mg of tixagevimab and 150 mg of cilgavimab.
- If the patient received their initial dose > 3 months ago, the patient should receive a dose of 300 mg of tixagevimab and 300 mg of cilgavimab.

Expert opinion is that COVID-19 vaccination can be administered 14 days after tixagevimab/cilgavimab injection.

Who:

Inclusion (All must be met)

- Age ≥12 years and ≥40 kg
- Not currently known or suspected to be infected with SARS-CoV-2
- No known recent exposure to an individual infected with SARS-CoV-2
- Has completed a primary vaccine series at least 2 weeks prior to administration OR is unable to due to a contraindication
- No known positive COVID-19 Spike IgG antibody test within the past 60 days
- Meets A or B:

A

Not COVID-19 vaccinated due to a history of severe adverse reaction and/or allergy to the vaccine(s) or their components AND is:

- Age ≥70, or
- BMI ≥ 40, or
- Has Severe Chronic Lung Disease, or
- Has **Immunocompromise** (see definition) regardless of vaccine status

Vaccinated = Received at least 2 doses of mRNA vaccine with last vaccine dose (primary or booster) being within last 6 months

B

Unlikely to mount an adequate immune response to COVID-19 vaccination due to **Immunocompromise** (see definition below) regardless of vaccine status.

Notes

- Spike IgG antibody testing is not required, but:
  - If negative following vaccination (for those vaccinated), patient should be prioritized for treatment
  - If positive within the past 60 days, PrEP should not be ordered. Spike IgG positivity prior to 60 days is permissible if criteria otherwise met as durability of responses may be blunted.

Immunocompromised

- Active treatment for solid tumor and hematologic malignancies
- Receipt of solid-organ transplant and taking immunosuppressive therapy
- Receipt of chimeric antigen receptor (CAR)-T-cell or hematopoietic stem cell transplant (within 2 years of transplantation or taking immunosuppression therapy)
- Moderate or severe primary immunodeficiency (e.g., DiGeorge syndrome, Wiskott-Aldrich syndrome)
- Advanced or untreated HIV infection (people with HIV and CD4 cell counts <200/mm3, history of an AIDS-defining illness without immune reconstitution, or clinical manifestations of symptomatic HIV)
- Active treatment with high-dose corticosteroids (i.e., ≥20 mg prednisone or equivalent per day when administered for ≥2 weeks), alkylating agents, antimetabolites, transplant-related immunosuppressive drugs, cancer chemotherapeutic agents classified as severely immunosuppressive, tumor-necrosis (TNF) blockers, and other biologic agents that are immunosuppressive or immunomodulatory (e.g., B-cell depleting agents)
- Active CLL not in remission

Post-Exposure Prophylaxis (PEP)

Why: PEP is administered to those with an exposure someone with known COVID-19 to prevent infection or to or developing severe disease, if they do.

What: At present, there is no agent authorized for use as PEP.

Who: Given no predicted active agent, **PEP is NOT being currently offered.**

Agents to TREAT Early COVID-19

Why: Early treatment of COVID-19 aims to prevent disease progression in those at risk for severe COVID-19.

What: Agents available as early COVID-19 therapeutics:

Nirmatrelvir/Ritonavir (Paxlovid) is an oral protease inhibitor combined with a cytochrome P450 inhibitor administered as three tablets twice a day for 5 days. The drug is expected to be active across SARS-CoV-2 variants. Potential drug-drug interactions need to be considered when used. A brief guide to the pharmacology of this agent and drug interactions can be found here.

→ **Paxlovid is the recommended first line agent for outpatients with symptomatic COVID-19 who meet treatment criteria and are not taking a concomitant medication that could not be held if there is a potential for a major drug-drug interaction.**

Bebtelovimab is a monoclonal antibody with activity against Omicron (BA.1 and BA.2) and Delta variants administered as an intravenous push.

→ **Bebtolevomab is recommended for those who cannot take Paxlovid (e.g., due to serious drug-drug interactions that cannot be managed).**

Molnupriavir (Lagevrio) is an oral antiviral administered as 4 tablets twice a day for 5 days. The drug has restrictions on use including pediatrics and pregnancy. Molnupirivir is expected to be active across SARS-CoV-2 variants.

→ **Molnupirivir can be used as an alternative when Paxlovid or Bebtelovimab are not options.**

Remdesivir (Veklury) is a parenteral antiviral that is FDA approved for the treatment of certain inpatients with COVID-19. Off-label use for early COVID-19 can be considered given results of clinical trial in which outpatients with COVID-19 received 3 days of drug intravenously. The drug is expected to be active across SARS-CoV-2 variants. As it requires 3 consecutive days of intravenous administration and is a commercial product the cost of which can be billed to patients, Remdesivir should be reserved for use when Paxlovid or monoclonals are indicated but not available or appropriate. In cases where an oral agent is preferred over a 3-day infusion, Molnupirivir (below) may be considered instead of Remdesivir.

→ **Remdesivir can be used as an alternative when Paxlovid or Bebtelovimab are not options. In choosing between Remdesivir and Molupirivir the time from symptom onset to treatment should be considered as data suggest sooner administration increases efficacy. In addition, there are infusion center capacity and patient cost issues associated with Remdesivir that should be considered.**

Note:
Sotrovimab (Xevudy) is a monoclonal antibody with activity against the Omicron BA.1 and BA.1.1 and Delta variants intravenously administered over ~30 minutes. In vitro studies indicate that Sotrovimab may have reduced activity against the Omicron subvariant BA.2 and therefore, its supply has been limited by the Federal government.

Casrivimab/Imdevimab (Regen-CoV) and **Bamlanivimab/Etesevimab**, are not predicted to be fully active against the Omicron variant and are no longer being administered.

Omicron:
With Omicron the dominant circulating variant of SARS-CoV-2, agent preference will be as follows with use of lower ranked agents if **Nirmatrelvir/Ritonavir (Paxlovid**) is not available or not clinically appropriate.

Nirmatrelvir/Ritonavir (Paxlovid)

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Bebtelovimab

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Molnupriavir (Lagevrio) or Remdesivir (Veklury)

Who: Eligibility for early COVID-19 is adjusted based on EUA criteria, which can be further restricted when supply of medications is limited. UNC Health has created a priority level system which can be found here.

Ordering

Tixagevimab/Cilgavimab (Evusheld) PrEP administration is provided at UNC clinics such as Transplant, Oncology, Eastowne medical specialty, and Neurology clinics where many eligible patients receive care; other sites may be added as venues for administration with additional supply of drug. A therapy plan must be placed in EPIC and clinic workflows followed.

Bebtelovimab, and Remdesivir are ordered using the existing COVID-19 Therapeutics referral process in EPIC (e.g., EPIC order. Link to instructions for ordering are here and here).

Paxlovid and Molnupirivir can be directly prescribed by UNC providers to a UNC pharmacy or an external pharmacy. UNC Shared Services can directly mail oral agents same or next day to patients within a 40-mile radius of this facility.

Both Paxlovid and Molnupirivir can be prescribed to a pharmacy external to UNC. The NC DHHS has created a COVID-19 treatment locator.

Providers are encouraged to download and read the FDA factsheets for Providers and for Patients. These factsheets provide useful information about the products and the Patient factsheet should be given to all patients receiving an authorized agent. In addition, **UNC Infectious Diseases COVID-19 Therapeutic Agents Infosheet** on these agents can be found here.

Links

UNC COVID-19 Treatment Criteria
US DHHS COVID-19 Treatment Algorithm
Paxlovid Pharmacology and Drug Interactions
UNC Pharmacies Oral COVID-19 Medication Inventories
NC DHHS COVID-19 Treatment Locators
Ordering COVID-19 Treatment
UNC Infectious Diseases COVID-19 Therapeutic Agent Infosheet