NEW YORK CITY DEPARTMENT OF
HEALTH AND MENTAL HYGIENE
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Commissioner

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COVID-19 ORAL ANTIVIRAL TREATMENTS AUTHORIZED AND SEVERE SHORTAGE OF ORAL ANTIVIRAL AND MONOCLONAL ANTIBODY TREATMENT PRODUCTS

- **Two COVID-19 oral antiviral therapies have received Emergency Use Authorization from the U.S. Food and drug Administration (FDA), Paxlovid (Pfizer) and molnupiravir (Merck).**
  - **Paxlovid and molnupiravir reduce the risk of hospitalization and death by 88% and 30% respectively, in patients at high-risk for severe COVID-19 disease when started early after symptom onset.**
  - **Prescriptions in New York City (NYC) will be filled by Alto Pharmacy to provide free, same day home delivery regardless of insurance or immigration status.**
  - **Paxlovid is the preferred product and is available for patients age 12 years and older.**
  - **Molnupiravir should be considered for patients age 18 years and older for whom alternative FDA- authorized COVID-19 treatment options are not accessible or clinically appropriate.**
- **At this time, Sotrovimab (Xevudy) is the only authorized monoclonal antibody product expected to be effective against the omicron variant of SARS-CoV-2.**
  - **There is a pause on allocations of bamlanivimab and etesevimab together, etesevimab alone, and REGEN-COV until further notice. These products do not retain activity against omicron and should not be used.**
- **Adhere to New York State Department of Health (NYS DOH) guidance on prioritization of high-risk patients for anti-SARS-CoV-2 therapies during this time of severe resource limitations.**
- **While therapeutic shortages continue, off-label use of remdesivir on an outpatient basis may be an option.**
- **Check nyc.gov/health/covidprovidertreatments regularly for updates.**

December 27, 2021

Dear Colleagues,

This HAN includes information about available COVID-19 outpatient therapeutics, including newly authorized oral antiviral treatment.

While the availability of oral antivirals for treatment of COVID-19 is an important milestone, it comes at a time of a significant surge in cases and reduced effectiveness of existing

therapeutics due to the omicron variant, which is now the predominant variant nationally and estimated by the Centers of Disease Control and Prevention (CDC) to account for over 90% of cases in New York. Supplies of oral antivirals will initially be extremely limited, and there is now only one monoclonal antibody product that is effective for treatment of infection caused by the omicron variant. While supplies remain low, adhere to the NYS DOH guidance on prioritization of anti-SARS-CoV-2 therapies for treatment and prevention of severe COVID-19 and prioritize therapies for people of any eligible age with moderate to severe immunocompromise regardless of vaccination status or who are age 65 and older and not fully vaccinated with at least one risk factor for severe illness.

COVID-19 Oral Antiviral Treatment

The FDA authorized the first oral antiviral therapies, Paxlovid from Pfizer and molnupiravir from Merck, to treat patients with mild-to-moderate COVID-19 who are at high risk for progression to severe disease, regardless of vaccination status. The oral antivirals work by interfering with several steps in the reproductive process of SARS-CoV-2 to prevent efficient replication of the virus in host cells. The U.S. Department of Health and Human Services (HHS) provides oral antivirals at no cost to patients.

Paxlovid is the preferred product, and molnupiravir can be considered for patients age 18 years and older for whom alternative FDA-authorized COVID-19 treatment options are not accessible or clinically appropriate. Limited supply will require providers to prioritize treatment for patients at highest risk for severe COVID-19 until more product becomes available.

Paxlovid clinical trials among 2,246 high-risk patients showed an 88% reduction in the risk for hospitalization and death among people taking Paxlovid compared to those taking placebo. Paxlovid is a combination treatment with PF-07321332 (or nirmatrelvir) and ritonavir. PF-07321332 inhibits the main protease of SARS-CoV-2 virus, the 3CL-like protease, that impedes synthesis of other non-structural proteins and ultimately inhibits viral replication. Ritonavir is a protease inhibitor (also used in HIV treatment) that acts as a pharmacokinetic enhancer of protease inhibitors.

Molnupiravir clinical trials among 1,433 high-risk patients showed a 30% reduction in the risk for hospitalization and death among people taking molnupiravir compared to those taking placebo. Molnupiravir is the pro-drug of a nucleoside analog that competes with the viral RNA polymerase and induces RNA mutations that ultimately have an antiviral effect.

Eligibility

Oral antiviral treatment is authorized for patients who meet all the following criteria:

- Age 12 years and older for Paxlovid, or 18 years and older for Molnupiravir
- Weigh at least 40 kg (88 pounds)

- Test positive for SARS-CoV-2 on a nucleic acid amplification test or antigen test; results from an FDA-authorized home-test kit should be validated through video or photo but, if not possible, patient attestation is adequate
- Have mild to moderate COVID-19 symptoms
    - Patient cannot be hospitalized or receiving oxygen therapy due to COVID-19
- Are able to start treatment within 5 days of symptom onset
- Have a medical condition or other factors that increase their risk for severe COVID-19 illness.
    - Consider race and ethnicity when assessing an individual's risk. Impacts of longstanding systemic health and social inequities put Black, Indigenous, and People of Color at increased risk of severe COVID-19 outcomes and death.

For Paxlovid only:

- Therapy is contraindicated for patients with history of clinically significant hypersensitivity reactions to its active ingredients or any other components of the product; are on drugs that are highly dependent on CYP3A for clearance and for which elevated concentrations are associated with serious and/or life-threatening reactions; or are on drugs that are potent CYP3A inducers where significantly reduced Paxlovid plasma concentrations may be associated with the potential for loss of virologic response and possible resistance. See list of medications in the Paxlovid Fact Sheet for Providers, Section 7.
- Therapy is not recommended for patients with severe kidney (eGFR <30 mL/min) or liver (Child-Pugh Class C) impairment. Dosage adjustments are needed for patients with moderate renal impairment. Providers should discuss with their patients with kidney or liver problems whether Paxlovid is right for them.
- Paxlovid may lead to a risk of HIV-1 developing resistance to HIV protease inhibitors in patients with uncontrolled or undiagnosed HIV-1 infection. Patients on ritonavir- or cobicistat-containing HIV or HCV regimens should continue their treatment as indicated.

For molnupiravir only:

- Molnupiravir should be prescribed for patients age 18 years and older for whom alternative COVID-19 treatment options authorized by FDA are not accessible or clinically appropriate.
- Molnupiravir is not recommended during pregnancy. Prescribing providers should assess whether a female of childbearing potential is pregnant or not. Advise individuals of childbearing potential to use effective contraception correctly and consistently for the duration of treatment and for 4 days after the last dose of molnupiravir.
- Breastfeeding is not recommended during treatment and for 4 days after the last dose of molnupiravir. A lactating individual may consider interrupting breastfeeding and pumping and discarding breast milk during this time.

- Males of reproductive potential who are sexually active with females of childbearing potential should use a reliable method of contraception correctly and consistently during treatment and for at least 3 months after the last dose.
- For more details, please refer to molnupiravir Fact Sheet for Providers.

Clinical Considerations

Treatment is most effective when given as soon as possible and no more than 5 days after symptom onset. High-risk patients who present within 6 to 10 days of symptoms onset should be referred for monoclonal antibody therapy.

The most common side effects reported during treatment and within 14 days after the last dose of molnupiravir were mild or moderate diarrhea, nausea, dizziness, and headache. For Paxlovid, mild or moderate dysgeusia, diarrhea, hypertension, and myalgia were reported.

Oral antivirals are not authorized for pre-exposure or post-exposure prophylaxis for prevention of COVID-19 and should not be used for longer than 5 consecutive days.

Referring Patients for Oral Antivirals

To ensure equitable access to oral antivirals, the NYC Department of Health and Mental Hygiene (Health Department) has partnered with Alto Pharmacy, a pharmacy delivery service. At this time, this is the only way NYC patients can receive oral antivirals. As supplies increase, additional pharmacies will be added.

Prescriptions placed with Alto Pharmacy will be delivered to the patient's preferred address at no cost. Once the prescription is placed, patients can schedule their delivery on the Alto mobile app, by text, or by phone with Alto pharmacists. Alto Pharmacy can offer direct support in English and Spanish and support in numerous other languages through language line. Prescriptions confirmed by 5 p.m. on weekdays or 1 p.m. on weekends will be delivered the same night. For instructions on how to prescribe oral antivirals in NYC, visit nyc.gov/health/covidprovidertreatments and look for "Referring or Offering Oral Antiviral Therapy" in the "Oral Antiviral Treatment" section.

Providers who would like to automatically have molnupiravir substituted when Paxlovid is unavailable must submit two prescriptions, one for each medication, and state in the notes section of the molnupiravir prescription, "to be used in case Paxlovid prescription cannot be filled because of supply limitation." Substituting with molnupiravir can only be done for patients meeting eligibility criteria and with no contraindications for either product.

Changes to Monoclonal Antibody Use

At this time, Sotrovimab (Xevudy) is the only authorized monoclonal antibody therapeutic that is expected to be effective against the omicron variant of SARS-CoV-2. Supplies of Sotrovimab

are extremely limited and providers should adhere to NYS DOH prioritization guidance, and refer to the NYC Health Department's Letter to Providers: Omicron and Monoclonal Antibodies.

As of December 23, 2021, there is a pause on further allocations of bamlanivimab and etesevimab together, etesevimab alone, and REGEN-COV until further notice. Bamlanivimab with etesevimab and REGEN-COV do not retain activity against omicron and should not be used. Monoclonal antibody treatment can no longer be used as post-exposure prophylaxis.

Outpatient Use of Remdesivir

The National Institute of Health (NIH) has issued treatment recommendations given therapeutics shortages and inactivity of some therapeutics against the omicron variant. This includes the use of remdesivir via IV infusion on an outpatient basis. Remdesivir is FDA-approved for hospitalized patients only; use of the drug for outpatient treatment would be an off-label indication. It is currently unknown if this treatment option will be available for patients in NYC. Do not send patients to the hospital to request treatment unless first identifying a facility and making arrangements in advance. See NIH COVID-19 Treatment Guidelines for more information.

Providers not offering treatment can refer patients to NYC Health + Hospitals. Patients can be connected to a health care provider by calling 212-COVID19 (212-268-4319). Treatment is available regardless of immigration status or ability to pay.

Thank you for all you are doing to help support the safety of your patients and our city. Please check nyc.gov/health/covidprovidertreatments regularly for updated guidance, including on treatment supply and prioritization.

Sincerely,

Celia Quinn MD, MPH
Deputy Commissioner
Division of Disease Control