NC DEPARTMENT OF HEALTH AND HUMAN SERVICES

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Division of Public Health

To: All North Carolina Clinicians
From: Elizabeth Tilson, MD, MPH NC State Health Director and Chief Medical Officer
Subject: Currently Available Therapeutics for the Treatment and Prevention of COVID-19
Date: April 21, 2022

This memo provides guidance to providers for outpatient treatment and prevention of coronavirus disease 2019 (COVID-19) in patients who are at high risk of progressing to severe disease.

Background

Therapeutics are an important tool to protect patients from severe illness from COVID-19. Large supplies of therapeutics, especially oral antivirals, are now widely available and can be utilized for any patient who meets the criteria in the Emergency Use Authorization. In addition, all providers can prescribe therapeutics for their high-risk patients, even if they don't dispense them.

There are several therapeutics available for prevention and treatment of mild to moderate COVID-19 in patients who are at high risk for progressing to severe illness, including hospitalization or death. Individuals at high risk include older adults and those with underlying conditions including, but not limited to, heart disease, overweight or obesity (BMI 25 or greater), asthma, diabetes, or depression. More information on who is considered high risk is available here.

A large proportion of the North Carolina population is considered high risk based on age or underlying conditions. Therefore, anyone with a COVID-19 diagnosis should be carefully evaluated for potential treatment options. These therapies have demonstrated effectiveness against currently circulating SARS-CoV-2 variants, and many have been clinically proven to be effective in preventing hospitalization or death.

Overview of Treatment Options

Monoclonal Antibodies(mAbs):

There are currently two mAb products under Emergency Use Authorization (EUA) by the Food and Drug Administration (FDA) available and effective for treatment or prevention of COVID-19 in high-risk individuals aged 12 years and older. There have been previously approved mAbs (e.g. sotrovimab) that are no longer authorized for use as they are not effective against currently circulating SARS-CoV-2 variants.

Generic Name and Link to Fact Sheet for Providers	Also known as	Authorized Indication	Route of Administration	Dosage and Administration	Authorized Patient Population	Standing Order?	Efficacy
Bebtelovimab	**Bebtelovimab**	Treatment of mild-to-moderate COVID-19	Intravenous (IV) Infusion	175 mg of bebtelovimab administered as a single IV injection over at least 30 seconds Administer within **seven (7) days** of symptom onset	Adults and pediatric patients (12 years of age and older weighing at least 40 kg) who are at high risk of progression to severe COVID-19 and for whom alternative COVID-19 treatment options approved or authorized by the FDA are not accessible or clinically appropriate Bebtelovimab is not authorized for use in patients who are hospitalized, require respiratory support, or require increase in baseline oxygen flow rate due to COVID-19	Yes, as of February 15th, 2022	Placebo controlled trial data not available to determine % effectiveness at reducing hospitalization Retains efficacy against Omicron and the BA.2 Omicron subvariant
Tixagevimab/ cilgavimab	**EVUSHELD AZD7442**	Pre-exposure prophylaxis of COVID-19	Intramuscular (IM) Injection	300 mg of tixagevimab and 300 mg of cilgavimab administered as two separate consecutive IM injections	Adults and pediatric patients (12 years of age weighing at least 40 kg) who are not currently infected with SARS-CoV-2 and who have not had a known recent exposure to an individual infected with SARS-CoV-2 who are immunocompromised or have a contraindication for COVID-19 vaccines EVUSHELD is not authorized for use in individuals for treatment of COVID-19 or for post-exposure prophylaxis of COVID-19 in individuals who have been exposed to someone infected with SARS-CoV-2.	No - per FDA/HHS	**77% effective** in preventing SARS-CoV-2 RT-PCR symptomatic illness Retains efficacy against the Omicron BA.2 subvariant

**Per the Public Readiness and Emergency Preparedness Act, pharmacies were added to the eligible providers and can now administer monoclonal antibody treatment*

Oral Antivirals:

The FDA has issued EUAs for two types of oral antivirals for treatment of mild-to-moderate COVID-19 in patients who are at risk of severe illness.

Generic Name and Link to Fact Sheet for Providers	Also known as	Authorized Indication	Route of Administration	Dosage and Administration	Authorized Patient Population	Standing Order?	Efficacy
Nirmatrelvir/ Ritonavir	**PAXLOVID Pfizer**	Treatment of mild-to-moderate COVID-19	Oral	300 mg of nirmatrelvir and 100 mg of ritonavir twice-daily for five (5) days Initiate **within five (5) days** of symptoms onset Dose adjustment required for moderate renal impairment (eGFR ≥30 to <60 mL/min) Extensive drug interactions list	Adults and pediatric patients (12 years of age and older weighing at least 40 kg) who are at high risk for progression to severe COVID-19 PAXLOVID is not authorized for initiation of treatment in patients requiring hospitalization due to severe or critical COVID-19, for pre- or post-exposure prophylaxis for prevention of COVID-19, or for use longer than five (5) consecutive days.	No – per FDA/HHS	**88% effective** in preventing hospitalization or death when initiated within five (5) days of symptom onset Expected to maintain effectiveness across all variants
Molnupiravir	**LAGEVRIO MK-4482 Merk**	Treatment of mild-to-moderate COVID-19	Oral	800 mg twice-daily for five (5) days Initiate **within five (5) days** of symptom onset Not recommended during pregnancy	Adult patients who are at high risk for progression to severe COVID-19 and for whom alternative COVID-19 treatment options approved or authorized by the FDA are not accessible or clinically appropriate LAGEVRIO is not authorized for use in patients less than 18 years of age, for initiation of treatment in patients requiring hospitalization due to COVID-19, for pre- or post-exposure prophylaxis for prevention of COVID-19, or for use longer than five (5) consecutive days.	No – per FDA/HHS	**30% effective** in preventing hospitalization or death when initiated within five (5) days of symptom onset Retains efficacy against all Omicron subvariants

IV Antiviral:

Veklury (remdesivir) is approved by the FDA for treatment in both hospitalized and non-hospitalized patients aged 12 years and older. The FDA has issued an EUA for Veklury (remdesivir) for treatment in both hospitalized and non-hospitalized patients less than 12 years of age. **Please note that Veklury (remdesivir) is not allocated by the federal government and is only available commercially.**

Generic Name and Link to Fact Sheet for Providers	Also known as	Authorized Indication	Route of Administration	Dosage and Administration	Authorized Patient Population	Standing Order?	Efficacy
Remdesivir	**VEKLURY**	Treatment of COVID-19	Intravenous (IV) Infusion	**For patients weighing 40 kg or greater:** 200 mg loading dose on Day 1, followed by a once-daily maintenance dose of 100 mg from Day 2 via IV infusion **For patients weighing less than 40 kg:** 5 mg/kg loading dose on Day 1, followed by a once-daily maintenance dose of 2.5 mg/kg from Day 2 via IV infusion **Non-hospitalized patients:** Initiate within **seven (7) days** of symptom onset; recommended total treatment duration is 3 days **Hospitalized patients**: Initiate as soon as possible after diagnosis of symptomatic COVID-19 has been made; recommended total treatment duration is 5-10 days	**Full FDA Approval** Adult and pediatric patients (12 years of age and older and weighing at least 40 kg) who are hospitalized, **or** not hospitalized and have mild-to-moderate COVID-19, and are at high risk for progression to severe COVID-19 **EUA** Pediatric patients weighing 3.5 kg to less than 40 kg or pediatric patients less than 12 years of age weighing at least 3.5 kg who are hospitalized, **or** not hospitalized and have mild-to-moderate COVID-19, and are at high risk for progression to severe COVID-19 VEKLURY is not authorized for patients weighing less than 3.5 kg	No	**87% effective** at preventing hospitalization/ death compared to placebo in non-hospitalized patients considered high-risk for progression to severe COVID-19 Retains efficacy against all Omicron subvariants

Prioritization of Treatment Products

For non-hospitalized adults with mild to moderate COVID-19 who are at high risk of disease progression, the National Institutes of Health (NIH) Panel recommends using one of the following treatment options:

- Preferred Therapies (listed in order of preference):
  - Nirmatrelvir/ritonavir (Paxlovid)
  - Remdesivir (Veklury)
- Alternative Therapies, *for use ONLY when neither of the preferred therapies are available, feasible to use, or clinically appropriate* (listed in alphabetical order):
  - Bebtelovimab
  - Molnupiravir (Lagevrio)

How to Provide COVID-19 Therapies to Your Patients

Option 1**:** Send a prescription for oral antiviral drugs to the nearest pharmacy that has drug in stock. This option can be used for all prescribing providers in North Carolina.

- Please utilize the state's mAbs and Oral Antivirals Site Finder Tool to find the nearest pharmacy that has drug in stock.

Option 2**:** Become a dispensing provider for monoclonal antibodies and/or oral antivirals.

- New dispensing providers must register with the state's COVID-19 treatment program in order to request COVID-19 therapeutics (with the exception of Veklury which is available commercially) by completing the NC DHHS Therapeutics New Provider Request Form. NCDHHS will then create your account in the Health Partners Ordering Portal (HPOP) as a registered provider. Specific therapeutics can be requested using their respective allocation request forms located on the Therapeutics Provider Hub. Allocation requests for all products are due every Monday by 12:00 PM.
- Physicians, advanced practice registered nurses, and physician's assistants with active licensure and in good standing with their respective governing bodies can prescribe and dispense oral

antivirals for treatment of COVID-19 in accordance with the Paxlovid and Lagevrio EUAs, from their offices, if the following conditions are met:

1. The provider is registered with the NC Board of Pharmacy as a dispensing provider **OR** there is absolutely no charge to the patient for the drug or act of dispensing, including seeking reimbursement of dispensing fees through third-party payors.
    - Physicians, nurse practitioners, or physician's assistants who wish to dispense oral antivirals for the treatment of COVID-19 and charge a dispensing fee must be registered with the NC Board of Pharmacy as a dispensing physician.
    - For more information on becoming a dispensing physician, nurse practitioner, or physician's assistant please visit the NC Board of Pharmacy Dispensing Physician, Physician Assistant and Nurse Practitioners Registration Requirements.
2. Products are labeled in accordance with State and Federal dispensing laws. Details from the NC Board of Pharmacy on what information must be included on a prescription label can be found here.

Option 3**:** Direct patients to the nearest dispensing provider.

- Please utilize the state's mAbs and Oral Antivirals Site Finder Tool and EVUSHELD Site Finder Tool to direct your patients who would benefit from these treatments to the nearest sites with available inventory of these products.

Additional Resources

- National Institute of Health (NIH) COVID-19 Treatment Guidelines
- COVID-19 Therapeutics EUA Factsheets
- NCDHHS Therapeutics Information for Providers
- Register for NCDHSS Therapeutics Communications

Please submit any COVID-19 Therapeutics-related inquiries, issues, and feedback to the Therapeutics Mailbox (therapeutics.covid19@dhhs.nc.gov).