Alabama Department of Public Health (ADPH)
Alabama Emergency Response Technology (ALERT)
Health Alert Network (HAN)
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ADPH Health Advisory-Precautions for COVID-19 Therapeutics

With COVID-19 continuing to circulate in Alabama, it is crucial that providers be aware of current treatment guidelines from the National Institutes of Health (NIH) and the CDC. Along with guidelines regarding the best options for treatment comes the concern that therapeutics be used safely. **Treatment of organ transplant recipients with chronic immunosuppression requires a very high level of caution in prescribing antivirals, including carefully reviewing information regarding drug-drug interactions.** Clinicians should be aware of indications, appropriate dosing, and precautions regarding the use of therapeutics for all patients.

UAB has partnered with ADPH providing the document, UAB Medicine Paxlovid Guidance for Drug Interaction Management, as part of ongoing efforts to assist clinicians. Additional important links are included in this HAN and should be thoroughly reviewed as part of patient safety.

UAB Medicine Paxlovid Guidance for Drug Interaction Management:

https://www.alabamapublichealth.gov/covid19/assets/cov-paxlovid-di-mgmt.pdf

CDC and NIH Guidance:

Updated Outpatient Treatments or COVID-19
https://emergency.cdc.gov/han/2022/pdf/CDC_HAN_463.pdf

NIH COVID Treatment Guidelines:

https://www.covid19treatmentguidelines.nih.gov/

Persons eligible for outpatient therapeutics include:

Those who have tested positive for SARS-CoV-2 (PCR or antigen) within 5 days of symptom onset.

Those who have symptoms consistent with mild to moderate COVID-19.

Those who are at risk for progressions to severe COVID-19 disease.
https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-care/underlyingconditions.html

Those who are not hospitalized due to COVID-19 disease.

Persons age 12 years and above may be eligible for nirmatrelvir/ritonavir

Persons age 18 years or older may be eligible for molnupiravir

Prior to prescribing Paxlovid (nirmatrelvir/ritonavir), review the following:

Date of onset of symptoms since the treatment needs to start within 5 days from the beginning of symptoms.

Age of patient - must be at least 12 years old

Patient's risk of progression to severe COVID-19 disease.

Confirmation of a positive test for SARS-CoV-2.

Determine dosing and make adjustments for renal impairment:

Mild impairment (eGFR higher than 60, but lower than 90 ml/min): No change.

Moderate impairment (eGFR higher than 30, but lower than 60 ml/min): Reduce regular dose to 150 mg of nirmatrelvir (one 150 mg tablet) with 100 mg of ritonavir (one 100 mg tablet), taken together twice daily for five days.

Severe impairment (eGFR lower than 30 ml/min): Paxlovid is NOT recommended.

Determine dosing and make adjustments for hepatic impairment:

Mild to moderate impairment: No dose adjustment needed.

Severe impairment (Child-Pugh Class C or higher-Paxlovid-NOT recommended) Score calculator:

https://www.mdcalc.com/calc/340/child-pugh-score-cirrhosis-mortality

Review the patient's medication regimen-(including over-the-counter medications, herbal supplements, and any recreational drugs) for **potentially serious drug interactions:**

https://www.covid19treatmentguidelines.nih.gov/therapies/antiviral-therapy/ritonavir-boosted-nirmatrelvir--paxlovid-/paxlovid-drug-drug-interactions/

Paxlovid Fact Sheet:

https://www.fda.gov/media/155050/download

Paxlovid checklist:

https://www.fda.gov/media/158165/download

Drug Interaction Tool from University of Liverpool:

https://www.covid19-druginteractions.org/checker

Drug classes of particular concern are those that include drugs that are prone to concentration-dependent toxicities, including certain antiarrhythmics, oral anticoagulants, immunosuppressants, anticonvulsants, antineoplastics, and neuropsychiatric drugs.

If the patient is taking any medication(s) that are contraindicated for co-administration with Paxlovid:

Consider specialist review (e.g., HIV provider, transplant provider, specialist pharmacist) for patients receiving highly specialized therapies, such as immunosuppressants or antineoplastics.

Strategies for management of the concomitant medication may include dose adjustment, use of an alternative agent, increased monitoring, or temporary withholding. Note: the dose of Paxlovid should not be adjusted to avoid a drug interaction.

In settings where using these management strategies is not feasible, or where the effectiveness of ritonavir-boosted nirmatrelvir may be compromised, consider using alternative COVID-19 therapies.

For patients ages 12-17 years being considered for treatment with Paxlovid:

The same eligibility considerations as above apply, **plus:**

Confirm weight is more than 40 kg (about 88 lbs).

Additional information for pediatric patients with high-risk conditions: https://www.covid19treatmentguidelines.nih.gov/special-populations/children/#:~:text=The%20majority%20of%20children%20with,the%20risk%20factors%20outlined%20above

Prior to prescribing molnupiravir, review the following:

Date of onset of symptoms since the treatment needs to start within 5 days from the beginning of symptoms.

Age of patient - must be at least 18 years old

Assess patient's risk of progression to severe COVID-19 disease.

Confirmation of a positive test for SARS-CoV-2.

For females of childbearing potential being considered for molnupiravir:

Assess whether pregnant or not (based on report of last menstrual period in individual with regular menstrual cycles and using reliable contraception correctly and consistently or based on a negative pregnancy test).

If pregnant:

Counsel patient regarding known and potential risks and benefits of molnupiravir use during pregnancy and document that patient is aware.

Counsel patient on the pregnancy surveillance program and provide patient name and contact information to Merck, if the patient agrees (at 877-888-4231 or Report a Pregnancy Exposure:

https://pregnancyreporting.msd.com/#:~:text=Report%20a%20pregnancy%20exposure&text=To%20report%20an%20adverse%20event,contact%20your%20local%20MSD%20office.

If not pregnant:

Recommend using effective contraception during treatment and for four days after the last dose.

If breastfeeding:

Confirm education has been provided that breastfeeding is not recommended during treatment and for four days after the last dose of molnupiravir.

Recommend interrupting breastfeeding or pumping and discarding breast milk during treatment and for four days after the last dose of molnupiravir.

For males being considered for treatment with molnupiravir:

Confirm education has been provided recommending sexually active individuals with partners of childbearing age use a reliable method of contraception correctly and consistently during treatment and for at least three months after the last dose of molnupiravir.

Molnupiravir FAQ:

https://www.fda.gov/media/155056/download

Molnupiravir Fact Sheet:

https://www.fda.gov/media/155054/download

For information concerning Veklury and Bebtelovimab, see NIH guidelines:

https://www.covid19treatmentguidelines.nih.gov/tables/antiviral-characteristics/

https://www.fda.gov/media/156152/download

Medication errors and serious adverse events:

Prescribing healthcare providers and/or designees must report all medication errors and serious

adverse events potentially related to these medications to the FDA MedWatch within 7 calendar days from the healthcare provider's awareness of the event.

https://www.fda.gov/safety/medwatch-fda-safety-information-and-adverse-event-reporting-program