Indiana Health Alert Network Notification

Guidelines for Use of COVID-19 Monoclonal Antibody and Antiviral Therapeutics

January 3, 2022

Summary:

Therapeutic	Use	Prescription Course	Limitations
AZ Evusheld Injectable monoclonal	Outpatient IM injection for most severely immunocompromised at risk	Outpatient injection only *Available at hospitals that directly care for these pts*	Not as effective against omicron, very limited use and supplies
Lilly Bam/Ete mAb Roche Regeneron Infusion monoclonals **SOON NOT AVAILABLE DUE TO OMICRON**	Outpatient infusion center, COVID + and high-risk, requires a prescription	Outpatient infusion centers	NOT effective against Omicron and not available currently
GSK Sotrovimab *ONLY mAb effective against Omicron* Infusion monoclonal	Outpatient infusion center, COVID + and high-risk requires a prescription	Outpatient infusion centers	VERY Limited Supply- Only COVID + high risk for severe illness and hospitalized patients
Remdesivir (direct order) Infusion antiviral	In-patient hospital (study showed outpatient use with decrease in hospitalization vs placebo)	5 days of infusion inpatient 3 days of infusion outpatient	Restricted in hospitalized patients (not authorized for outpatient use but can be used off label)
Merck Molnupiravir Oral antiviral	Outpatient treatment, requires a prescription, within 5 days of symptoms	800 mg (four 200 mg capsules) twice daily for 5 days *Retail Pharmacies*	VERY Limited supply, no pregnant patients, birth control recommendations
Pfizer Paxlovid Oral antiviral	Outpatient treatment, requires a prescription, within 5 days of symptoms	Nirmatrelvir (150 mg tab) 2 tabs plus 1 tab of ritonavir (100 mg tab), twice daily for 5 days. *Hospitals for now*	VERY LIMITED supply, prioritize high risk for severe illness and hospitalization

Key Recommendations for Monoclonal Antibody Therapies:

AstraZeneca Evusheld®

- Evusheld is a combination product that includes two recombinant human monoclonal antibodies (tixagevimab and cilgavimab) targeting the spike protein of SARS-CoV-2; these monoclonal antibodies are administered as two separate consecutive intramuscular (IM) injections

- This long-acting monoclonal antibody therapy can be used for pre-exposure prophylaxis (PrEP) in:
    - Persons 12 years of age or older, who weigh at least 40 kg, and who are either
        - moderately to severely immunocompromised (see FDA Fact Sheet below for medical conditions or treatments that might result in moderate to severe immunosuppression), or
        - not recommended to receive COVID-19 vaccination due to a history of a vaccine contraindication.
    - NOT for treatment of people infected with SARS-CoV-2 and NOT for post-exposure prophylaxis (PEP). Providers administering this product should review and follow the instructions found in the FDA EUA.
- PROVENT Phase 3 clinical trial found that tixagevimab/cilgavimab recipients experienced a 77% reduction in incidence of COVID-19 compared placebo and showed effect for 6 months post administration (re-dosing can be considered every 6 months).
- Not a substitute for vaccination and any age-eligible person who is immunocompromised should still be vaccinated against COVID-19; can be administered at least two weeks after vaccination.
- Unfortunately, preliminary data show that the neutralizing capability of tixagevimab/cilgavimab is 12- to 30-fold lower against the Omicron variant.
- Hospitals have been asked to develop processes to take referrals for tixagevimab/cilgavimab from non-affiliate providers and healthcare organizations.
- Given the very limited supply hospitals are asked to start with people considered the most immunocompromised and unlikely to mount an adequate immune response at any point from vaccination.

<u>GSK Sotrovimab</u>

- Early in vitro data suggests sotrovimab retains activity against the Omicron variant.
- Federal government's current supply of sotrovimab is extremely limited, and additional doses of the product will not be available until the week of January 3.
- **Continue to use the bam/ete and REGEN-COV monoclonal antibody products while reserving sotrovimab for treatment of eligible outpatients at highest risk who are either**:
    - diagnosed with a test that may identify a potential case of the Omicron variant (e.g., by S gene Target Failure (SGTF) in the ThermoFisher TaqPath assay); or
    - are present in local settings where reported prevalence of Omicron is greater than 20%.
- **Until local prevalence of Omicron is greater than 20%, jurisdictions are encouraged to direct sotrovimab to sites that can provide IV treatment (within 48 hours of collection of a patient sample) to highest risk, eligible individuals diagnosed with a test that may identify a potential case of the Omicron variant.**

Key Recommendations for Antiviral Therapies:

<u>Gilead Remdesivir (Veklury®)</u>

- In an analysis of 562 participants randomly assigned in a 1:1 ratio to receive Veklury or placebo, Veklury demonstrated a statistically significant 87% reduction in risk for the composite primary endpoint of COVID-19 related hospitalization or all-cause death by Day 28 (0.7% [2/279]) compared with placebo (5.3% [15/283]) p=0.008.
- Results also showed an 81% reduction in risk for the composite secondary endpoint of medical visits due to COVID-19 or all-cause death by Day 28 for participants treated with Veklury (1.6% [4/246]) compared with placebo (8.3% [21/252]) p=0.002.
- VEKLURY is indicated for the treatment of adults and pediatric patients ≥12 years old and weighing ≥40 kg requiring hospitalization for COVID-19. VEKLURY should only be administered in a hospital or healthcare setting capable of providing acute care comparable to inpatient hospital care.

Merck Molnupiravir

- Primary data supporting this EUA for molnupiravir are from MOVe-OUT, a randomized, double-blind, placebo-controlled clinical trial studying molnupiravir for the treatment of non-hospitalized patients with mild to moderate COVID-19 at high risk for progression to severe COVID-19 and/or hospitalization.
    - Of the 709 people who received molnupiravir, 6.8% were hospitalized or died within this time period compared to 9.7% of the 699 people who received a placebo.
    - Of the people who received molnupiravir one died during the follow-up period compared to nine people who received placebo.
- **Not recommended for use during pregnancy.**
    - Molnupiravir is only authorized to be prescribed to a pregnant individual
        - after the prescribing healthcare provider has determined that the benefits of being treated with molnupiravir would outweigh the risks
        - after the prescribing health care provider has communicated the known and potential benefits and the potential risks
    - **Females** of childbearing potential are advised to use a **reliable method of birth control** correctly and consistently during treatment with molnupiravir and **for four days after the final dose**.
    - **Males** of reproductive potential who are sexually active with females of childbearing potential are advised to use a reliable method of birth control correctly and consistently during treatment with molnupiravir and **for at least three months** after the final dose.
    - Questions and concerns about reliable birth control methods that are appropriate for use during treatment with molnupiravir, as well as how molnupiravir may affect sperm cells, should be directed at one's healthcare provider.
    - Lactation: Breastfeeding is not recommended during treatment and for 4 days after the last dose of molnupiravir. A lactating individual may consider interrupting breastfeeding and may consider pumping and discarding breast milk during treatment and for 4 days after the last dose of molnupiravir.
- Molnupiravir is not authorized for use in patients under 18 years of age, for initiation of treatment in patients requiring hospitalization for COVID-19, in patients following hospitalization for COVID-19, for longer than five consecutive days, for pre- or post-exposure prophylaxis for prevention of COVID-19.
- Prescribing
    - 800 mg (four 200 mg capsules) taken orally every 12 hours for 5 days, with or without food.
    - Take molnupiravir as soon as possible after a diagnosis of COVID19 has been made and within 5 days of symptom onset.
    - 800 mg (four 200 mg capsules) taken orally every 12 hours for 5 days, with or without food.
    - Completion of the full 5-day treatment course and continued isolation in accordance with public health recommendations are important to maximize viral clearance and minimize transmission of SARS-CoV-2

Pfizer Paxlovid®

- Dosage and administration
    - Nirmatrelvir tablets co-packaged with ritonavir tablets.
    - Initiate PAXLOVID treatment **as soon as possible** after diagnosis of COVID-19 and within 5 days of symptom onset.
    - Dosage: 300 mg nirmatrelvir (two 150 mg tablets) with 100 mg ritonavir (one 100 mg tablet), with all three tablets taken together twice daily for 5 days, administered orally with or without food,
    - **Dose reduction for moderate renal impairment** (eGFR ≥30 to <60 mL/min): 150 mg nirmatrelvir (one 150 mg tablet) with 100 mg ritonavir (one 100 mg tablet), with both tablets taken together twice daily for 5 days.
    - PAXLOVID is **not recommended in patients with severe renal impairment** (eGFR <30 mL/min).
    - PAXLOVID is **not recommend in patients with severe hepatic impairment**

- Treatment course
    - 5-day treatment course of PAXLOVID should be initiated as soon as possible after a diagnosis of COVID-19 has been made, and within 5 days of symptom onset.
    - Should a patient require hospitalization due to severe or critical COVID-19 after starting treatment with PAXLOVID, the patient should complete the full 5-day treatment course per the healthcare provider's discretion.
    - If the patient misses a dose of PAXLOVID within 8 hours of the time it is usually taken, the patient should take it as soon as possible and resume the normal dosing schedule.
    - If the patient misses a dose by more than 8 hours, the patient should not take the missed dose and instead take the next 5 dose at the regularly scheduled time. The patient should not double the dose to make up for a missed dose.
    - Tablets should be swallowed whole and not chewed, broken, or crushed.

- Paxlovid is not authorized for:
    - Initiation of treatment in patients requiring hospitalization due to severe or critical COVID-19
    - Pre- or post-exposure prophylaxis for prevention of COVID-19
    - Use for longer than five consecutive days
- Paxlovid adverse events
    - Hepatotoxicity: Hepatic transaminase elevations, clinical hepatitis, and jaundice have occurred in patients receiving ritonavir.
    - HIV-1 Drug Resistance: PAXLOVID use may lead to a risk of HIV-1 developing resistance to HIV protease inhibitors in individuals with uncontrolled or undiagnosed HIV-1 infection.
    - Adverse events (incidence ≥1% and ≥5 subject difference) were dysgeusia, diarrhea, hypertension, and myalgia.

For questions related to COVID-19 therapeutics, please contact Dr. Lindsay Weaver, IDOH Chief Medical Officer, at 317-233-7400 or lweaver@isdh.in.gov.