

Provider resources: COVID-19 therapeutics options
(Updated 2/22/22)



Looking to place your first order for mAB infusions?

Complete the [order form](#) with the clinically responsible [attestation form](#), and email to OEMS@delaware.gov.

I. Treatment recommendations¹

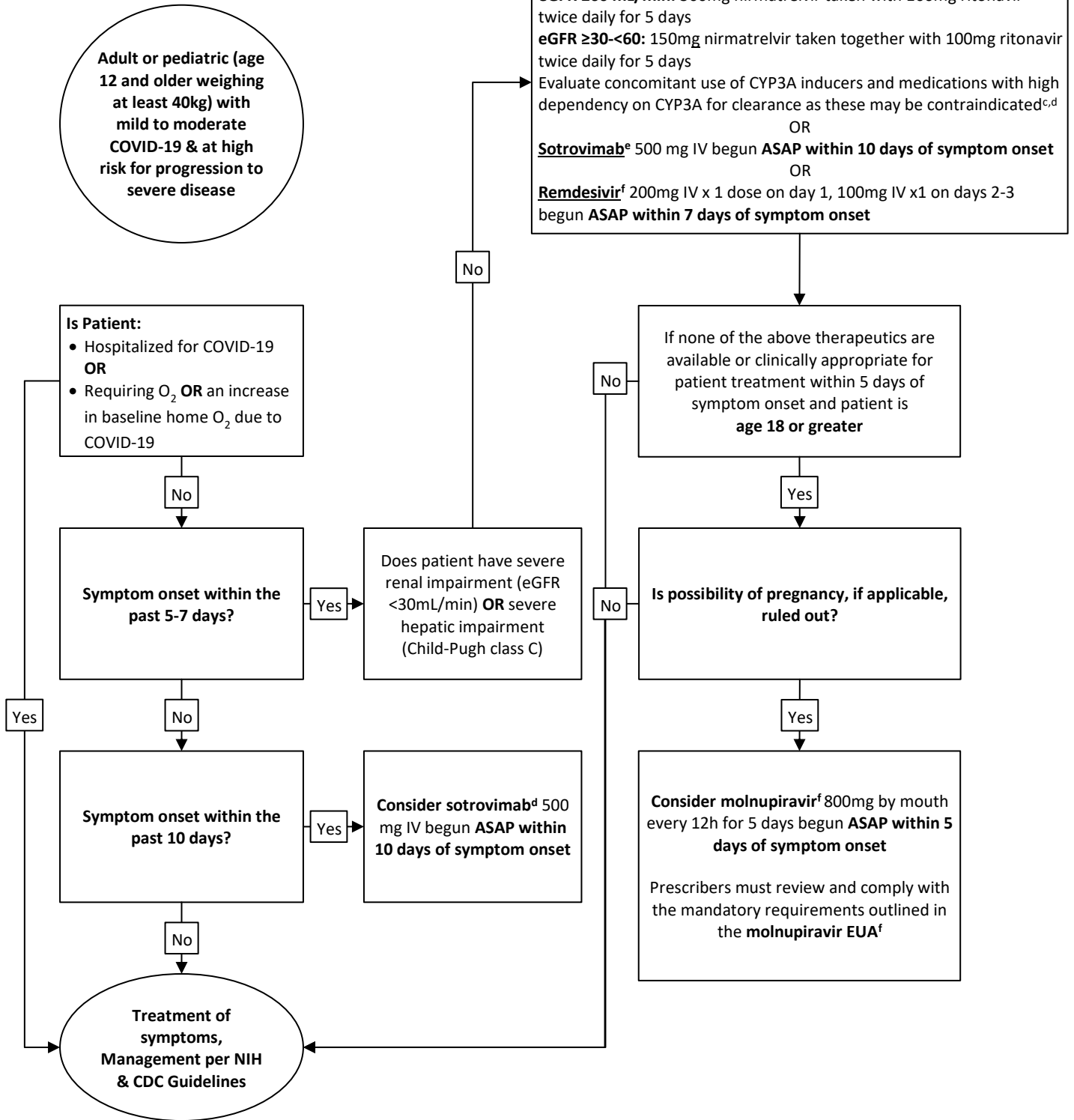
Please refer to the flow chart below for guidance around how to determine the best course of treatment for a patient. A side-by-side comparison of treatment options may also be found [here](#).

¹The COVID-19 Treatment Guidelines Panel's Statement on the Use of Anti-SARS-CoV-2 Monoclonal Antibodies or remdesivir for the Treatment of COVID-19 in Nonhospitalized Patients When Omicron Is the Predominant Circulating Variant (NIH, 12/23/21). Additional information available here: <https://www.covid19treatmentguidelines.nih.gov/>

Therapeutics Decision Aid (phe.gov)

Flow chart for treatment selection

As of Feb 01, 2022



^{2a} [NIH's COVID-19 Treatment Guidelines Panel's Statement on Therapies for High Risk, Non-hospitalized patients With Mild to Moderate COVID-19.](https://www.covid19treatmentguidelines.nih.gov/therapies/statement-on-therapies-for-high-risk-nonhospitalized-patients/) <https://www.covid19treatmentguidelines.nih.gov/therapies/statement-on-therapies-for-high-risk-nonhospitalized-patients/>

^b [PAXLOVID EUA.](https://www.fda.gov/media/155050/download) <https://www.fda.gov/media/155050/download>

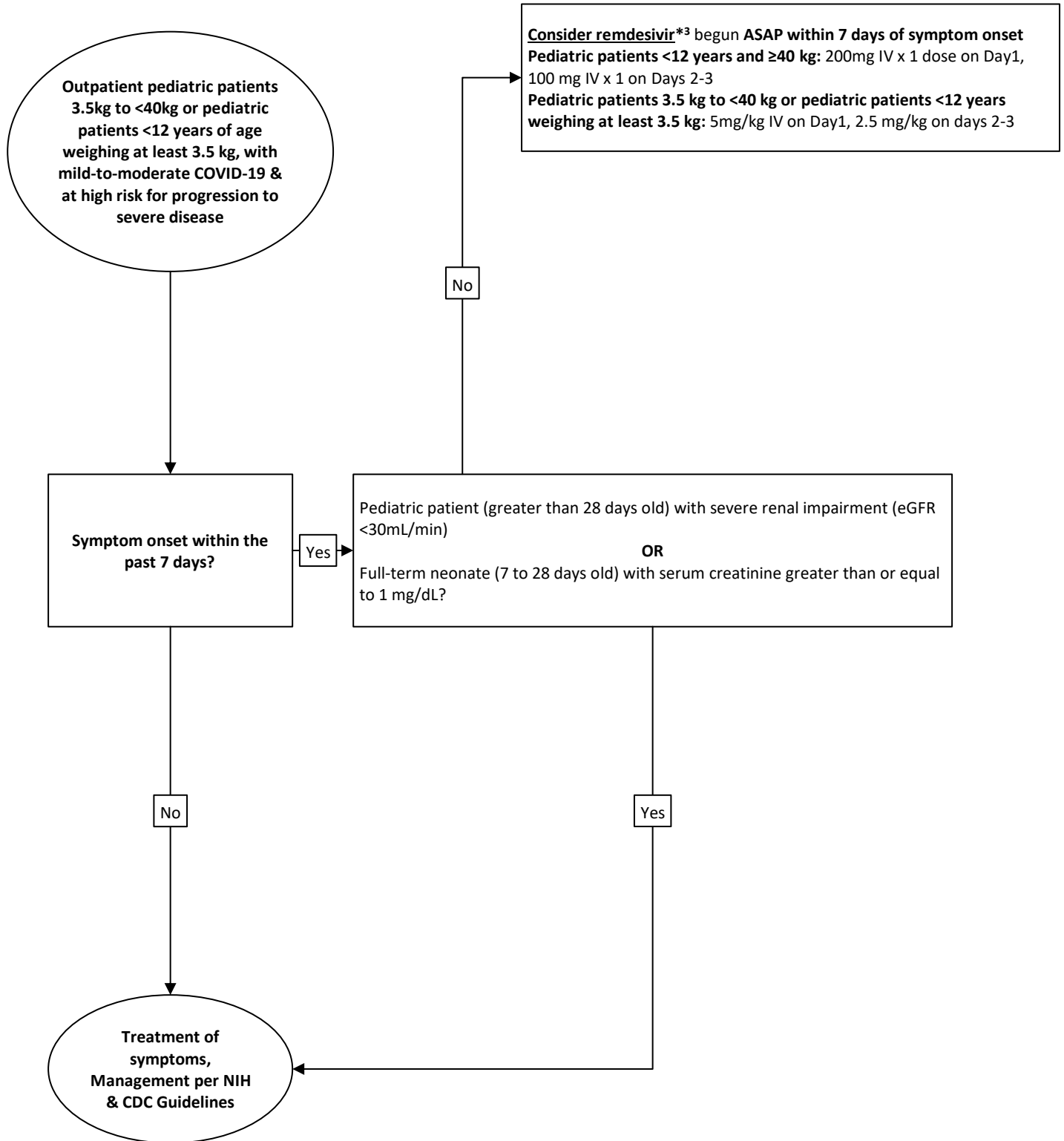
^c [NIH's COVID-19 Treatment Guidelines Panel's Statement on Potential Drug-Drug Interactions Between Ritonavir-Boosted Nirmatrelvir \(Paxlovid\) and Concomitant Medications.](https://www.covid19treatmentguidelines.nih.gov/therapies/statement-on-paxlovid-drug-drug-interactions) <https://www.covid19treatmentguidelines.nih.gov/therapies/statement-on-paxlovid-drug-drug-interactions>

^d [Sotrovimab EUA.](https://www.fda.gov/media/149534/download) <https://www.fda.gov/media/149534/download>

^e [Veklury \(remdesivir\) Prescribing Information.](https://www.gilead.com/-/media/files/pdfs/medicines/covid-19/veklury/veklury_pi.pdf) https://www.gilead.com/-/media/files/pdfs/medicines/covid-19/veklury/veklury_pi.pdf

^f [Molnupiravir EUA.](https://www.fda.gov/media/155054/download) <https://www.fda.gov/media/155054/download>

Flow chart for treatment selection, Outpatient Pediatric
As of Feb 01, 2022



* Use 100mg lyophilized vial for EUA pediatric use

³ [Remdesivir EUA](https://www.fda.gov/media/137566/download): <https://www.fda.gov/media/137566/download>.

II. Monoclonal Antibody (mAb) treatments overview⁴

a. Pre-Exposure Prophylactics (PrEP):

AstraZeneca: EVUSHELD (tixagevimab and cilgavimab)

- Use Case: EUA for PrEP only for individuals who do not have SARS-CoV-2 infection nor exposure to anyone with SARS-COV-2 infection
 - Who are moderately to severely immunocompromised and potential inadequate immune response to COVID-19 vaccination **OR**
 - Previously documented history of severe adverse reaction to a COVID-19 vaccine or any vaccine components
- Considerations: Not a substitute for COVID-19 vaccination and should not be used in unvaccinated individuals for whom vaccination is recommended and anticipated to have an adequate response.
 - Can be re-dosed every 6 months for those individuals who continue to qualify for PrEP
- **Expected to be effective against Omicron, but effectiveness should be monitored**

b. **mAb Post-Exposure Prophylactics (PEP)** – There are no current therapies recommended as PEP against the Omicron VOC. Follow the latest HHS announcement [here](#).

c. mAB Treatments

GSK: Sotrovimab (Xevudy)

- Use Case: EUA for treatment only
- Considerations: None reported at this time.
- Variant impact: **Remains effective against Omicron BA.1 variant**

Eli Lilly: Bebtelovimab

- Use Case: EUA for treatment in patients for whom alternative FDA-approved COVID-19 therapies are not accessible or appropriate
- Considerations: None reported at this time.
- Variant impact: **Effective against Omicron BA.1 variant and the BA.2 subvariant**
 - Potential for Bebtelovimab to Affect Other Drugs – **UNLIKELY**
 - Bebtelovimab is not renally excreted or metabolized by cytochrome P450 enzymes

III. Antiviral treatments overview⁵

a. Oral treatments:

Pfizer: Paxlovid (nirmatrelvir + ritonavir)

- Use Case: EUA for treatment of mild to moderate disease for patients ages 12 or older.
- **Considerations: Significant number of drug interactions; overview below, but full fact sheet should be consulted for details, found [here](#)**
 - **Potential for PAXLOVID to Affect Other Drugs**
 - PAXLOVID is an inhibitor of CYP3A and may increase plasma concentrations of drugs that are primarily metabolized by CYP3A. Co-administration of PAXLOVID with drugs highly dependent on CYP3A for clearance and for which elevated plasma concentrations are

⁴ [NIH treatment guidelines; CDC Health Advisory \(12/31/21\)](#)

⁵ [NIH treatment guidelines; CDC Health Advisory \(12/31/21\)](#)

associated with serious and/or life-threatening events is contraindicated. Co-administration with other CYP3A substrates may require a dose adjustment or additional monitoring.

- **Potential for Other Drugs to Affect PAXLOVID**
 - Nirmatrelvir and ritonavir are CYP3A substrates; therefore, drugs that induce CYP3A may decrease nirmatrelvir and ritonavir plasma concentrations and reduce PAXLOVID therapeutic effect.
- **Table 1 (section 7.3 [here](#)) from the FDA fact sheet provides listing of clinically significant drug interactions, including contraindicated drugs.** Drugs listed in Table 1 are a guide and not considered a comprehensive list of all possible drugs that may interact with PAXLOVID. Healthcare providers should consult appropriate references for comprehensive information.
- Variant impact: **Expected to be active against Omicron**

Merck: Molnupiravir

- Use Case: EUA for treatment of mild to moderate disease for patients, ages 18 or older.
- **Considerations:** Not recommended for pregnant, breastfeeding, or pediatric patients. Females with reproductive potential must use reliable contraception for the duration of treatment and **up to 4 days after last dose**. Men sexually active with individuals with reproductive potential should abstain or use reliable contraception **for 3 months after last dose of Molnupiravir**
 - **Has the lowest efficacy of all treatments and should ONLY be used when Paxlovid, Sotrovimab or Remdesivir are not available.**
- Variant impact: **Expected to be active against Omicron**

b. Intravenous treatments

Gilead: Remdesivir (Veklury)

- Use Case: FDA approval for treatment of hospitalized patients with COVID-19
- **Considerations: FDA does not consider Remdesivir to be an acceptable outpatient alternative to Bebtelovimab because administration is not feasible nor practical in certain patients⁶**
- Variant impact: **Expected to be active against Omicron**

IV. Ordering therapeutics

a. Order process: Given supply considerations, Delaware is currently managing allocations of mAb infusions.

- **First-time orders:** Complete the [order form](#) with the clinically responsible [attestation form](#), and email to OEMS@delaware.gov
- **Repeat/ subsequent orders:** Follow the same process as first-time orders above

b. Order timeline

Decisions regarding requests for product infusion are made within 1 business day of a completed request

c. Other ordering guidance

Anyone providing infusion treatment must sign and submit the attestation letter prior to receiving product.

⁶ [FDA Guidelines Bebtelovimab](#)

Any provider referring a patient for therapeutics of any type is responsible for being up to date with the latest safety and prescribing standards

d. Guidance for ordering antivirals

Ordering for any therapeutic, including antivirals, is routed the same request form outlined above

V. COVID-19 Therapeutics Locator

- a. Providers can use the HHS COVID-19 Therapeutics Locator Tool to identify pharmacies, hospitals, clinics, or other approved locations that have COVID therapeutics (anti-viral medications, and monoclonal antibody treatments including Evusheld).
- b. DPH has coordinated with these locations to ensure therapeutics are readily available across all three counties and to those who have requested them. Precise inventory may differ, but all dispensing locations have been provided contacts at DPH and informed how they can request additional supply prior to the next weekly allocation. The locator can be found with either the QR code or link [here](#)⁷:



COVID-19 Therapeutics Locator
covid-19-therapeutics-locator-dhhs.hub.arcgis.com

VI. COVID-19 Therapeutics Reporting Requirements

Providers who order and use monoclonal antibodies should adhere to the following reporting and treatment requirements.

- a. **Requirements for Sotrovimab – Reporting required weekly, by 11:59 pm ET**
- b. **Requirements for Paxlovid, Bebtelovimab, EVUSHELD – Reporting required daily, by 11:59 pm ET**
- c.

VII. Treatment prioritization given logistical and supply constraints

Providers should use their clinical judgment when prioritizing the use of mAbs PEP given limited supply. Prioritization schemes should consider equitable distribution to populations that may include individuals who may have less knowledge of and/or access to these therapies.

The NIH panel prioritized tiered risk groups based on age, vaccination status, immune status, and clinical risk factors.

Tier	Risk Group⁸
1	<ul style="list-style-type: none">• Immunocompromised individuals not expected to mount adequate immune response to vaccination or infection, regardless of vaccine status• Unvaccinated individuals at the highest risk of severe disease (anyone aged ≥75 years or anyone aged ≥65 years with additional risk factors)

⁷ [COVID Therapeutics Locator](#)

⁸ Immunocompromising conditions outlined [here](#); additional detail on prioritization available [here](#)

2	<ul style="list-style-type: none"> • Unvaccinated individuals at risk of severe disease not included in Tier 1 (anyone aged ≥ 65 years or anyone aged < 65 years with clinical risk factors)
3	<ul style="list-style-type: none"> • Vaccinated individuals at high risk of severe disease (anyone aged ≥ 75 years or anyone aged ≥ 65 years with clinical risk factors) • Note: those who have not received a booster are likely at higher risk for severe disease; patients in this situation within this tier should be prioritized for treatment.
4	<ul style="list-style-type: none"> • Vaccinated individuals at risk of severe disease (anyone aged ≥ 65 years or anyone aged < 65 with clinical risk factors) • Note: those who have not received a booster are likely at higher risk for severe disease; patients in this situation within this tier should be prioritized for treatment.

VIII. Further Resources:

- NIH: Statement on therapies for high-risk Nonhospitalized patients: [Here](#)
- NIH: Statement on Paxlovid Drug-Drug Interactions: [Here](#)
- NIH: Statement on patient prioritization for outpatient therapies: [Here](#)
- COVID-19 monoclonal antibody side-by-side comparison (updated 01/12/22): [Here](#)
- NIH: Anti-SARS-CoV-2 mAbs treatment guidelines: [Here](#)
- NIH: Information on Anti-SARS-CoV-2 Antibody products: [Here](#)
- NIH: COVID-19 Clinical Management summary: [Here](#)
- NIH: Statement on EVUSHELD for PrEP: [Here](#)
- CDC: Underlying medical conditions associated with higher risk for severe COVID-19: [Here](#)
- COVID-19 Therapeutics for Nonhospitalized Patients Overview: [Here](#)

Important COVID-19 therapeutics updates from December 2021

- New FDA EUA for Eli Lilly's monoclonal antibody, **Bebtelovimab**. Effective against Omicron BA.1 variant **and** BA.2 subvariant (February 11, 2022). *Please note: current NIH guidelines do not include recommendations regarding Bebtelovimab.*
- With new Bebtelovimab mAB, Remdesivir no longer acceptable alternative as off-label outpatient use due to 3-day administration. However, it is still recommended over Molnupiravir.
- Molnupiravir has lowest efficacy of all COVID-19 therapeutics (For oral anti-virals: Molnupiravir 30% efficacy vs. Paxlovid 88% efficacy) **with significant reproductive toxicity**.
 - o Recommended as last line of defense for patients ages 18 or older. Counseling required regarding abstinence or reliable contraception methods for individuals with reproductive potential.
- **Eli Lilly's Bamlanivimab and Etesevimab and Regeneron's Casirivimab and Imdevimab mAB's no longer approved for Post-Exposure Prophylaxis (PEP) or treatment as these agents are not effective against the Omicron variant.** Distribution is paused, however EUA is still in place for susceptible variants (January 24, 2022)
- Expanded qualifications for EVUSHELD as PrEP to include patients with documented adverse reaction(s) to COVID-19 vaccine or any of its components

Appendix

Figure 1. Therapeutic Management of Nonhospitalized Adults with COVID-19 (latest [here](#))

PATIENT DISPOSITION	PANEL'S RECOMMENDATIONS
Does Not Require Hospitalization or Supplemental Oxygen	All patients should be offered symptomatic management (AIII). For patients who are at high risk of progressing to severe COVID-19 ^a (treatments are listed in order of preference based on efficacy and convenience of use): <ul style="list-style-type: none">• Ritonavir-boosted nirmatrelvir (Paxlovid)^{b,c} (Alla)• Sotrovimab^d (Alla)• Remdesivir^{c,e} (BIIa)• Molnupiravir^{c,f} (CIIa) The Panel recommends against the use of dexamethasone or other systemic corticosteroids in the absence of another indication (AIII). ^g
Discharge From Hospital Inpatient Setting in Stable Condition and Does Not Require Supplemental Oxygen	The Panel recommends against continuing the use of remdesivir (Alla) , dexamethasone^g (Alla) , or baricitinib^g (Alla) after hospital discharge.
Discharged From Hospital Inpatient Setting and Require Supplemental Oxygen <i>For those who are stable enough for discharge but who still require oxygen^h</i>	There is insufficient evidence to recommend either for or against the continued use of remdesivir or dexamethasone.
Discharged From ED Despite New or Increased Need For Supplemental Oxygen <i>When hospital resources are limited, inpatient admission is not possible, and close follow-up ensuredⁱ</i>	The Panel recommends using dexamethasone 6 mg PO once daily for the duration of supplemental oxygen (dexamethasone use should not exceed 10 days) with careful monitoring for AEs (BIII). Since remdesivir is recommended for patients with similar oxygen needs who are hospitalized ^j , clinicians may consider using it in this setting. Given that remdesivir requires IV infusions for up to 5 consecutive days, there may be logistical constraints to administering remdesivir in the outpatient setting.

Rating of Recommendations: A = Strong; B = Moderate; C = Optional

Rating of Evidence: I = One or more randomized trials without major limitations; IIa = Other randomized trials or subgroup of analyses of randomized trials; IIb = Nonrandomized trials or observational cohort studies; III = Expert opinion

^a For a list of risk factors, see the CDC webpage [Underlying Medical Conditions Associated With Higher Risk for Severe COVID-19](#) and the Patient Prioritization for Treatment section below.

^b Ritonavir-boosted nirmatrelvir has significant drug-drug interactions. Clinicians should carefully review a patient's concomitant medications and evaluate potential drug-drug interactions.

^c If a patient requires hospitalization after starting treatment, the full treatment course can be completed at the health care provider's discretion.

^d The B.1.1.529 (Omicron) VOC is currently the dominant SARS-CoV-2 variant in the United States. Sotrovimab is the only anti-SARS-CoV-2 mAb that is active against the Omicron VOC.

^e Administration of remdesivir requires 3 consecutive days of IV infusion.

^f Molnupiravir has a lower efficacy than the other treatment options. Therefore, it should be used **ONLY** when the other options are not available or feasible.

^g There is currently a lack of safety and efficacy data on the use of these agents in outpatients with COVID-19; using systemic glucocorticoids in this setting may cause harm.

^h These individuals should receive oximetry monitoring and close follow-up through telehealth, visiting nurse services, or in-person visits.

ⁱ Provide an advanced level of home care, including supplemental oxygen (whether patients are receiving oxygen for the first time or are increasing their baseline oxygen requirements), pulse oximetry, laboratory monitoring, and close follow-up through visiting nurse services, telehealth, or in-person visits.

^j See [Therapeutic Management of Hospitalized Adults With COVID-19](#).

Figure 2. Therapeutic Management of Hospitalized Adults With COVID-19 Based on Disease Severity (latest [here](#))

DISEASE SEVERITY	PANEL'S RECOMMENDATIONS
Hospitalized but Does Not Require Supplemental Oxygen	<p>The Panel recommends against the use of dexamethasone (AIIa) or other corticosteroids (AIII)^a</p> <p>There is insufficient evidence to recommend either for or</p>
Hospitalized and Requires Supplemental Oxygen	<p>Use 1 of the following options:</p> <ul style="list-style-type: none"> • Romdesivir^{bc} (e.g. for patient who require minimal supplemental oxygen) (BIIa) • Dexamethasone plus romdesivir^{bc} (BIIb) • Dexamethasone (BI)
Hospitalized and Requires Oxygen Through a High-Flow Device or NIV	<p>Use 1 of the following options:</p> <ul style="list-style-type: none"> • Dexamethasone (AI) • Dexamethasone plus romdesivir^b (BIII) <p>For patients with rapidly increasing oxygen needs and systemic</p>
Hospitalized and Requires MV or ECMO	<ul style="list-style-type: none"> • Dexamethasone (AI)^g <p>For patients who are within 24 hours of admission to the ICU:</p> <ul style="list-style-type: none"> • Dexamethasone plus IV tocilizumab (BIIa)

Rating of Recommendations: A = Strong; B = Moderate; C = Optional

Rating of Evidence: I = One or more randomized trials without major limitations; IIa = Other randomized trials or subgroup of analyses of randomized trials; IIb = Nonrandomized trials or observational cohort studies; III = Expert opinion

^a Corticosteroids prescribed for an underlying condition should be continued.

^b If the patient progresses to requiring high-flow oxygen, NV, MV, or ECMO, complete the full course of remdesivir (refer to table A).

^c Evidence suggests that the benefit of remdesivir is greatest when the drug is given early in the course of COVID-19 (e.g., within 10 days of symptom onset). Clinical trials have not demonstrated a mortality benefit for remdesivir, but a large placebo-controlled trial showed that remdesivir reduced time to clinical recovery in hospitalized patients. See Rationale for the use of Remdesivir below.

^d Drugs are listed alphabetically. There are no studies directly comparing baricitinib and tocilizumab, and there is insufficient evidence to recommend 1 drug or 1 class of drug (i.e., JAK inhibitors, anti-IL-6 receptor mAbs) over the other. Treatment decision should be based on local guidance, drug availability, and patient comorbidities.

^e If baricitinib and IV tocilizumab are not available or not feasible to use, **tofacitinib** can be used instead of baricitinib **(BIIa)** and **IV sarilumab** can be used instead of IV tocilizumab **(BIIa)**.

^f The panel **recommends against** the use of **baricitinib** in combination with **tocilizumab** for the treatment of COVID-19, except in a clinical trial **(AIII)**. Because both baricitinib and tocilizumab are potent immunosuppressants, there is the potential for an additive risk of infections.

^g The combination of **dexamethasone plus remdesivir** may be considered for patients who have recently been intubated **(CIII)**. The Panel **recommends against** the use of **remdesivir** monotherapy in these patients **(AIIa)**.

Key: ECMO = extracorporeal membrane oxygenation; ICU = intensive care unit; IL = interleukin; IV = intravenous; JAK = Janus kinase; mAb = monoclonal antibody; MV = mechanical ventilation; NIV = noninvasive ventilation; the Panel = the COVID-19 Treatment Guidelines Panel; PO = orally