Anti-SARS-CoV-2 monoclonal antibody and anti-viral educational information (9/22/22):

Patients with risk factors for progression to severe COVID-19 may qualify for pre-emptive treatment with an anti-SARS-CoV-2 monoclonal antibody (mAb) or antiviral agent. The NIH suggests the following preference order for therapy to prevent progression to severe COVID-19 in at-risk patients: Paxlovid, remdesivir x 3 days, bebtelovimab, and molnupiravir- NIH Treatment Guidelines. The choice of specific agent for a patient may depend on product availability, patient eligibility by age/weight, hospitalization status, and drug contraindications (such as drug-drug interactions, liver/kidney dysfunction, history of infusion reactions, and pregnancy status). For example, mAb is preferred for patients at least 12 years of age and 40 kg who have significant drug-drug interactions to Paxlovid or are unable to access the drug during the eligibility window (within 5 days of symptom onset).

a. As of 5/19/22, resources allow us to approve Tier 1 patients, Tier 2 patients, and Tier 4 patients for monoclonal antibody therapy, Paxlovid prescription from hospital supply, or outpatient remdesivir infusion (depending on patient eligibility factors). Additional patients may qualify for Paxlovid prescription from community pharmacy sources based on the full CDC list of risk factors for severe COVID-19. The NIH Tier definitions are listed in Table 1, followed by specific pediatric conditions that meet these criteria.

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<th>Table 1. NIH Patient Prioritization Tiers</th>
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Pediatric Tier 1- High priority, Immunocompromised individuals not expected to mount an adequate immune response to vaccine
1. Any patients with absent or near absent T cells (<300 cells in infants or <100 cells in older children)
   a. Organ transplant recipients receiving anti-thymocyte globulin (ATG) or high dose immunosuppression within 3 months
   b. Patients with recent conditioning for bone marrow transplant (BMT), hemophagocytic lymphohistiocytosis (HLH) treatment, or high-dose immunosuppression for aplastic anemia
   c. Patients receiving induction therapy which depletes T cells for malignancy
2. Patients with common variable immunodeficiency, congenital agammaglobulinemias, or other primary immunodeficiencies characterized by an absent or poor specific Ab response to vaccination.
3. Patients with autoimmune diseases with high dose immunosuppression (i.e. systemic lupus erythematosus, steroids greater than 40mg daily and Cytoxan therapy, multiple T cell inhibitors, or rituximab)

Pediatric Tier 2- Medium priority, Unvaccinated individuals with clinical risk factors for severe disease

1. Patients with at least two risk factors for severe COVID-19 including obesity (>95%ile for age), moderate-severe asthma, hypertension, poorly-controlled diabetes, DKA, chronic lung disease, congenital heart disease, developmental disability, chronic liver disease, and chronic kidney disease
2. Patients on less intensive immunosuppression or mild-moderate immunodeficiency AND with chronic organ damage
3. Patients with end-stage lung or cardiac disease (including dependence on chronic respiratory support, pulmonary hypertension, single ventricle disease with significant cyanosis, ventricular-assist devices, surfactant deficiency, or CF with FEV1<40% predicted or after lung transplant)
4. Sickle cell disease
5. Severe obesity (>99%ile for age)

Pediatric Tier 4- Low priority, Vaccinated individuals with clinical risk factors for severe disease

1. Same risk factors of Tier 2
2. Priority within this group to individuals who have not received a booster dose

The CDC lists additional clinical factors that may increase risk for severe disease. CDC list of risk conditions. Patients with these risk factors and eligibility for oral Paxlovid may be considered for Paxlovid prescriptions from community pharmacies.

Additional information on anti-SARS-CoV-2 mAbs

Information on sotrovimab, bamlanivimab/etesevimab, casirivimab/imdevimab, and bebtelovimab is summarized in the CW guideline on connect updated mAb guidelines. On 1/24/22, the EUAs were changed to remove authorization in geographic regions where exposure is likely to have been to a non-susceptible SARS-CoV-2 variant. There are some
notable differences between each product’s efficacy against variants of concern and patient eligibility.

- Sotrovimab- ≥12 years, ≥40 kgs, only treatment (no post-exposure prophylaxis), active against omicron and delta (not omicron subvariant BA.2)
- Bamlanivimab/etesevimab- any age, any weight, both treatment and post-exposure prophylaxis, active against delta (not omicron)
- Casirivimab/imdevimab- ≥12 years, ≥40 kgs, both treatment and post-exposure prophylaxis, active against delta (not omicron)
- Bebtelovimab- ≥12 years, ≥40 kgs, only treatment (no post-exposure prophylaxis), active against omicron including subvariants

Healthcare providers who prescribe sotrovimab, bamlanivimab/etesevimab, casirivimab/imdevimab, and bebtelovimab under the emergency use authorization are required to provide patients and/or their caregivers with information consistent with the conditions of authorization listed in the EUA, and provide a copy of the sotrovimab, bamlanivimab/etesevimab, casirivimab/imdevimab, bebtelovimab Fact Sheet for Patients, Parents and Caregivers.

Additional information on oral anti-viral agents (Paxlovid, molnupiravir)

A map showing pharmacies that received allocations of the oral anti-SARS-CoV-2 medications is posted by the state:  https://www.dhs.wisconsin.gov/covid-19/therapeutics.htm

- Paxlovid- patients at high risk of progressing to severe COVID-19, 12 years of age and older weighing at least 40 kg, with positive SARS-CoV-2 testing and symptom onset within 5 days of initiating treatment. Highest efficacy of the oral antiviral drugs. Take the full 5 days to avoid emergence of resistant virus. **Check the NIH guide on drug-drug interactions or the other resources below before prescribing.** Some drugs are absolute contraindications (including some antiarrhythmics and anticonvulsants). Therapy adjustment for other interacting medications (holding drug, decreasing dose, or increased monitoring) will be required for the 5-day duration of Paxlovid plus 3-5 days after treatment completion. Notable drugs on the list include cyclosporine, everolimus, sirolimus, tacrolimus, opioids, statins, some steroids. The official EUA states that Paxlovid may not be crushed, however medical information provided by Pfizer does allow for the dissolution of the tablets immediately prior to administration to facilitate administration via feeding tubes. Please contact the COVID liaison for more details.

https://www.covid19treatmentguidelines.nih.gov/therapies/antiviral-therapy/ritonavir-boosted-nirmatrelvir-paxlovid-/ (Table A)

https://www.med.umich.edu/asp/pdf/outpatient_guidelines/Paxlovid-DDI.pdf

https://www.covid19-druginteractions.org/checker
Molnupiravir- patients at high risk of progressing to severe COVID-19, 18 years and older, with positive SARS-Co-V-2 testing and symptoms onset within 5 days of initiating treatment if patient unable to receive Paxlovid due to drug-drug interactions or availability. Lowest efficacy of the oral antiviral drugs, but better availability. Avoidance of pregnancy is necessary for 4 days (females) or 3 months (males) after completing therapy.

Healthcare providers who prescribe molnupiravir and Paxlovid under the emergency use authorization are required to provide patients and/or their caregivers with information consistent with the conditions of authorization listed in the EUA, and provide a copy of the molnupiravir or Paxlovid Fact Sheet for Patients, Parents and Caregivers.

Additional information on intravenous anti-viral agents (remdesivir)

Remdesivir is FDA approved for the treatment of COVID-19 in hospitalized patients and nonhospitalized patients who are at high risk of progression to severe COVID-19 (new 1/21/22). On 4/25/22, the FDA approval was extended to include children <12 years with the following restrictions, ≥28 days and >3 kg. It is administered as an intravenous (IV) medication daily for 5-10 days (hospitalized patient with moderate-severe COVID) or 3 days (nonhospitalized or hospitalized patient with mild-moderate early COVID at risk for progression to severe infection).

Patients treated with remdesivir who required supplemental oxygen demonstrated a reduction in mortality, improved time to recovery, and fewer progression to invasive ventilation compared with placebo (ACTT-1 Trial). However, in an open-label trial, there was no significant difference in mortality or initiation of ventilation between remdesivir and standard of care across all illness severities (WHO Solidarity trial). The randomized-controlled PINETREE Trial demonstrated an 87% reduction in hospitalization and death in nonhospitalized patients with mild to moderate disease at high risk of progression if given remdesivir for 3 days. This is the basis for recommending a short course of remdesivir IV for outpatients positive for SARS-CoV-2 and at high risk of progression to severe disease. In an updated guideline from the NIH for pediatric patients on 8/8/22, the guideline panel notes that there is insufficient evidence to recommend for or against routine use of remdesivir in children <12 years with risk factors for progression to severe COVID-19.

Pre-exposure prophylaxis with monoclonal antibody (mAb)

Evusheld (tixagevimab/cilgavimab): monoclonal antibody (mAb) that provides ~6 months of protection from COVID-19 infection (77% reduction in symptomatic COVID-19 in an unpublished trial).

- EUA for adults and pediatric patients with age ≥ 12 years and weight ≥ 40 kg who are unlikely to respond to vaccination due to moderate to severe immunocompromise or is not recommended to receive any available COVID-19 vaccine due to history of severe adverse reaction
• Administration is authorized in previously vaccinated patients as long as last dose >2 weeks prior to Evusheld
• Not authorized for patients with recent exposure to or active COVID-19 infection
• Adverse effects: risk of anaphylaxis, bleeding at injection site, headache, fatigue, cough, increased rate of serious cardiac adverse events in those with risk factors for cardiac disease or a history of pre-existing CV disease. See page 8 in the Fact Sheet for Healthcare Providers for description of the cardiac issues
• Administered as 2 IM injections (3 ml) in a large muscle (gluteal) or 4 IM injections (1.5 ml) at the same visit, followed by 1-hour observation period. The authorized dose was increased on 2/24/22 to provide better coverage for circulating variants.
• Redosing after 6 months in patients with continued eligibility was added to the FDA authorization on 6/29/22.