Children's Wisconsin Pediatric Guidelines for outpatient anti-SARS-CoV2 treatment and prevention

06/14/23

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Overview: outpatient COVID-19 therapeutics*

- **Treatment** (current + test, patient at high risk for severe illness)
  - Paxlovid if ≥12 years and ≥40 kg or adult (slides 3, 5)
  - Remdesivir any age (including <12 years or <40 kg) (slides 3, 5)
  - Molnupiravir if ≥18 years
  - Start within 5 days of sx onset for oral antiviral, 7 days for remdesivir
- **Post-exposure prophylaxis** (no current infection, yes recent exposure)
  - Not available as of 1/24/22 (slide 7)
- **Pre-exposure prophylaxis** (no current infection, no recent exposure)
  - Vaccination: all patients ≥ 6 months (slide 8)
  - Evusheld mAb: Not available as of 1/26/23 (slide 9)

*ID approval required for inpatient Paxlovid and outpatient remdesivir (slides 5, 6)
No approval required for Paxlovid or Molnupiravir prescribing at community pharmacies.
**no treatment monoclonal antibody available as of 11/30/22

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Outpatient Treatment Details

- Patients with risk factors for progression to severe COVID-19 may qualify for pre-emptive treatment with an anti-SARS-CoV-2 antiviral agent.
  - NIH Treatment Guidelines for adult and pediatric patients
  - Choice of specific agent will depend on product availability, product authorizations status, 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)
  - Treatment agents are not authorized for use when agent has no activity against the dominant circulating variant
- Paxlovid* is an anti-SARS-CoV-2 oral antiviral
  - FDA approved for adults (5/25/2023)
  - Emergency Use Authorization (EUA) from the FDA for pediatric patients with age ≥12 years and weight ≥40 kg
  - Available through the CW investigational drug pharmacy and many community pharmacies
- Remdesivir** is an anti-SARS-CoV-2 intravenous antiviral
  - FDA approved for adults and pediatric patients with age ≥28 days and weight ≥3 kg (4/25/22 pediatric FDA approval)
  - May be used outpatient as 3 daily infusions in the Special Isolation Unit (Infusion Center)

*Requires ID approval to use CW supply
**Requires ID approval for outpatient use; no approval required for inpatient use

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Pediatric risk factors for progression to severe COVID-19 infection

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)

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 (i.e. dependence on chronic respiratory support, pulmonary hypertension, single ventricle disease with significant cyanosis, ventricular-assist devices, surfactant deficiency, CF with FEV1<40% predicted)
4. Sickle cell disease
5. Severe obesity (>99%ile for age)

Tier 4, Low Priority: Vaccinated individuals with clinical risk factors for severe disease

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

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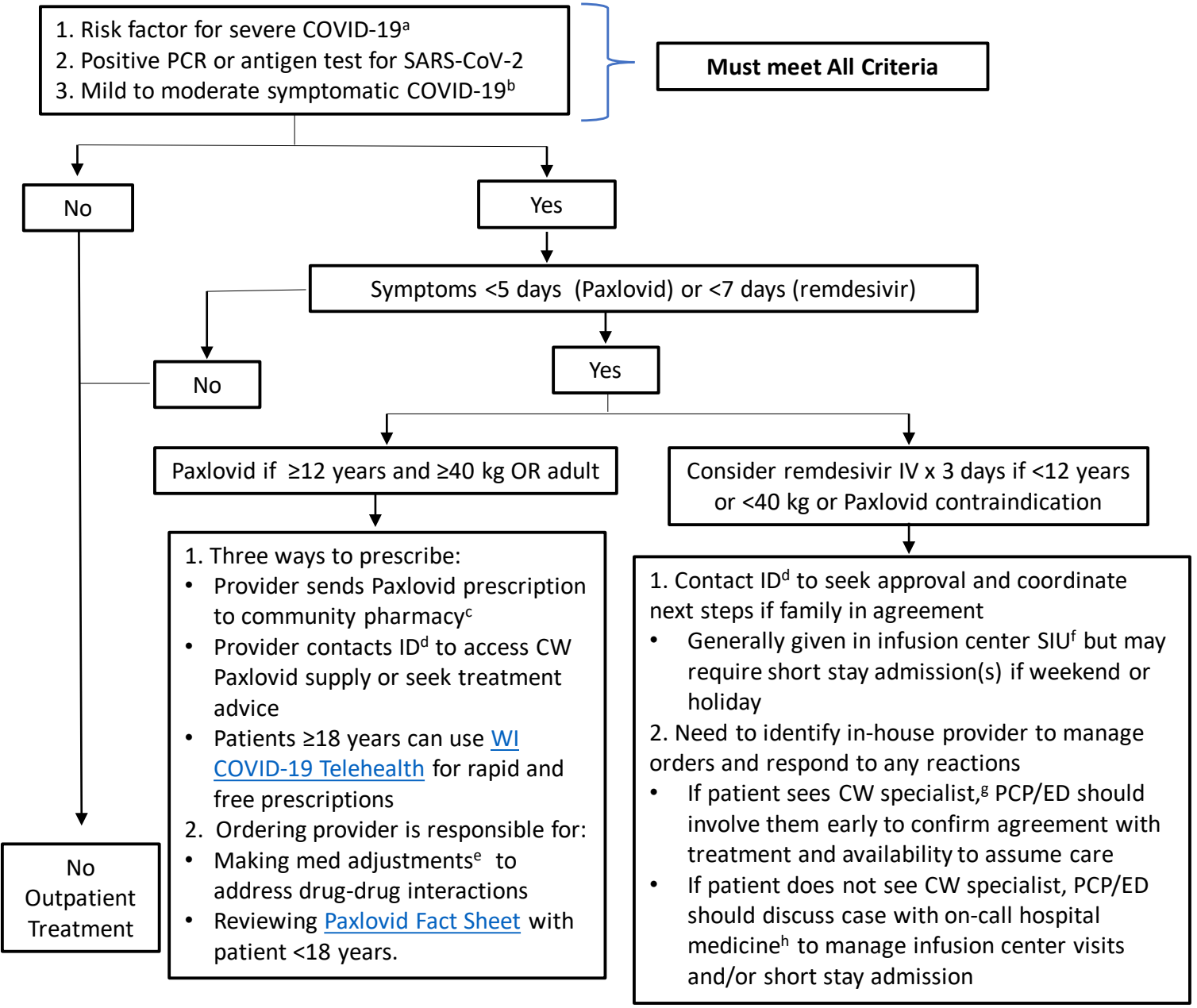
Treatment of mild-moderate COVID-19 at CW



a. Risk factors for severe COVID-19 from CDC https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-care/underlyingconditions.html

b. Mild to moderate symptomatic COVID-19 = NOT requiring hospitalization due to COVID-19 AND no new or increased oxygen requirement or respiratory support

c. Pharmacies with Paxlovid: https://www.dhs.wisconsin.gov/covid-19/treatments.htm. Epic and other EMRs will not alert providers if a pharmacy does not carry Paxlovid.

d. ID office M-F/7-3, 414-337-7070 or page ID on-call with urgent or after-hours requests. Additional resources on COVID treatment page on intranet or https://childrenswi.org/medical-professionals/tools-and-resources/covid-19-resources).

e. Questions about managing Paxlovid drug-drug interactions can be directed to the ambulatory clinic pharmacist on Voalte or contact the central pharmacy (414-266-3302). Additional resources:
https://www.covid19-druginteractions.org/checker
https://www.med.umich.edu/asp/pdf/outpatient_guidelines/Paxlovid-DDI.pdf
https://www.covid19treatmentguidelines.nih.gov/therapies/antiviral-therapy/ritonavir-boosted-nirmatrelvir--paxlovid-/
Work with relevant CW specialist for difficult to manage interactions[d]. Do not assume that community pharmacy will identify interactions

f. Infusion center visits will include ~1 hr infusion + 1 hr observation period. Potential side effects include infusion reactions and anaphylaxis (fever, chills, nausea, headache, pruritis, rash including urticaria, throat irritation, myalgia, dizziness, bronchospasm, hypotension). AST/ALT baseline check with remdesivir.

g. Relevant specialists: oncology/BMT, cardiology, pulmonary, gastroenterology, rheumatology, hematology, immunology, endocrine, nephrology. Page via CW operator 414-266-2000 or physician access center.

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Roles and responsibilities for outpatient drug requests

PCP

- Identify potentially eligible patient
- Confirm that patient/family interested in antiviral therapy
- **For IV infusions**, reach out to CW specialist on patient's care team to take over next steps
- Offer COVID-19 vaccine after infection isolation period

- If no CW specialist available or oral drug request, request drug or advice via ID on- call.
- **Verbally consent patient** for drug and provide FDA Fact Sheet
- Provide sign-out to Hospital Med for care during infusion visit
- **Order** Paxlovid Rx

ED/UC

CW Specialist

- Identify potentially eligible patient or receive call from PCP/ED
- Confirm that patient/family interested in antiviral therapy
- Request drug via or advice via ID on-call
- **Verbally consent patient** for drug and provide FDA Fact Sheet
- **Order** remdesivir using orderset or Paxlovid Rx to print
- **Designate** a team member to be available on-campus during infusion to review treatment-related lab results (per order set) and in case of infusion reaction
- Provide sign-out to PCP that COVID-19 vaccine should be offered after infection isolation period

ID physician and nurse

- Receive antiviral request phone or page
- Share approval decision and **resources** to assist with talking points for family/patient
- **Communicate** approval with pharmacy
- **Direct** requester to infusion staff for scheduling and ordering process
- **Facilitate** identification of on-campus team member for infusion (subspecialist or Hospital Med)

ID will not order medication or speak to outpatient family/patient directly

https://childrenswi.org/medical-professionals/tools-and-resources/covid-19-resources

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Anti-SARS-CoV-2 mAb for Post-exposure Prophylaxis of COVID-19

1/24/22- Post-exposure prophylaxis program on hold

- mAb products are not authorized for post-exposure prophylaxis of COVID-19 in geographic regions where exposure is likely to have been to a non-susceptible SARS-CoV-2 variant
- All mAb products with previous authorization for post-exposure prophylaxis have no activity against the current circulating variant in our area

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PEDIATRIC COVID-19 vaccination

- Recommended for all patients 6 months through adult
- Schedule depends on age, health status and product
- See COVID-19 Vaccine Interim Schedule for current vaccine schedules
  - Footnotes include information on booster doses and extended intervals between doses 1 & 2 for some people to minimize the small risk of myocarditis and pericarditis

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Anti-SARS-CoV-2 mAb for Pre-exposure Prophylaxis of COVID-19

- **Evusheld (tixagevimab/cilgavimab):** monoclonal antibody (mAb) that provides 6 months of protection from COVID-19 infection (77% reduction in symptomatic COVID-19 in 2021, early 2022)
  - **Update 1/26/23- no longer authorized for use due to resistance in the predominant circulating variants**

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