OUR LADY OF THE LAKE CHILDREN'S HOSPITAL

Treatment Guidance for Pediatric Patients with Acute COVID-19

(V.14 September 1, 2023)

Outline

1. Treatment of hospitalized children
2. Treatment of outpatients

Table 1: Treatment of hospitalized children

Disease severity	Specific therapy
Asymptomatic	Not recommended
Mild illness [a]	Supportive care only
Pneumonia without new or increased oxygen requirement in patient who is **NOT** high-risk [b] for progression to severe COVID-19	Supportive care only
Pneumonia without new or increased oxygen requirement in patient who is high-risk [b] for progression to severe COVID-19 ***If high risk and hospitalized for reasons other than COVID, refer to guideline for outpatient treatment (table 3)	Consider use of Remdesivir if 12 years or older (See table 2 below for dosages and considerations)
Pneumonia with any of the following regardless of risk level:	Remdesivir **PLUS** Steroids

-oxygen saturation (SpO2) ≤ 94% on room air for children without home oxygen requirements - need for new supplemental oxygen (conventional oxygen i.e NOT high flow oxygen or NIMV) . -need for increased conventional oxygen to maintain goal oxygen saturations for children with chronic lung or cardiac disease.	(See table 2 below for dosages and considerations) For patients ≥ 2 years who cannot receive or tolerate steroids, substitute steroids with baricitinib (see table 2)
Pneumonia requiring high flow oxygen or NIMV	Remdesivir **PLUS** Steroids
Pneumonia requiring high flow oxygen or NIMV WITH worsening respiratory status after 24h of remdesivir PLUS Steroids	Remdesivir **PLUS** Steroids **PLUS** Baricitinib OR Tocilizumab if ≥ 2 years (see table 2)
Patient admitted to the PICU with pneumonia and need for MV	Steroids only **Include** Baricitinib OR Tocilizumab if ≥ 2 years and does not improve 24 h after steroids were started. (Remdesivir does not improve recovery)

a. upper respiratory tract infection, fever, fatigue, cough, anorexia, malaise, myalgia, sore throat, headache, conjunctivitis, anosmia, loss of taste, diarrhea, nausea, and vomiting. No dyspnea, tachycardia, tachypnea, or other signs of respiratory distress. No oxygen requirement. Normal chest X-ray if obtained. No alterations in mental status. No features suggestive of multisystem inflammatory syndrome in children related to COVID-19 (MIS-C). See MIS-C guidance document for MIS-C treatment recommendations.

b. High risk includes patients with 1 of the following:
   1. Moderate or severe immunocompromise
      - Are receiving active treatment for solid tumor and hematologic malignancies.
      - Have hematologic malignancies (e.g., Lymphoma, acute leukemia) and are known to have poor responses to COVID-19 vaccines or an increased risk of severe COVID-19, regardless of the treatment status for the hematologic malignancy.
      - Received a solid-organ or islet transplant and are receiving immunosuppressive therapy.
      - Received chimeric antigen receptor T cell (CAR T-cell) therapy or a hematopoietic cell transplant (HCT) and are within 2 years of transplantation or are receiving immunosuppressive therapy.
      - Have a moderate or severe primary immunodeficiency (e.g., severe combined immunodeficiency, DiGeorge syndrome, Wiskott-Aldrich syndrome, common variable immunodeficiency disease).
      - Have advanced or untreated HIV infection (defined as people with HIV and CD4 T lymphocyte [CD4] cell counts <200 cells/mm3, a history of an AIDS-defining illness without immune reconstitution, or clinical manifestations of symptomatic HIV).
      - Are receiving active treatment with high-dose corticosteroids (i.e., ≥20 mg prednisone or equivalent per day when administered for ≥2 weeks), alkylating agents, antimetabolites, transplant-related immunosuppressive drugs, cancer chemotherapeutic agents classified as severely immunosuppressive, or immunosuppressive or immunomodulatory biologic agents (e.g., B cell–depleting agents).

   2. Unvaccinated PLUS any of the following
      - Obesity (BMI ≥95th percentile for age)
      - Medical complexity with dependence on respiratory technology
      - Severe neurologic, genetic, metabolic, or other disability that results in impaired airway clearance or limitations in self-care or activities of daily living
      - Severe asthma or other severe chronic lung disease requiring ≥2 inhaled or ≥1 systemic medications daily.
      - Severe congenital or acquired cardiac disease.
      - Diabetes
      - Multiple moderate to severe chronic diseases

Table 2: Drug Table

Drug	Dosage	Duration	Monitoring parameters & adverse effects	Contraindications
Remdesivir ("Veklury") FDA-approved for children ≥ 28 days and ≥ 3 kg For children < 28 days or < 3kg, discuss use with infectious disease.	**3 kg to < 40 kg** Loading dose: 5 mg/kg IV x1. Maintenance dose: 2.5 mg/kg IV q24h from days 2 through 5 **≥ 40 kg** Loading dose: 200 mg IV x1 Maintenance dose: 100 mg IV q24h from days 2 through 5	5 days or until discharge. May extend to 10 days if not significantly improved by day 5. May discharge prior to completion of 5-day course	Obtain baseline CBC, CMP, PT. May repeat during treatment as clinically appropriate. **Adverse effects**: Infusion-related reactions e.g., hypotension, nausea, vomiting, diaphoresis, and shivering. If clinically significant, immediately discontinue & initiate appropriate treatment. Increases in transaminases. Nausea and vomiting Prolonged PT	-Hypersensitivity to any ingredient of remdesivir. - ALT ≥ 10 times the upper limit of normal or any ALT elevation with signs or symptoms of hepatic dysfunction. -Recommended in pregnancy and breastfeeding after shared decision-making.
Steroids [c]	**Dexamethasone** PO/IV/NGT/GT 0.15 mg /kg/dose (max 6mg) q24h *** Higher dose of dexamethasone may be considered in critically ill patients with ARDS weighing ≥ 40 kg on	Up to 10 days May discharge prior to completion and need not be tapered	Hyperglycemia, hypertension, agitation, bacterial or fungal superinfection	Consult OBGYN prior to use of dexamethasone in pregnant patients. Prednisone may be preferable. Use higher dose dexamethasone with caution in patients on

	heated HFNC, NIMV or MV Higher dose dexamethasone: 20 mg IV q24 h for 5 days followed by 10 mg q24h IV for 5 days **Methylprednisolone** 0.8 mg/kg/dose IV (max 32 mg) q24h **Prednisolone** PO/NGT/GT 1 mg /kg/dose q24h (max 40 mg)			immunosuppressive drugs, cytotoxic chemotherapy in the past 21 days, neutropenia due to malignancies or expected death in the next 24 hours
Baricitinib **(*"Olumiant")*** (1 mg or 2 mg tabs) EUA for ≥ 2 years [d] Use in combination with remdesivir and dexamethasone	PO/NGT/GT ≥ 2 to 8 years: 2 mg once daily ≥ 9 years: 4 mg once daily	Up to 14 days	Baseline and daily CBC, CMP and eGFR Baseline T spot or QuantiFERON **Adverse effects:** Secondary infections, thromboembolic events, hepatotoxicity, hypersensitivity reactions	CI: Active tuberculosis, AKI, eGFR < 15 ml/min for all children, eGFR 15 to < 30 ml/min for ages 2 to < 9 years, ESRD, dialysis, ALC < 200 cells/µL, ANC < 500 cells/µL Dose adjustments needed for eGFR 15 to < 60. Avoid use in patients with active bacterial or fungal infection or HSV. Avoid use with live vaccines. Recommended in pregnancy after shared-decision making Lactating mothers should avoid breastfeeding while taking baricitinib and for 4 days after the last dose. Patients on OAT3 inhibitors such as

				probenecid need dose adjustments. **Not to be used with tocilizumab**
Tocilizumab (*"Actemra"*) EUA for ≥ 2 years [e]	**< 30 kg** 12 mg/kg/dose IV once If patient does not improve after initial dose, may repeat dose once 8 hours after initial dose. **≥30 kg** 8 mg/kg/dose IV once max dose 800 mg/dose If patient does not improve after initial dose, may repeat dose once 8 hours after initial dose		Daily CBC, CMP **Adverse effects:** constipation, diarrhea, insomnia, anxiety, hypertension, nausea, infusion reactions, anemia, hepatitis, GI perforation, opportunistic infections, neutropenia, thrombocytopenia	CI: Concurrent active infection, ALT or AST ≥ 10 times the upper limit of normal, active liver disease, ANC < 1,000/mm^3, platelet count < 50,000/mm^3, risk for GI perforation Avoid live vaccines. Use with caution in immunocompromised patients. Recommended in pregnancy and breastfeeding after shared-decision making. Use with caution in preexisting or recent onset demyelinating disorders. **Not to be used with baricitinib**

c. For patients admitted with asthma exacerbation and acute COVID-19, we recommend steroid choice of methylprednisolone, dexamethasone, or prednisone with dosing per the asthma treatment recommendations. If asthma steroid course is complete, and patient qualifies for steroid continuation based on their COVID-19 disease severity, please continue steroid of choice with dosing as referenced in Table 2.

For patients with adrenal insufficiency or who are receiving chronic steroid therapy for endocrine disorders, please contact the on-call Endocrinologist for steroid dosing guidance.

d: Baricitinib EUA: Health Care Providers must review FDA Fact Sheet for Health Care Providers available at https://www.fda.gov/media/143823/download And provide caregiver with the Fact Sheet for Patients/Caregivers available at https://www.fda.gov/media/143824/download. Provider must communicate with the caregiver and document in the EMR that 1. Baricitinib is not an FDA approved therapy 2. The patient or caregiver has the option to accept or refuse administration of Baricitinib 3. The significant known and potential risks and benefits of Baricitinib and the extent to which such risks and benefits are unknown 4. Information on available alternative treatments and the risks and benefits of those alternatives.

e: Tocilizumab EUA: Provider must communicate to the patient and/or caregiver information consistent with the "FACT SHEET FOR PATIENTS, PARENTS AND CAREGIVERS" (https://www.gene.com/download/pdf/actemra_eua_patient_fact_sheet.pdf) and provide them with a copy of this Fact Sheet prior to administration of ACTEMRA. However, if providing this information will delay the administration of ACTEMRA to a degree that would endanger the life of a patient, the information must be provided to the parent and/or caregiver as soon as feasible after ACTEMRA administration.

Table 3: Treatment of children with COVID-19 in the outpatient setting

Recommendations applicable only to children with SYMPTOMATIC mild to moderate COVID-19

Risk group for progression to severe COVID-19	Recommended therapy
High risk **1. [f] Moderate or severe immunocompromise** **2. [g] Unvaccinated PLUS any of the following** • Obesity (BMI ≥95th percentile for age • Medical complexity with dependence on respiratory technology • Severe neurologic, genetic, metabolic, or other disability that results in impaired airway clearance or limitations in self-care or activities of daily living • Severe asthma or other severe chronic lung disease requiring ≥2 inhaled or ≥1 systemic medications daily. • Severe congenital or acquired cardiac disease. • Multiple moderate to severe chronic diseases • Diabetes **Additional high-risk conditions qualify at the discretion of covering physician	Paxlovid tablets (nirmatrelvir tablets co-packaged with ritonavir tablets) if ≥ 12 years and within 5 days of symptom onset. If < 12 years, supportive care
Low risk	Supportive care Seek emergency medical attention for concerning symptoms. Standard dose multivitamins. No evidence of benefit from high dose vitamins or zinc

f: Moderate or severe immunocompromise includes the following:

- Are receiving active treatment for solid tumor and hematologic malignancies.

- Have hematologic malignancies (e.g. lymphoma, acute leukemia) and are known to have poor responses to COVID-19 vaccines or an increased risk of severe COVID-19, regardless of the treatment status for the hematologic malignancy.
- Received a solid-organ or islet transplant and are receiving immunosuppressive therapy.
- Received chimeric antigen receptor T cell (CAR T-cell) therapy or a hematopoietic cell transplant (HCT) and are within 2 years of transplantation or are receiving immunosuppressive therapy.
- Have a moderate or severe primary immunodeficiency (e.g., severe combined immunodeficiency, DiGeorge syndrome, Wiskott-Aldrich syndrome, common variable immunodeficiency disease).
- Have advanced or untreated HIV infection (defined as people with HIV and CD4 T lymphocyte [CD4] cell counts <200 cells/mm^3, a history of an AIDS-defining illness without immune reconstitution, or clinical manifestations of symptomatic HIV).
- Are receiving active treatment with high-dose corticosteroids (i.e., ≥20 mg prednisone or equivalent per day when administered for ≥2 weeks), alkylating agents, antimetabolites, transplant-related immunosuppressive drugs, cancer chemotherapeutic agents classified as severely immunosuppressive, or immunosuppressive or immunomodulatory biologic agents (e.g., B cell–depleting agents).

g : Unvaccinated = individuals who are not eligible for COVID-19 vaccination or are <2 weeks from the final dose of the primary series.

Table 4: Paxlovid dosing guidance

Treatment	EUA criteria	Dosage and administration instructions	Monitoring & adverse effects	Contraindications/ precautions
Paxlovid tablets nirmatrelvir 150 mg (3) ritonavir 100 mg (3) ***CHECK DRUG-DRUG INTERACTIONS!!*** EUA for ≥ 12 years [g]	Age 12-17 years **AND** b. Weight ≥40kg **AND** c. Documented +SARS CoV-2 viral test **AND** d. within 5 days of symptom onset **AND** e Outpatient status (not hospitalized) **AND** f. Not requiring oxygen due to COVID -19 or no increase in oxygen requirement **AND** g. Evidence of at least **ONE** high risk condition for progression to severe COVID-19 disease	Nirmatrelvir 300 mg (two 150 mg tablets) + Ritonavir 100 mg (one 100 mg tablet), taken together twice daily for a total of 5 days. Administer with or without food. Tablets cannot be split, crushed or chewed. If patient is hospitalized after starting treatment, the full 5-day course may be	Dsygeusia, diarrhea, hypertension, myalgia, hepatotoxicity, HIV resistance	Ritonavir is a strong CYP3A inhibitor and may cause significant drug-drug interactions. Co-administration with drugs highly dependent on CYP3A for clearance may lead to elevated concentrations associated with serious and/or life-threatening reactions. Consult the full prescribing information prior to and during treatment for potential drug interactions. ID approval not needed.

		completed at the provider's discretion, using patient's home meds		Prescriber should ensure compliance with EUA requirement. For eGFR 30-60 mL/min, use 150 mg nirmatrelvir. Avoid use when eGFR < 30 mL/min. Avoid in severe hepatic impairment (Child-Pugh Class C) History of significant hypersensitivity reactions to the active ingredients (nirmatrelvir or ritonavir) or any other components. Recommended in pregnancy and can be offered to lactating mothers after shared-decision making

g: As a healthcare practitioner, you must communicate to the patient and/or caregiver information consistent with the "FACT SHEET FOR PATIENTS, PARENTS, AND CAREGIVERS" and provide them with a copy of this Fact Sheet prior to administration of PAXLOVID.

FACT SHEET FOR PATIENTS, PARENTS, AND CAREGIVERS EMERGENCY USE AUTHORIZATION (EUA) OF PAXLOVID FOR CORONAVIRUS DISEASE 2019 (COVID-19) (fda.gov)

FACT SHEET FOR HEALTHCARE PROVIDERS: EMERGENCY USE AUTHORIZATION FOR PAXLOVID (fda.gov)