OUR LADY OF THE LAKE CHILDREN'S HOSPITAL

Treatment Guidance for Pediatric Patients with Acute COVID-19

(V.7 1/25/2021)

Disclaimer: Currently, the only FDA-approved treatment for COVID-19 is remdesivir. However, the FDA has issued emergency use authorizations (EUAs) for the use of barcitinib, convalescent plasma, and monoclonal antibodies (bamlanivimab, and casirivimab/imdevimab) in children and adults with COVID-19.

Supportive care remains the cornerstone of treatment for most children given that the course of the illness is typically mild. Based on guidance documents from the Pediatric Infectious Diseases Society, the Infectious Diseases Society of America, the FDA EUAs and expanding literature, the OLOL Children's Hospital COVID-19 task force suggests the following treatment plan for children with COVID-19 infections. This guidance document will be updated as more experimental data becomes available.

This guidance document does not address the management of children with the Multisystem Inflammatory Syndrome in Children (MIS-C).

Outline

1. Treatment of hospitalized children
2. Treatment of outpatients

Table 1: Treatment of hospitalized children

Clinical syndrome	Specific therapy [a]
Asymptomatic	Not recommended
Mild illness [b]	Not recommended. Supportive care only.
Pneumonia without new or increased oxygen requirement	Not recommended. Supportive care only.
Pneumonia with any of the following: -oxygen saturation (SpO2) ≤ 94% on room air for children without home oxygen requirements - need for new supplemental oxygen. -need for increased supplemental oxygen to maintain goal oxygen saturations for children with chronic lung or cardiac disease. -need for mechanical ventilation. -need for extracorporeal membrane oxygenation (ECMO)	Remdesivir **PLUS** Steroids See tables 2 and 3 for dosages and considerations. For patients ≥ 2 years who cannot receive or tolerate steroids, consider barcitinib (see table 4) as a replacement for steroids on a case-by-case basis. Discuss with on-call pediatric infectious diseases specialist.

a. Currently, there are insufficient data to recommend the routine use of convalescent plasma and tocilizumab for the treatment of COVID-19 in children outside a clinical trial. As such, the task force recommends reviewing all cases for eligibility for ongoing clinical trials.

b. 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)

REMDESIVIR

Remdesivir is FDA-approved for children 12 years or older and weighing at least 40 kg. For these children who meet clinical criteria for remdesivir use per Table 1, the medication can be ordered without additional documentation. See table below for dosages.

For children below age 12 years of age or children older than 12 years weighing 3.5 kg to < 40 kg, Remdesivir is only available via an EUA and the following steps must be taken prior to prescribing and administering the medication.

1. Healthcare providers should review the "Fact Sheet for Healthcare Providers" for information at https://www.gilead.com/remdesivir

2. The health care provider must communicate to the patient or parent/caregiver information consistent with the "Fact Sheet for Patients and Parents/Caregivers" (available at https://www.gilead.com/remdesivir) prior to the patient receiving remdesivir. Health care providers (to the extent practicable given the circumstances of the emergency) must document in the patient's medical record that the patient/caregiver has been:

a. Given the Fact Sheet for Patients and Parents/Caregivers.

b. Informed of alternatives to receiving remdesivir.

c. Informed that remdesivir is unapproved below age 12 years but is authorized for use under EUA.

3. The following tests should be performed in all patients prior to starting remdesivir and daily while receiving remdesivir: CBC with differential, CMP and PT.

4. It is mandatory for the healthcare provider to complete the FDA MedWatch Form to report all medication errors and serious adverse events within calendar 7 days from the onset of the event.

Table 2: REMDESIVIR DOSAGE

Weight	Remdesivir Loading Dose	Remdesivir Maintenance Dose	Duration of treatment	Considerations
3.5 kg to < 40 kg	5 mg/kg IV x1	2.5 mg/kg IV q24h from days 2 through 5	5 days or until hospital discharge	

≥ 40 kg	200 mg IV x1	100 mg IV q24h from days 2 through 5		Obtain baseline and daily CBC, CMP and PT 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

Remdesivir contraindications or precautions

-contraindicated in patients with known hypersensitivity to any ingredient of remdesivir.

- ALT ≥ 10 times the upper limit of normal or ALT elevation with signs or symptoms of hepatic dysfunction.

-not recommended for children >28 days old with eGFR less than 30 mL/min or full-term neonates (≥7 days to ≤28 days old) with serum creatinine greater than or equal to 1 mg/dL unless the potential benefit outweighs the potential risk.

-use in pregnancy only if the potential benefit justifies the potential risk for the mother and the fetus.

-no manufacturer dosing recommendations for children weighing < 3.5 kg.

Table 3: USE OF STEROIDS FOR COVID-19 IN CHILDREN

Recent evidence from a randomized controlled trial showed that dexamethasone decreased mortality in hospitalized adult patients with COVID-19 on supplemental oxygen or mechanical ventilation. The effect of steroid use in children is yet unknown. It is reasonable to recommend a short course of steroids for children hospitalized with COVID-19 pneumonia who require oxygen support. The task force recommends steroid use on a case-by-case basis after weighing the risks of steroid use (such as increased risk of bacterial and fungal infections, adrenal suppression, hyperglycemia, and agitation) against potential benefits in lowering mortality.

The task force discourages steroid use in children without the need for supplemental oxygen as data from the randomized trial showed no mortality benefit from dexamethasone and a non-statistically significant trend towards harm.

Steroid	Recommended dose and duration
***Dexamethasone PO/IV/NGT/GT *** Consult OBGYN prior to use in pregnant patients. Prednisone may be preferable	0.15 mg /kg/dose (max 6mg) q24h for up to 10 days
Methylprednisolone	0.8 mg/kg/dose IV (max 32 mg) q24h for up to 10 days
Prednisolone PO/NGT/GT	1 mg /kg/dose q24h (max 40 mg) for up to 10 days

Table 4: BARCITINIB

Available as “Olumiant “(Barcitinib 1 mg, Barcitinib 2 mg) film-coated, immediate-release tablets. Tablets can be taken orally or can be crushed, dispersed in water, and given via a G tube or NG tube.

Dosage and duration	Considerations
≥ 2 to 8 years: 2 mg PO/NGT/GT once daily for up to 14 days ≥ 9 years: 4 mg PO/NGT/GT once daily for up to 14 days	Use in combination with remdesivir. Obtain baseline and daily CBC, CMP and eGFR Due to risk of VTE, prophylaxis for VTE is recommended unless contraindicated.

	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. The following must be communicated with the caregiver and documented in the EMR. 1. FDA has authorized emergency use of Baricitinib, which 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. The prescribing healthcare provider and/or the provider's designee are/is responsible for mandatory reporting of all medication errors and all serious adverse events potentially related to baricitinib treatment within 7 calendar days from the onset of the event. **Adverse effects:** Secondary infections, thromboembolic events, hepatotoxicity, hypersensitivity reactions **Not recommended:** Active tuberculosis, AKI, eGFR < 15 ml/min, ESRD, dialysis, ALC < 200 cells/µL, ANC < 500 cells/µL **Caution:** Avoid use with live vaccines, adjust dose for AKI with eGR > 15 ml/min, be aware of the potential for significant drug interactions

Treatment of children with COVID-19 in the outpatient setting

Supportive care is the mainstay of treatment for non-hospitalized children. We do not recommend the use of antiviral therapy or steroids in children with COVID-19 who are not hospitalized except in a clinical trial setting.

Monoclonal antibodies (bamlanivimab and REGN-COV2 (casirivimab plus imdevimab) have received emergency use authorization (EUA) by the FDA for children 12 years or older weighing at least with 40 kg with risk factors that may increase the risk of progression to severe COVID-19/hospitalization. However, there is currently a lack of efficacy or safety data in children and the approved risk factors have not all been definitively shown to increase the risk of severe COVID-19 in the pediatric population. More so, children are generally at lower risk for severe manifestations of COVID-19.

Thus, in line with guidance from the Pediatric Infectious Disease Society (PIDS) and the Infectious Diseases Society of America (IDSA), we recommend against the routine use of monoclonal antibodies (bamlanivimab and REGN-COV2 (casirivimab plus imdevimab) for children with COVID-19 in the ambulatory setting. We encourage providers who wish to prescribe or consider the use of monoclonal antibodies in their perceived “high-risk” patients to consult pediatric infectious diseases to discuss these patients on a case-by-case basis and provide directions for administration.