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Evidence Based Practice Guideline:

Date: September 2024

Anti-Infective Medication Management for Pediatric Patients with Coronavirus Disease-2019 (COVID-19)

Background & Scope

COVID-19 (coronavirus disease 2019) is a disease caused by the SARS-CoV-2 virus. The clinical spectrum of COVID-19 ranges from asymptomatic/mild disease with non-specific signs and symptoms of acute respiratory illness, to severe pneumonia with respiratory failure and septic shock. Transmission of SARS-CoV-2 occurs primarily through exposure to respiratory droplets. Exposure can occur when individuals inhale droplets or particles that contain the virus or touch mucous membranes with hands that have been contaminated with the virus. Exhaled droplets or particles can also deposit the virus onto exposed mucous membranes.

COVID-19 is generally milder in children than in adults, and a substantial proportion of children with the infection are asymptomatic. Data from the Centers for Disease Control and Prevention (CDC) demonstrate that severe disease and death due to COVID-19 occur less often in children than in adults. However, weekly hospitalization rates for children aged <6 months are high, exceeded only by the rates for adults aged ≥75 years. Most non-hospitalized children with COVID-19 will not require any specific therapy. A small subset of children and young adults with SARS-CoV-2 infection may develop multisystem inflammatory syndrome in children (MIS-C) and many patients with MIS-C require intensive care management. See Multi-System Inflammatory Syndrome in Children (MIS-C) Associated with Coronavirus Disease in 2019 guideline for additional treatment and management considerations.

It is important to note that at the time of writing this guideline, results from pediatric clinical trials evaluating COVID-19 therapies mostly arise from retrospective analyses. Data evaluating the use of pharmacologic therapy in children with COVID-19 are limited largely to descriptive reports. This guideline will summarize the anti-infective management for pediatric patients treated in both the outpatient and hospitalized setting as recommended by the National Institute of Health (NIH) as of February 29, 2024. Recommendations that have been modified by local content experts will be stated as such. In regards to the neonatal population there is even more of a paucity of data.

Pediatric - Anti-infective Management of COVID-19 Disease Clinical Pathway v4.0

Summary of Key Management Statements

- Most non-hospitalized children with COVID-19 will not require any specific therapy.
- Children with ≥1 of the following comorbidities are at increased risk of progression to severe COVID-19:
  - Moderately or severely immunocompromised
  - Obesity (especially severe obesity)
  - 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
  - Pregnancy
  - Patient age (<1 year and 10–14 years) and non-White race/ethnicity are associated with severe disease.
- The risk of severe disease is an important factor to consider when making treatment decisions for children with COVID-19. The children most likely to benefit from antiviral treatment are those who have mild to moderate COVID-19, and are at the highest risk of severe COVID-19 (e.g., those with severe comorbidities).
- A small subset of children and young adults with SARS-CoV-2 infection may develop multisystem inflammatory syndrome in children (MIS-C). Many patients with MIS-C require intensive care management. The majority of children with MIS-C do not have underlying comorbidities.
- Patients with severe or critical respiratory symptoms should be hospitalized. Treatment with steroids, anti-virals, and/or immunomodulators is recommended based on oxygenation and level of respiratory support required.

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Inclusion and Exclusion Criteria

- This guideline is intended for physicians, advanced practice providers, clinical pharmacy specialists, and nurses caring for pediatric patients with confirmed COVID-19.

INCLUSION CRITERIA

a. All neonates and pediatric patients ≥ 1.5 kg and < years 18 yrs old with confirmed COVID-19

EXCLUSION CRITERIA

a. Neonates < 1.5 kg

Risk Factors for Severe Disease

- A meta-analysis of individual patient data showed that among hospitalized children with COVID-19, patients aged <1 year and those aged 10 to 14 years had the highest risks of intensive care unit (ICU) admission and death.
- Many published studies reported an increased relative risk of severe disease in children with comorbidities, but the overall risk of severe COVID-19 among children remains low.
- The table below is adapted from the NIH and outlines the panel's framework for assessing risk of progression to severe COVID-19 using the patient co-morbidity. Vaccination status was removed from the original NIH table as it is unclear of the level of protection it provides against current circulating strains. Recent SARS-CoV-2 infection may also provide substantial immunity form closely related variants and should also be considered in risk assessment. According to NIH guideline, the degree of risk conferred by obesity in younger children is less clear than it is in older adolescents. Also, the data for non-severe cardiac, neurologic, or metabolic disease are particularly limited.

Risk Level for Progression to Severe COVID-19 Based on Association with Patient Comorbidity

Patient Comorbidity	Risk Level for Progression to Severe COVID-19
Strong or Consistent Association with Progression to Severe COVID-19	
• Moderately or severely immunocompromised	High
• Obesity (BMI ≥95th percentile for age), especially severe obesity (BMI ≥120% of 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 • Pregnancy	High
Moderate or Inconsistent Association with Progression to Severe COVID-19	
• Aged <1 year • Prematurity in children aged ≤2 years • Sickle cell disease • Diabetes mellitus (poorly controlled) • Chronic kidney disease • Non-severe cardiac, neurologic, or metabolic disease	Intermediate
Weak or Unknown Association with Progression to Severe COVID-19	
• Mild asthma • Overweight • Diabetes mellitus (well controlled)	Low

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Clinical Spectrum of SARS-CoV-2 Infection

- The following severity classifications are adapted from adult definitions established by the NIH.
- In children with COVID-19, radiographic abnormalities are common and should not be the only criteria used to determine the severity of illness.
- The normal values for respiratory rate also vary with age in children. Therefore, hypoxemia should be the primary criterion used to define severe COVID-19, especially in younger children. With that being said, clinicians must acknowledge the limitation of pulse oximetry in some circumstances and SpO2 should always be interpreted within the context of a patient's entire clinical presentation.

Asymptomatic or pre-symptomatic infection	Individuals who test positive for SARS-CoV-2 using a virologic test (i.e., a nucleic acid amplification test [NAAT] or an antigen test) but have no symptoms consistent with COVID-19
Mild Illness	Individuals who have any of the various signs and symptoms of COVID-19 (e.g., fever, cough, sore throat, malaise, headache, muscle pain, nausea, vomiting, diarrhea, loss of taste smell) but do not have shortness of breath, dyspnea, or abnormal chest imaging
Moderate Illness	Individuals who show evidence of lower respiratory disease during clinical assessment or imaging and who have an oxygen saturation measured by pulse oximetry (SpO2) ≥94% on room air
Severe Illness	Individuals who have an SpO2 <94% on room air, tachypnea for age, or presence of lung infiltrates
Critical Illness	Individuals who have respiratory failure, septic shock, or multiple organ dysfunction

Prevention, Initial Management and Treatment Recommendations

(See "How was this guideline developed?")

Prevention

- COVID-19 vaccination is recommended for everyone who is eligible by the Centers for Disease Control and Prevention's Advisory Committee on Immunization Practices (ACIP) (Source: NIH Strong recommendation, high quality evidence). Visit the CDC website for the most up to date vaccine recommendations from the ACIP. (https://www.cdc.gov/vaccines/hcp/acip-recs/vacc-specific/covid-19.html)
- Vaccine response rates may be lower in patients who are moderately or severely immunocompromised. Specific guidance on administering vaccines to these individuals is provided by the Centers for Disease Control and Prevention.
- Clinicians should strongly encourage all household members and close contacts of patients who are immunocompromised to be vaccinated against COVID-19. (Source: NIH, Strong recommendation, high quality evidence)

Assessment

- The majority of children with mild to moderate COVID-19 will not progress to more severe illness; therefore, the NIH panel recommends managing these patients with supportive care alone. (Source: NIH Strong recommendation, high quality evidence)
- Assessing patients with confirmed COVID-19 for risk of progression to severe disease using patient co-morbidity is recommended in determining anti-viral treatment.
- When selecting treatments for COVID-19 in children, clinicians should consider factors such as the underlying disease; immune status, immunosuppressant use; disease severity of COVID-19; and potential for drug-drug interactions, overlapping toxicities, and secondary infections. Contact pediatric sub-specialists involved in patient's care if indicated. (Local consensus, expert opinion)

Treatment (Non-Hospitalized)

- Non-hospitalized adolescents aged ≥12 years and weighing ≥40 kg who have mild to moderate COVID-19 and associated with the highest risk of progression to severe COVID-19 (See *Risk Level for Progression to Severe COVID-19 Based on Association with Patient Comorbidity*) are recommended to be treated with ritonavir-boosted nirmatrelvir (Paxlovid®). (Source: NIH Moderate recommendation, expert opinion).
- The evidence to recommend anti-viral treatment in non-hospitalized children <12 years who have mild to moderate COVID-19 and are at the highest risk of progression to severe is limited. Clinicians should consider age and risk factors in the decision to treat with remdesivir. (Local consensus, expert opinion).
- Given the demonstrated efficacy, favorable side effect profile, and clinical experience in hospitalized patients, remdesivir can be

considered as an alternative to ritonavir-boosted nirmatrelvir for children aged ≥12 years who are at the highest risk of progression to severe COVID-19. (Source: NIH Weak recommendation, expert opinion).

- Clinicians should consider age and risk factors in the decision to treat with remdesivir for neonates and pediatrics that are intermediate risk for progression to severe COVID-19. (Local consensus, expert opinion).

Summary: Therapeutic Management of Non-Hospitalized Children with COVID-19 by Risk Level
(See *Risk Level for Progression to Severe COVID-19 Based on Association with Patient Comorbidity)*

Risk of Severe COVID-19	Recommendations (modified from NIH with local consensus)	
	Aged < 12 years	Aged 12-17 years
High Risk of Progression to Severe Disease	Clinicians should consider age and risk factors in the decision to treat with remdesivir *(outpatient remdesivir administration is not available at pediatric infusion centers and requires hospitalization)*	**Preferred**: Ritonavir-boosted nirmatrelvir (Paxlovid®) within 5 days of symptom onset OR **Alternative**: Remdesivir within 7 days of symptom onset (if unable to take Paxlovid®)
Intermediate Risk of Progression to Severe Disease	Clinicians should consider age and risk factors in the decision to treat with remdesivir *(outpatient remdesivir administration is not available at pediatric infusion centers and requires hospitalization)*	
Low Risk of Progression to Severe Disease	Supportive care	

Treatment (Hospitalized)

- Hospitalized pediatric patients with confirmed COVID-19 should undergo the following diagnostic studies: CBC with differential, CRP, RFP, LFT, blood cultures (if signs or concern for sepsis and considering antibiotics), and chest x-ray (Local consensus, expert opinion).
- All patients ≥ 12 years of age hospitalized for COVID-19 are at risk for development of thromboembolism and are recommended to receive anticoagulation unless treatment is contraindicated. See *Anticoagulation Therapy and Reversal of Anticoagulants Guideline* (Source: NIH Moderate recommendation, expert opinion).
- Patients < 12 years of age hospitalized for COVID-19 may also benefit from pharmacologic prophylaxis for thromboembolism. Consult hematology to assess for additional risk factors and determine the need for anticoagulation (Local consensus, expert opinion).
- Children admitted for COVID-19 who are at the highest risk of progression to severe COVID-19 with no oxygen requirement, especially those who are severely immunocompromised), consider using remdesivir x 3 days (Source: NIH Moderate recommendation, expert opinion).
- Among children admitted for reasons other than COVID-19, who are found to have mild to moderate COVID-19 and are at the highest risk of progression, treat with remdesivir for 3 days (Local consensus, expert opinion).
- Consult infectious diseases (ID) for treatment in neonates less than 30 days or considering baricitinib or tocilizumab.
- For hospitalized children requiring conventional oxygen therapy, treat with dexamethasone for 5-10 days + remdesivir for 5 days or until hospital discharge, whichever comes first (Source: NIH Moderate recommendation, expert opinion).
- For hospitalized children requiring oxygen through high flow nasal cannula or non-invasive ventilation, treat with dexamethasone for 5-10 days + remdesivir for 5 days or until hospital discharge, whichever comes first (Source: NIH Moderate recommendation, expert opinion).
  - For those who do not have rapid (e.g., within 24 hours) improvement in oxygenation after initiation of dexamethasone, baricitinib can be considered for children aged ≥ 2 years old (Source: NIH Moderate recommendation, expert opinion).
  - Baricitinib is available through an Emergency Use Authorization only (EUA). Consult ID if considering baricitinib.
- Completion of dexamethasone +/- remdesivir course is not required if patient has clinical improvement and deemed ready for discharge.
- For hospitalized children requiring mechanical ventilation or extracorporeal membrane oxygenation (ECMO), treat with dexamethasone for 5-10 days + remdesivir for 5 days (Source: NIH Strong recommendation, expert opinion for dexamethasone) (Local consensus, expert opinion for remdesivir).
  - For those who do not have rapid (e.g., within 24 hours) improvement in oxygenation after initiation of dexamethasone, tocilizumab can be considered for children aged ≥ 2 years old (Source: NIH Weak recommendation, expert opinion).

- Tocilizumab is available through an Emergency Use Authorization only (EUA). Consult ID if considering tocilizumab.
- Duration of remdesivir therapy can be extended to 10 days if patient requiring mechanical ventilation upon initiation of antiviral therapy.
- COVID-19 may lead to critical illness in children, including hypoxemic respiratory failure, acute respiratory distress syndrome, septic shock, cardiac dysfunction, thromboembolic disease, hepatic or renal dysfunction, central nervous system disease, and exacerbation of underlying comorbidities. In addition, multisystem inflammatory syndrome in children (MIS-C) is a rare, post-infectious complication of SARS-CoV-2 and is frequently associated with critical illness.
- See Pediatric Sepsis Recognition and Initial Management and/or Initial Empiric Antibiotic Recommendations for Pediatric Suspected Sepsis or Sepsis for guideline for additional information.

Therapeutic Management of Hospitalized Children with COVID-19

Does not require supplemental oxygen	Children admitted for COVID-19 who are at the highest risk of progression to severe COVID-19 (especially those who are severely immunocompromised): consider remdesivir for 3 days Children admitted for reasons other than COVID-19 who are found to have mild to moderate COVID-19 and are at the highest risk of progression: consider remdesivir for 3 days
Requires conventional oxygen therapy	Dexamethasone for 5-10 days + remdesivir for 5 days or until hospital discharge, whichever comes first Completion of 5-day course is not required if patient has clinical improvement and deemed ready for discharge
Requires oxygen therapy with high flow nasal cannula or non-invasive ventilation (i.e. beyond low-flow nasal cannula)	Dexamethasone for 5-10 days + remdesivir for 5 days or until hospital discharge, whichever comes first Completion of 5-day course is not required if patient has clinical improvement and deemed ready for discharge For children who do not have rapid (e.g., within 24 hours) improvement in oxygenation after initiation of dexamethasone, consider baricitinib for children aged ≥ 2 years old. Consult ID
Requires oxygen mechanical ventilation or ECMO	Dexamethasone for 5-10 days plus remdesivir for 5 days. Duration of remdesivir therapy can be extended to 10 days if patient requiring mechanical ventilation upon initiation of antiviral therapy For children who do not have rapid (e.g., within 24 hours) improvement in oxygenation after initiation of dexamethasone, consider tocilizumab for children aged ≥ years old. Consult ID

Medications Prescribed in the Treatment of COVID-19

Medication	Indication	Prescribing Considerations

Ritonavir-boosted nirmatrelvir (Paxlovid)	Non-hospitalized adolescents aged ≥12 years and weighing ≥40 kg who have mild to moderate COVID-19 and are at the highest risk of progression to severe COVID-19	• Nirmatrelvir 300 mg and ritonavir 100 mg twice daily for 5 days
		• Initiate as soon as possible following COVID-19 diagnosis and within 5 days of symptom onset.
		• Assess for drug-drug interactions and contraindications (https://covid19-druginteractions.org/checker)
		• Renal function adjustments:
		  ○ eGFR ≥60 ml/min no adjustment necessary
		  ○ eGFR ≥30-60 ml/min: 150 mg nirmatrelvir/100 mg ritonavir BID x 5 days

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Remdesivir	Remdesivir is approved by the FDA for use in hospitalized and non-hospitalized pediatric weighing ≥1.5kg	• Dosing, Neonates and Children
		  ○ ≥ 1.5kg to 3kg: IV 2.5mg/kg x 1 dose, then 1.25 mg/kg once daily x 4 days
		  ○ 3kg to < 40kg: IV 5mg/kg x 1 dose, then 2.5 mg/kg once daily x 4 days
		  ○ ≥40kg: IV 200mg x 1 dose, then 100mg once daily x 4 days

Prophylactic anticoagulation	All patients ≥ 12 hospitalized for COVID-19 are at risk for development of thromboembolism and are recommended to receive anticoagulation unless treatment is contraindicated. Patients < 12 hospitalized for COVID-19 may also benefit from pharmacologic prophylaxis for thromboembolism.	• ≥ 12 years old: *Anticoagulation Therapy and Reversal of Anticoagulants Guideline* • < 12: Consult hematology for assess for additional risk factors and the need for anticoagulation
Dexamethasone	Hospitalized patients with severe disease requiring any oxygen support	• Dosing: 0.15mg/kg/dose once daily IV or PO, max of 6mg; duration is a max of 10 days • Concern in patients that are immunocompromised, may cause harm and consider on case by case basis

Tociluzumab
 	
Tociluzumab is available for hospitalized pediatric patients that meet criteria through an Emergency Use Authorization (EUA)* only.
	Interleukin-6 inhibitor that has received an FDA Emergency Use Authorization for the treatment of hospitalized adults and children with COVID-19 who are aged ≥2 years; receiving systemic corticosteroids; and require supplemental oxygen, non-invasive ventilation, mechanical ventilation, or ECMO
	
	EUA fact sheet must be given to families
		• **Consult Infectious Diseases**
		• Contraindications:
		  ○ Active or known tuberculosis infection
		  ○ Clear evidence of bacterial, viral (other than COVID-19) or fungal infection
		  ○ Hepatotoxicity defined as: AST/ALT >5 times ULN, neutrophils <0.5, platelets <50
		  ○ High risk of bowl perforation (diverticulitis, small bowel obstruction)
		  ○ Condition or treatment resulting in ongoing immune suppression
		• Dosing:
		  ○ <30 kg: 12 mg/kg/dose IV, max of 800mg; duration one dose
		  ○ ≥30kg: 8 mg/kg/dose IV, max of 800mg; duration one dose
		• Warnings/Precautions
		  ○ Serious infections
		  ○ GI perforation
		  ○ Hypersensitivity
		• Monitoring: CBC with differential and LFTs
		• See link to Tociluzimab EUA Fact sheet. Fact sheet required to be given to families

Baricitinib
 	
Baricitinib is available for hospitalized pediatric patients that meet criteria through an Emergency Use Authorization (EUA)* only.
	Immunomodulator that has received FDA EUA for treatment of
	treatment of coronavirus disease 2019 (COVID-19) in hospitalized pediatric patients 2 to less than 18
	years of age requiring supplemental oxygen, non-invasive or invasive mechanical ventilation, or extracorporeal membrane oxygenation (ECMO).
	
	EUA fact sheet must be given to families
		• **Consult Infectious Diseases**
		• Precaution: Active or known tuberculosis infection
		• Dosing:
		  ○ 2-≤9 years old: 2mg flat dose PO once daily, max 14 days or until hospital discharge (whichever comes first)
		  ○ ≥9 years old: 4mg flat dose PO once daily, max 14 days or hospital discharge (whichever comes first)
		  ○ Dosing adjustments are required for reduced eGFR, increased liver enzymes, or immunosuppression noted by ANC or ALC.
		• Warnings/Precautions
		  ○ Serious infections
		  ○ Thrombosis
		  ○ GI perforation
		• Monitoring: renal function, CBC, LFTs
		• See link to Baricitinib EUA Fact Sheet. Fact sheet required to be given to families

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Antibiotics for suspected co-infection	Blood culture and antibiotics may be warranted if the patient has signs or symptoms of sepsis and/or respiratory co-infection.	• See Pediatric Sepsis Recognition and Initial Management • See Initial Empiric Antibiotic Recommendations for Pediatric Suspected Sepsis or Sepsis

**EUA: The FDA may authorize unapproved medical products or unapproved uses of approved medical products to be used in an emergency to diagnose, treat, or prevent serious or life-threatening diseases or conditions caused by a chemical, biological, radiological, and nuclear threat agents when certain criteria are met, including there are no adequate, approved, and available alternatives.*

Major References

1. COVID-19 Treatment Guidelines Panel. Coronavirus Disease 2019 (COVID-19) Treatment Guidelines. National Institutes of Health. Available at https://www.covid19treatmentguidelines.nih.gov/. Accessed June 22, 2024.
2. Aparicio, C., Willis, Z. I., Nakamura, M. M., Wolf, J., Little, C., Maron, G. M., Sue, P. K., Anosike, B. I., Miller, C., Bio, L. L., Singh, P., James, S. H., & Oliveira, C. R. (2024). Risk Factors for Pediatric Critical COVID-19: A Systematic Review and Meta-Analysis. Journal of the Pediatric Infectious Diseases Society, 13(7), 352–362. https://doi.org/10.1093/jpids/piae052

How was this Guideline Developed?

- This guideline was developed by a multi-disciplinary group of caregivers and subject matter experts experienced in the management of pediatric patients requiring treatment for COVID-19.
- This guideline was adopted and/or adapted from the National Institute of Health (NIH) COVID-19 Treatment guidelines that were published in February 2024. The NIH published guidance on the treatment of COVID-19 in children was extrapolated mostly from recommendations for adults with COVID-19, recommendations for children with other viral infections, and expert opinion. The NIH and local consensus recommendations are all rated as expert opinion.

Acronyms and Abbreviations

COVID-19	Coronavirus-19
ECMO	Extracorporeal membrane oxygenation
EUA	Emergency Use Authorization
ID	Infectious diseases
NIH	National Institute of Health
MIS-C	Multi-System inflammatory syndrome in children
SpO^2	Oxygen saturation

Disclaimer: Practice recommendations are based upon the evidence available at the time the clinical practice guidance was developed. Clinical practice guidelines (including summaries and pathways) do not set out the standard of care and are not intended to be used to dictate a course of care. Each physician/practitioner must use his/her independent judgement in the management of any specific patient and is responsible, in consultation with the patient and/or the patient's family to make the ultimate judgement regarding care. If you have questions about any of the clinical practice guidelines or about the guideline development process please contact the Rainbow Evidence Practice Program at RainbowEBPprogram@uhhospitals.org

Initial Approval April 2020
Revised June 2020, Dec 2020, Oct 2021, Sep 2024

Pediatric patient with confirmed COVID-19
All neonates and pediatric patients > 1.5 kg and < years 18 yrs old with confirmed COVID-19

This guideline does not include the diagnosis or management of MIS-C

Severe or Critical Illness? See Box 1

YES

Severity of illness requires hospitalization.

Consult ID for admitted neonates < 30 days

NO

Risk Level for Progression to Severe COVID-19 (See Box 2)	**Recommendations (modified from NIH with local consensus)**	
	Aged < 12 years	Aged ≥ 12-17 years
High Risk of Progression to Severe Disease	Clinicians should consider age and risk factors in the decision to treat with remdesivir *(outpatient remdesivir administration is not available at pediatric infusion centers and requires hospitalization)*	Preferred: Ritonavir-boosted nirmatrelvir (Paxlovid®) within 5 days of symptom onset OR Alternative: Remdesivir within 7 days of symptom onset (if unable to take Paxlovid®)
Intermediate Risk of Progression to Severe Disease	Clinicians should consider age and risk factors in the decision to treat with remdesivir *(outpatient remdesivir administration is not available at pediatric infusion centers and requires hospitalization)*	
Low Risk of Progression to Severe Disease	Supportive care	

Decision to treat with IV antiviral necessitating hospital admission?

NO

YES

- Provide supportive care
- Script for ritonavir-boosted nirmatrelvir if agreed
- Discharge with return precautions

See Box 3 for anti-infective agent dosing

Does not require supplemental oxygen	Children admitted for COVID-19 who are at the highest risk of progression to severe COVID-19 (especially those who are severely immunocompromised): consider remdesivir for 3 days Children admitted for reasons other than COVID-19 who are found to have mild to moderate COVID-19 and are at the highest risk of progression: consider remdesivir for 3 days
Requires conventional oxygen therapy	Dexamethasone 5-10 days + remdesivir for 5 days or until hospital discharge, whichever comes first Completion of 5-day course is not required if patient has clinical improvement and deemed ready for discharge
Requires oxygen therapy with high flow nasal cannula or non-invasive ventilation (i.e. beyond low-flow nasal cannula)	Dexamethasone 5-10 days + remdesivir for 5 days or until hospital discharge, whichever comes first Completion of 5-day course is not required if patient has clinical improvement and deemed ready for discharge For children who do not have rapid (e.g., within 24 hours) improvement in oxygenation after initiation of dexamethasone, consider baricitinib for children aged ≥ 2 years old. Consult ID
Requires oxygen mechanical ventilation or ECMO	Dexamethasone 5-10 days plus remdesivir for 5 days. Duration of remdesivir therapy can be extended to 10 days if patient requiring mechanical ventilation upon initiation of antiviral therapy For children who do not have rapid (e.g., within 24 hours) improvement in oxygenation after initiation of dexamethasone, consider tocilizumab for children aged ≥ years old. Consult ID

Blood culture and antibiotics may be warranted if the patient **has signs or symptoms of sepsis** and/or respiratory co-infection.

See **Pediatric Sepsis Recognition and Initial Management Guideline**

Box 1: COVID-19 Disease Severity

Asymptomatic	Individuals who test positive for SARS-CoV-2 but have no symptoms consistent with COVID-19.
Mild Illness	Individuals who have any of the various signs and symptoms of COVID-19 but do not have shortness of breath, dyspnea, or abnormal chest imaging
Moderate Illness	Evidence of lower respiratory disease during clinical assessment or imaging and an SpO2 ≥94% on room air
Severe Illness	Individuals who have an SpO2 <94% on room air, tachypnea for age, or presence of lung infiltrates
Critical Illness	Individuals who have respiratory failure, septic shock, or multiple organ dysfunction

Box 2: Risk Level for Progression to Severe COVID-19 Based on Association with Patient Comorbidity

Patient Comorbidity	Risk Level for Progression to Severe COVID-19
Strong or Consistent Association with Progression to Severe COVID-19	
• Moderately or severely immunocompromised	High
• Obesity (BMI ≥95th percentile for age), especially severe obesity (BMI ≥120% of 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 • Pregnancy	High
Moderate or Inconsistent Association with Progression to Severe COVID-19	
• Aged <1 year • Prematurity in children aged ≤2 years • Sickle cell disease • Diabetes mellitus (poorly controlled) • Chronic kidney disease • Non-severe cardiac, neurologic, or metabolic disease	Intermediate
Weak or Unknown Association with Progression to Severe COVID-19	
• Mild asthma • Overweight • Diabetes mellitus (well controlled)	Low

Box 3: Medications Prescribed in the Treatment of COVID-19

Medication	Indication	Prescribing Considerations

Ritonavir-boosted nirmatrelvir (Paxlovid)	Non-hospitalized adolescents aged ≥12 years and weighing ≥40 kg who have mild to moderate COVID-19 and are at the highest risk of progression to severe COVID-19	• Nirmatrelvir 300 mg and ritonavir 100 mg twice daily for 5 days
		• Initiate as soon as possible following COVID-19 diagnosis and within 5 days of symptom onset.
		• Assess for drug-drug interactions and contraindications (https://covid19-druginteractions.org/checker)
		• Renal function adjustments:
		  ○ eGFR ≥60 ml/min no adjustment necessary
		  ○ eGFR ≥30-60 ml/min: 150 mg nirmatrelvir/100 mg ritonavir BID x 5 days

Remdesivir	Remdesivir is approved by the FDA for use in hospitalized and non-hospitalized pediatric weighing ≥1.5kg	• Dosing, Neonates and Children
		  ○ ≥ 1.5kg to 3kg: IV 2.5mg/kg x 1 dose, then 1.25 mg/kg once daily x 4 days
		  ○ 3kg to < 40kg: IV 5mg/kg x 1 dose, then 2.5 mg/kg once daily x 4 days
		  ○ ≥40kg: IV 200mg x 1 dose, then 100mg once daily x 4 days

Prophylactic anticoagulation	All patients ≥ 12 hospitalized for COVID-19 are at risk for development of thromboembolism and are recommended to receive anticoagulation unless treatment is contraindicated. Patients < 12 hospitalized for COVID-19 may also benefit from pharmacologic prophylaxis for thromboembolism.	• ≥ 12 years old: *Anticoagulation Therapy and Reversal of Anticoagulants Guideline* • < 12: Consult hematology for assess for additional risk factors and the need for anticoagulation
Dexamethasone	Hospitalized patients with severe disease requiring any oxygen support	• Dosing: 0.15mg/kg/dose once daily IV or PO, max of 6mg; duration is a max of 10 days • Concern in patients that are immunocompromised, may cause harm and consider on case by case basis

Tociluzumab
 	
Tociluzumab is available for hospitalized pediatric patients that meet criteria through an Emergency Use Authorization (EUA)* only.
	Interleukin-6 inhibitor that has received an FDA Emergency Use Authorization for the treatment of hospitalized adults and children with COVID-19 who are aged ≥2 years; receiving systemic corticosteroids; and require supplemental oxygen, non-invasive ventilation, mechanical ventilation, or ECMO
	
	EUA fact sheet must be given to families
		• **Consult Infectious Diseases**
		• Contraindications:
		  ○ Active or known tuberculosis infection
		  ○ Clear evidence of bacterial, viral (other than COVID-19) or fungal infection
		  ○ Hepatotoxicity defined as: AST/ALT >5 times ULN, neutrophils <0.5, platelets <50
		  ○ High risk of bowl perforation (diverticulitis, small bowel obstruction)
		  ○ Condition or treatment resulting in ongoing immune suppression
		• Dosing:
		  ○ <30 kg: 12 mg/kg/dose IV, max of 800mg; duration one dose
		  ○ ≥30kg: 8 mg/kg/dose IV, max of 800mg; duration one dose
		• Warnings/Precautions
		  ○ Serious infections
		  ○ GI perforation
		  ○ Hypersensitivity
		• Monitoring: CBC with differential and LFTs
		• See link to Tociluzimab EUA Fact sheet. Fact sheet required to be given to families

Baricitinib
 	
Baricitinib is available for hospitalized pediatric patients that meet criteria through an Emergency Use Authorization (EUA)* only.
	Immunomodulator that has received FDA EUA for treatment of treatment of coronavirus disease 2019 (COVID-19) in hospitalized pediatric patients 2 to less than 18 years of age requiring supplemental oxygen, non-invasive or invasive mechanical ventilation, or extracorporeal membrane oxygenation (ECMO).
	
	EUA fact sheet must be given to families
		• **Consult Infectious Diseases**
		• Precaution: Active or known tuberculosis infection
		• Dosing:
		  ○ 2-≤9 years old: 2mg flat dose PO once daily, max 14 days or until hospital discharge (whichever comes first)
		  ○ ≥9 years old: 4mg flat dose PO once daily, max 14 days or hospital discharge (whichever comes first)
		  ○ Dosing adjustments are required for reduced eGFR, increased liver enzymes, or immunosuppression noted by ANC or ALC.
		• Warnings/Precautions
		  ○ Serious infections
		  ○ Thrombosis
		  ○ GI perforation
		• Monitoring: renal function, CBC, LFTs
		• See link to Baricitinib EUA Fact Sheet. Fact sheet required to be given to families

Antibiotics for suspected co-infection	Blood culture and antibiotics may be warranted if the patient has signs or symptoms of sepsis and/or respiratory co-infection.	• See Pediatric Sepsis Recognition and Initial Management • See Initial Empiric Antibiotic Recommendations for Pediatric Suspected Sepsis or Sepsis