

Brenner Children's Hospital Treatment Guidelines for Pediatric Patients with COVID-19 (10/15/2021)

The emergence of the delta variant has resulted in a COVID-19 surge in the United States primarily affecting unvaccinated individuals. Since the onset of the COVID-19 pandemic, children represented 16% of total cumulated cases. For the week ending Sep 23, 2021, children accounted for 26.7% of reported weekly COVID-19 cases in the U.S. (children, under age 18, make up 22.2% of the US population). Most children with mild or moderate disease can be managed with supportive care alone.

NIH Treatment Guidelines

<https://www.covid19treatmentguidelines.nih.gov/about-the-guidelines/whats-new/>

(last updated Sep 29, 2021)

<https://www.covid19treatmentguidelines.nih.gov/special-populations/children> *(last updated April 21, 2021)*

Treatment Pearls

- Conservative fluid management is a reasonable approach
- Consider obtaining baseline labs such as CMP, CBC, CRP, and procalcitonin for evaluation of secondary bacterial pneumonia; ferritin if critically ill
- Nebulized therapies should be avoided in suspected or confirmed COVID-19 patients who are not intubated or who have an uncuffed tracheostomy
 - o Bronchodilator therapy may be provided via MDI, see bronchodilator section, page 14
 - o Uncuffed tracheostomies may be changed to cuffed and nebulized therapies given
 - o Consider placing home vent patients on a hospital ventilator to reduce aerosolization and use cuffed trachs if possible.
 - o Non-bronchodilator nebulized therapeutic agents such as nebulized hypertonic sodium may not have a treatment alternative. Risk and benefit must be considered.
- In COVID-19 patients with acute hypoxic respiratory failure
 - o Early prone positioning may be helpful
 - o Fluid restriction may be beneficial
 - o Early positive pressure respiratory support (non-invasive ventilation or intubation) may be beneficial for patients with progressive hypoxic respiratory failure
 - PUI/COVID-19 patients with hypoxic or hypercarbic respiratory failure may benefit from non-invasive ventilation support such as Optiflow, CPAP, or bipap.
 - Consider early consultation with pediatric critical care if aerosol generating procedures such as NIV support are needed or if intubation is deemed necessary. Permissive hypoxia may be well tolerated.
 - o Higher PEEP may be beneficial if ventilator waveforms show lung to be recruitable

Specific Clinical Scenarios warranting additional consideration

- Patient admitted with potential COVID-19 and asthma exacerbation or status asthmaticus
 - o Treat asthma exacerbations according to all current protocols with the exception of utilizing MDIs in place of nebulizers:
 - For alternative MDI dosing, see bronchodilator section, page 14
 - o There is not adequate data to support avoiding steroids in the setting of COVID-19 and asthma exacerbation, while there is a risk of worsening asthma symptoms. Both inhaled and systemic corticosteroids should be used for treatment of asthma in patients with COVID-19
- Patient admitted with potential COVID-19 and chest pain or other signs of myocardial depression
 - o Appropriate cardiac evaluation and monitoring including CXR, EKG, troponin, and BNP

- Risk factors for poor outcome of COVID-19 related to immune suppression
 - o Active myelosuppressive chemotherapy
 - o History of transplantation (solid organ or stem cell)
 - o Immune suppression due to medication (e.g. prednisone equivalent doses of ≥ 2 mg/kg or 20mg/day for ≥ 14 days, cyclophosphamide)
 - o Any immune suppressed patient with more than a mild disease should have a Peds ID consult
- Children with chronic respiratory illnesses, tracheostomies, or chronic ventilation
 - o *Recommend Peds Pulmonary Consult.*
 - o Discuss need for acute and/or chronic aerosol generating procedures with Peds Pulmonary (nebulized therapies such as saline or albuterol, and use of cough assist devices)
- BCH process for deliveries and admissions of infants with COVID+ mothers
 - o Contact neonatology and/or labor and delivery
- Wake Forest Baptist Health Adult Treatment Guide for COVID-19 ([link](#))

COVID-19 Treatment Algorithm for Pediatric Patients

INPATIENTS:

Compared with adults, SARS-CoV-2 infection is generally milder in children. Specific therapy is not necessary for most children with SARS-CoV-2 infection. Hospitalized patients with asymptomatic, mild or moderate COVID-19 disease without a new or increase in baseline oxygen requirement can be managed with supportive care alone.

Antiviral (Remdesivir) is recommended for:

- Hospitalized children aged ≥ 12 years with COVID-19 who have risk factors for severe disease and have an emergent or increasing need for supplemental oxygen.
- Hospitalized children aged ≥ 16 years with COVID-19 who have an emergent or increasing need for supplemental oxygen regardless of whether they have risks factors for severe disease
- In consultation with a pediatric infectious disease specialist, consider remdesivir for hospitalized children of all ages with COVID-19 who have an emergent or increasing need for supplemental oxygen

Corticosteroids (Dexamethasone): In the RECOVERY trial, a decrease in 28-day mortality in patients treated with dexamethasone (29.3%) compared with the usual care group (41.4%) was seen in hospitalized adult patients with COVID-19 receiving oxygen or mechanical ventilation. In contrast, no benefit for dexamethasone was seen in patients not requiring oxygen at the time of randomization, with 28-day mortality of 17.8% and 14.0% for the dexamethasone group and the usual care group, respectively.

The safety and efficacy of dexamethasone or other corticosteroids for COVID-19 treatment have not been sufficiently evaluated in pediatric patients and thus caution is warranted when extrapolating recommendations for adults to patients aged <18 years. Dexamethasone is recommended for children with COVID-19 who require high-flow oxygen, noninvasive or invasive ventilation, or ECMO. Dexamethasone should be considered for patients who require new or increase from baseline oxygen requirement. Use of dexamethasone for treatment of COVID-19 who are profoundly immunocompromised should be considered on a case-by-case basis as it may be harmful.

Consideration for Remdesivir and Dexamethasone therapy may be guided by illness severity:

- A. Mild to Moderate COVID-19 disease (without new or increase from baseline oxygen requirement) – **Supportive care alone***

*Consult Peds ID for patients who have received a solid organ, bone marrow, or stem cell transplant and admitted with confirmed COVID-19, but do not have an oxygen requirement

- B. Severe COVID-19 disease (new or increase from baseline oxygen requirement) – **Supportive care plus consideration of Remdesivir and Dexamethasone** for hospitalized children of all ages with COVID-19 who have an emergent or increasing need for supplemental oxygen, unless there are contraindications.
- C. Critical COVID-19 disease (IMC/PICU) – **Supportive care plus Remdesivir and Dexamethasone for all children, unless there are contraindications.** If Remdesivir cannot be used, consider Tocilizumab (in addition to dexamethasone) on a case-by-case basis after Peds ID consultation for patients meeting criteria (see below).
- Critical disease defined as
 - Patients with new or increased requirement for non-invasive ventilation (high-flow nasal cannula, CPAP, BiPAP) or invasive mechanical ventilation, ECMO, sepsis, or multiorgan failure.

Administration of Remdesivir and Dexamethasone:

Consult Peds ID for consideration of remdesivir and dexamethasone in critically ill patients and/or immunocompromised patients with COVID-19.

Remdesivir

Remdesivir is FDA approved for adult and pediatric patients 12 years of age and older weighing at least 40 kg for the treatment of COVID-19 requiring hospitalization.

The FDA Emergency Use Authorization (EUA) permits use of unapproved remdesivir for treatment of laboratory-confirmed COVID-19 in hospitalized pediatric patients weighing 3.5 kg to < 40 kg or hospitalized pediatric patients < 12 years of age weighing at least 3.5 kg. Patients should be informed of risks and potential benefits before initiating treatment when possible.

Eligibility

- Patients who have a confirmed COVID-19 infection
 - Clinical symptoms for 10 days or LESS (if immune competent), no time restriction if immune compromised
 - Require new or increase from baseline oxygen requirement including mechanical ventilation and ECMO
- OR**
- Confirmed SARS-CoV-2 infection AND
 - Have received a solid organ, bone marrow, or stem cell transplant who are admitted with confirmed COVID-19, but do not have an oxygen requirement AND use is approved by Peds ID
- Hepatic impairment: Remdesivir should not be administered to patients with ALT ≥ 10 times the upper limit of normal OR to patients with ALT elevations associated with increased conjugated bilirubin, alkaline phosphatase, or INR
 - Complete Metabolic Panel (CMP) should be obtained daily to monitor liver function while patients are receiving Remdesivir

- Renal insufficiency: Remdesivir is not recommended for patients >28 days old with an eGFR <30 ml/min or term neonates (7-28 days of life) with a serum creatinine \geq 1 mg/dl, unless the benefit outweighs the risk. No dose adjustments have been performed for patients with eGFR > 30 ml/min.

Remdesivir dosing*

Weight	Remdesivir Loading Dose	Remdesivir Maintenance Dose
\geq 40 kg	200 mg IV x1	100 mg IV q24h x 4-9 doses
< 40 kg	5 mg/kg IV x1	2.5 mg/kg IV q24h x 4-9 doses

FDA Approved: \geq 12 years of age and \geq 40 kg.

EUA: <12 years & \geq 3.5 kg or >12 years & <40 kg

Duration: 5-10 days

Remdesivir treatment duration may be extended to up to 10 days if substantial clinical improvement has not occurred by day 5.

Clinicians are advised to seek review and guidance from a pharmacist regarding potential drug interactions for patients being treated for COVID-19. This website is also a useful reference: www.covid19-druginteractions.org.

Corticosteroids

Dexamethasone (preferred):

Preferred Drug	Dose	Duration
Dexamethasone	0.15 mg/kg once daily (Max: 6 mg)	5-10 days

Methylprednisolone:

If the patient is being treated for an asthma exacerbation in the setting of COVID-19, we suggest methylprednisolone 2 mg/kg/day divided twice daily (max: 30 mg/dose) per the asthma pathway. Higher doses of parenteral methylprednisolone should be considered for patients admitted to the PICU with status asthmaticus. Extension of steroid duration beyond 5 days with ongoing methylprednisolone or transition to dexamethasone should be determined on a case-by-case basis.

Preferred Drug for Asthma exacerbation in COVID-19 patients*	Dose	Duration
Methylprednisolone	2 mg/kg/day divided q 12h (Max: 60 mg/day)	5-10 days

*In critically ill patients with status asthmaticus (e.g. PICU admission), higher doses of parenteral methylprednisolone may be needed

Alternative steroids:

Alternative Drugs for Breastfeeding/Pregnant	Dose	Duration
Prednisolone	1 mg/kg once daily (Max: 40 mg)	5-10 days
Methylprednisolone	0.8 mg/kg once daily (Max 32 mg)	5-10 days

IL-6 receptor antagonist (Tocilizumab)

Tocilizumab, a recombinant humanized anti-IL6 monoclonal antibody has been used in the management of several rheumatologic conditions in children and adults (eg, polyarticular juvenile idiopathic arthritis, systemic juvenile idiopathic arthritis) and for chimeric antigen receptor T cell-induced severe or life-threatening cytokine release syndrome). In clinical trials of hospitalized adult patients with COVID-19, tocilizumab in addition to routine care, which included corticosteroids, was shown to reduce the risk of death through 28 days of follow-up and decrease the amount of time patients remained hospitalized. The risk of patients being placed on ventilators through 28 days of follow-up was also decreased.

Data is very limited to recommend for or against use of tocilizumab in hospitalized children with COVID-19. However, Tocilizumab may have a role in select critically ill pediatric patients with evidence of hyperinflammation, early in their hospital course. Pediatric ID service should be consulted for pediatric patients in whom tocilizumab is considered. If used, tocilizumab should be used in combination with dexamethasone.

Remdesivir should not be used if tocilizumab is determined to be the preferred treatment.

Consideration of Tocilizumab:

Actemra (tocilizumab) recently demonstrated a mortality benefit in the treatment of adult patients with severe COVID-19 in the Randomized Evaluation of COVID-19 therapy (RECOVERY) and the Randomized, Embedded, Multi-factorial, Adaptive Platform Trial for Community-Acquired Pneumonia (REMAP-CAP) trials. In June 2021, the FDA issued an emergency use authorization (EUA) for Actemra (tocilizumab), an IL-6 receptor antagonist for the treatment of hospitalized adults and pediatric patients 2 years of age and older with COVID-19 who are receiving systemic corticosteroids and require supplemental oxygen, non-invasive or invasive mechanical ventilation, or extracorporeal membrane oxygenation (ECMO). Tocilizumab is not authorized for use in outpatients with COVID-19.

Use of Tocilizumab (in addition to dexamethasone) can be considered on a case-by-case basis after Peds ID consultation for select patients meeting criteria (see below).

Indications

- Tocilizumab for the management of COVID-19 is restricted to pediatric patients 2 years of age and older hospitalized in the PICU with severe/critical COVID-19 who meet **ALL** of the following criteria:
 - Positive SARS-CoV-2 Test
 - Evidence of hyperinflammation (e.g. C-reactive protein ≥ 75 mg/L, ferritin > 500 ng/mL)
 - Requiring invasive mechanical ventilation, noninvasive mechanical ventilation (e.g. BiPap support with $>40\%$ FiO₂), heated high-flow nasal cannula oxygen* > 20 LPM, non-rebreather, or ECMO
 - Administered within 5 days of hospital admission
 - **Patient not receiving remdesivir (discontinue remdesivir if previously started or avoid initiation of remdesivir during hospitalization)**
- Do not initiate tocilizumab use after completion of remdesivir course
- Tocilizumab should be used in combination with dexamethasone
- Tocilizumab is **limited to 1 dose for the treatment of COVID-19.**
- Avoid use in the following patients:
 - Alanine transaminase (ALT) > 5 times the upper limit of normal
 - Absolute neutrophil count < 500 cells/microliter, or
- Patients with evidence of active tuberculosis infection or clear evidence of active bacterial, fungal, non-COVID viral, or other coinfection

- In non-COVID studies, tocilizumab has been associated with fatal infections in immunosuppressed patients. Tocilizumab use in the setting of immunosuppression and severe COVID-19 infection requires Peds ID consult service and approval.

**= Heated High Flow Nasal Cannula are specialized systems that delivers titratable oxygen and gas flow. Gas flow is typically 20-60 liters per minute. Heated High Flow in the Wake Forest system is usually delivered via the Optiflow device; however, some non-invasive and invasive mechanical ventilators are also capable of Heated High Flow and may be used. Heated High Flow Nasal Cannula differs from conventional High Flow Nasal Cannula oxygen devices that do not deliver titratable oxygen concentrations and do not exceed 15 liters per minute.*

Tocilizumab dosing (based on patient weight)*

Weight	Tocilizumab Dosing (Peds ID approval required for use)
≥ 30 kg	8 mg/kg IV in a single 60-min infusion (maximum 800 mg per infusion)
< 30 kg	12 mg/kg IV in a single 60-min infusion

*Fact sheet for healthcare providers. Emergency use authorization for actemra (tocilizumab). <https://www.fda.gov/media/150321/download> (Accessed on June 28, 2021).

OUTPATIENTS

Supportive care.

Do not recommend antiviral agents for ambulatory pediatric patients with suspected/proven COVID-19.

PEDIATRIC OUTPATIENT/AMBULATORY USE CRITERIA AND DOSING FOR MONOCLONAL ANTIBODIES

Anti-SARS-CoV-2 Monoclonal antibodies:

- Casirivimab and Imdevimab
- Bamlanivimab and Etesevimab
- Sotrovimab

The anti-SARS-CoV-2 Monoclonal antibodies are produced with recombinant DNA technology. Although Emergency Use Authorization (EUA) for anti-SARS-CoV-2 monoclonal antibodies includes patients aged ≥ 12 years and weighing ≥ 40 kg, there is insufficient data for the NIH to recommend routine use in pediatric patients. No *controlled* studies demonstrate which adolescents would benefit most from monoclonal antibody therapy.

Per the EUA(s), use of Casirivimab/Imdevimab and Bamlanivimab/Etesevimab for outpatient/ambulatory treatment or post-exposure prophylaxis of COVID-19 is permitted for outpatients 12 years of age and older weighing at least 40 kg who have **at least one of the following criteria** to identify as high risk for progression of severe disease: obesity, cardiovascular disease, chronic kidney disease, chronic lung disease, diabetes, immunosuppressive disease/therapy, sickle cell disease, medically complex neurodevelopmental, genetic or metabolic disorders, and medical-related technology dependence.

Clinical Considerations for Outpatient/Ambulatory Treatment and Post-Exposure Prophylaxis with Anti-SARS-CoV-2 Monoclonal Antibodies

Outpatient/Ambulatory Treatment	Post-Exposure Prophylaxis
Casirivimab and Imdevimab*	Casirivimab and Imdevimab
Bamlanivimab and Etesevimab	Bamlanivimab and Etesevimab
Sotrovimab**	

*If Casirivimab and Imdevimab is unavailable, other alternative anti-SARS-CoV-2 Monoclonal antibodies include Bamlanivimab/Etesevimab for treatment or post-exposure prophylaxis

**Per the EUA, Sotrovimab is permitted for outpatient/ambulatory treatment of COVID-19 in the same high-risk population. The EUA does NOT permit use of Sotrovimab for post-exposure prophylaxis at this time.

Pediatric Infectious Disease is available for consultation in patients > 12 years of age and ≤ 18 years of age when outpatient monoclonal antibody is considered. **Individual clinicians may choose to administer outpatient monoclonal antibody therapy on a case-by-case basis to non-hospitalized pediatric patients (≥12 years of age and <18 years of age and weighing ≥40 kg) who meet EUA criteria to identify as high risk for severe disease.** The **suggested clinical criteria** for use of monoclonal antibodies (**see TABLE on following page**) is based on expert opinion and are designed to assist **pediatric providers** to identify patients most at risk for severe disease and hospitalization who may be most likely to benefit from monoclonal antibody treatment.

Outpatient Monoclonal Antibody Infusion Sites:

Provider [link](#) for information around available *anti-SARS CoV2* monoclonal antibodies and prescribing these therapies to eligible outpatients. Due to frequent changes in product availability, a streamlined order entry process has been implemented. The updated order panel is available to providers in the ambulatory space.

Atrium Health-WFB primary care providers and subspecialists are able to input the order and schedule the patients at **Urgent Care – Clemmons or Urgent Care – Pisgah Church**. Non-WFBH providers are directed to contact the appropriate subspecialist for patients who may be eligible. The ordering provider’s clinic must call Urgent Care-Clemmons or Greensboro Urgent Care-Pisgah Church to schedule administration. Urgent Care staff will contact the patient to coordinate an appointment date and time. Peds ID is available for consultation.

Eligible outpatients may also self-refer to **Meeting Place - Wilkes (FEMA/DHHS site)** located at 1901 W. Park Drive, North Wilkesboro, NC, 28659. Appointments are required, but patients who qualify for treatment do not need a referral from a health care provider unless otherwise specified if they meet medical screening criteria when setting up their appointment necessary. Non-Atrium Health-WFB providers may refer patients who may be eligible to the FEMA site where provider orders are not necessary. [Link](#) to schedule treatment at this location or call 336-528-1637. Peds ID is available for consultation.

Anti-SARS-CoV-2 monoclonal antibodies are not authorized for use in patients who are hospitalized with COVID-19, or who require oxygen therapy due to COVID-19 or who require an increase in baseline oxygen flow rate due to COVID-19 in those on chronic oxygen therapy due to underlying non-COVID-19 related comorbidity. Casirivimab/Imdevimab, Bamlanivimab/Etesevimab, and Sotrovimab *should not be confused with* anti-IL 6 receptor antagonist (Tocilizumab). There are currently no data to support the use of anti-SARS-CoV-2 monoclonal antibodies in hospitalized children for COVID-19. Emerging data regarding the prevalence and clinical significance of SARS-CoV-2 variants, and the efficacy of monoclonal antibodies against variants, may inform the choice of specific anti-SARS-CoV-2 monoclonal antibody therapy in the future.

TABLE: Suggested High-Risk Clinical Criteria for Pediatric Outpatient Monoclonal Antibody Therapy

<p>General Pediatrics</p> <ul style="list-style-type: none"> • Obesity (BMI >97th percentile) 	<p>Immunology</p> <ul style="list-style-type: none"> • Primary or secondary cellular (T cell) immunodeficiency • HIV infection with history of opportunistic infection or with severe CD4 lymphocytopenia (CD4 count <200 cell/microL (<14%)) • Significant secondary immunosuppression due to pharmacologic agents: <ol style="list-style-type: none"> 1. <u>Agents used for malignant conditions and related complications.</u> <ol style="list-style-type: none"> a. Chemotherapeutic agents (e.g., cyclophosphamide, methotrexate, mycophenolate) b. Anti-B lymphocyte monoclonal antibodies (e.g. rituximab), or anti-T lymphocyte monoclonal antibodies (e.g. alemtuzumab) c. Cytotoxic T-lymphocyte-associated antigen 4 (CTLA-4) inhibitors (e.g., abatacept) d. Tumor necrosis factor-alpha (TNF-α) antagonists (e.g., adalimumab, certolizumab, infliximab, etanercept, golimumab) e. Select anti-cytokine antagonists (e.g., tocilizumab, ustekinumab, secukinumab, ixekizumab) * 2. <u>Daily corticosteroid therapy at a dose \geq20 mg of prednisone or equivalent for longer than 14 days</u> 3. <u>Immunosuppressive agents used for solid organ transplant, and rheumatologic and other autoimmune conditions (e.g., inflammatory bowel disease, hemolytic uremic syndrome)</u> <ol style="list-style-type: none"> a. Conventional immunosuppression: mycophenolate, sirolimus, tacrolimus, azathioprine ** b. Anti-B lymphocyte monoclonal antibodies or inhibiting agents (e.g., rituximab or belimumab) c. Cytotoxic T-lymphocyte-associated antigen 4 (CTLA-4) inhibitors (e.g., abatacept) d. Anti-C5 monoclonal antibody (e.g., eculizumab). e. Tumor necrosis factor-alpha (TNF-α) antagonists (e.g. adalimumab, certolizumab, infliximab, etanercept, golimumab) f. Select anti-cytokine antagonists (e.g., tocilizumab, ustekinumab, secukinumab, ixekizumab) * <p><i>*Does not include anakinra when used as monotherapy as there is no significant increase in the risk of severe infection. Tocilizumab is included because it can cause neutropenia and generally is associated with more infections.</i></p> <p><i>**Does not include low-dose methotrexate, hydroxychloroquine, colchicine, or leflunomide as used in rheumatic conditions.</i></p>
<p>Cardiology</p> <ul style="list-style-type: none"> • Single ventricle physiology (Fontan physiology or similar) • Complex conotruncal disease (interrupted aortic arch, pulmonary atresia, truncus) • Cardiac failure/transplant (decision-making in conjunction with heart failure/transplant team) • Pulmonary hypertension on oral or inhaled therapy (decision-making in conjunction with pulmonary and/or pulmonary HTN team) • Significant secondary immunosuppression due to pharmacologic agents (see Immunology) 	
<p>Endocrinology</p> <ul style="list-style-type: none"> • Obesity (BMI >97th percentile) • Type 1 diabetes mellitus • Type 2 diabetes mellitus • Significant secondary immunosuppression due to pharmacologic agents (see Immunology) 	
<p>Gastroenterology</p> <ul style="list-style-type: none"> • Significant secondary immunosuppression due to pharmacologic agents (see Immunology) 	
<p>Hematology/Oncology</p> <ul style="list-style-type: none"> • Receipt of CAR-T-cell or hematopoietic stem cell transplant (within the previous 1 year or taking immunosuppression therapy) (see Immunology) • Active treatment for solid tumor and hematologic malignancies • Receipt of solid-organ transplant and taking immunosuppressive therapy (see Immunology) • Sickle cell disease with significant pulmonary disease and/or greater than one hospitalization for confirmed or suspected acute chest episode • Significant secondary immunosuppression due to pharmacologic agents (see Immunology) 	
<p>Nephrology</p> <ul style="list-style-type: none"> • Dialysis (peritoneal or hemodialysis) • Receipt of renal transplant and taking immunosuppressive therapy • Significant secondary immunosuppression due to pharmacologic agents (see Immunology) 	

TABLE: Suggested High-Risk Clinical Criteria for Pediatric Outpatient Monoclonal Antibody Therapy

Neurology <ul style="list-style-type: none">• Oxygen- or ventilator-dependent neuromuscular disease• Cerebral palsy/spastic quadriplegia• Congenital chromosomal abnormality (e.g., trisomy 21, trisomy 18, 22q11del or other chromosome abnormalities, on an individual basis as recommended by a geneticist)• Mitochondrial disease and other inborn errors of metabolism with risk of metabolic decompensation (e.g., maple syrup urine disease (MSUD), organic acidemias, urea cycle disorders)• Significant secondary immunosuppression due to pharmacologic agents (see Immunology)	Pulmonology <ul style="list-style-type: none">• Oxygen- or ventilator-dependent chronic lung disease or neuromuscular disease• High-risk (severe or poorly controlled) asthma• History of bronchopulmonary dysplasia with lung function impairment or other fixed obstructive lung disease• Cystic fibrosis, primary ciliary dyskinesia, and other causes of bronchiectasis (e.g., primary immunodeficiency)• Significant secondary immunosuppression due to pharmacologic agents (see Immunology)
	Rheumatology <ul style="list-style-type: none">• Significant secondary immunosuppression due to pharmacologic agents (see Immunology)

Pediatric Outpatient/Ambulatory TREATMENT with Anti-SARS-CoV-2 Monoclonal Antibodies

Use of Casirivimab/Imdevimab, Bamlanivimab/Etesevimab, and Sotrovimab for treatment of COVID-19 is recommended for patients meeting **the following criteria**:

- Outpatients 12 years of age and older weighing at least 40 kg
- Positive SARS-CoV-2 viral test and able to be treated within 10 days of symptom onset
- Have at least one of the above suggested high-risk clinical criteria to identify as high risk for progression of severe disease (see above TABLE)

Due to frequent changes in product availability, a streamlined order entry process has been implemented. Product selection will be based on product availability at the time of infusion ([link](#)).

Casirivimab/Imdevimab TREATMENT Dose:

- 600 mg Casirivimab / 600 mg Imdevimab (1200 mg total) administered together for one dose
- **For treatment doses, intravenous infusion (IV) is strongly recommended for immunocompromised hosts.**
- *Subcutaneous injection is an alternative route of administration when intravenous infusion is not feasible and would lead to delay in treatment. The subcutaneous injection is four syringes administered consecutively.*

Bamlanivimab/Etesevimab TREATMENT Dose:

- Bamlanivimab 700 mg and Etesevimab 1400 mg IV infusion once
- Patients who have traveled to, resided in, or had close contact with an infected individual from an area where the frequency of resistant variants to bamlanivimab and etesevimab exceeds 5% should not receive bamlanivimab and etesevimab (CDC variant proportions [\[link\]](#); list of state/jurisdictions bamlanivimab and etesevimab are authorized for use [\[link\]](#)).
 - Providers will be contacted if patient is not eligible to receive bamlanivimab and etesevimab and alternative COVID monoclonal antibodies are not available.

Sotrovimab TREATMENT Dose: 500mg IV infusion once

COVID-19 vaccination should be deferred for at least 90 days following COVID-19 monoclonal antibody therapy. This may be an important clinical consideration to weigh in the decision to provide therapy to patients.

Pediatric Outpatient/Ambulatory POST-EXPOSURE PROPHYLAXIS with Anti-SARS-CoV-2 Monoclonal Antibodies

Use of Casirivimab/Imdevimab and Bamlanivimab/Etesevimab for post-exposure exposure prophylaxis is recommended for patients meeting **all the following criteria**:

- Outpatients 12 years of age and older weighing at least 40 kg who have **EITHER** been exposed to an individual infected with SARS-CoV-2 consistent with close contact criteria per Centers for Disease Control and Prevention (CDC) **OR** are at high risk of exposure to an individual infected with SARS-CoV-2 because of occurrence of SARS-CoV-2 infection in other individuals in the same institutional setting (e.g. adolescents living in group homes)
 - CDC Close Contact Definition: contact with an infected individual within 6 feet for a total of 15 minutes or more, providing care at home to someone who is sick having direct physical contact with the person (hugging or kissing, for example), sharing eating or drinking utensils or being exposed to respiratory droplets from an infected person (e.g. sneezing or coughing).
- Have at least one of the above suggested high-risk clinical criteria to identify as high risk for progression of severe disease (see above TABLE)
- Are **EITHER**
 - Not fully vaccinated (defined as people who were never vaccinated or those who received a full vaccination series (2-doses or 3-doses for immunosuppressed) or a single-dose vaccine <2 weeks ago); **OR**
 - Fully vaccinated, but not expected to mount an adequate immune response (e.g., those with immunocompromising conditions, including those who are taking immunosuppressive medications, definition below)
 - Active treatment for solid tumor and hematologic malignancies
 - Receipt of solid-organ transplant and taking immunosuppressive therapy
 - Receipt of CAR-T-cell or hematopoietic stem cell transplant (within 1 years of transplantation or taking immunosuppression therapy)
 - Moderate or severe primary immunodeficiency (e.g. DiGeorge, Wiskott-Aldrich syndromes)
 - Advanced or untreated HIV infection
 - Active treatment with high-dose corticosteroids (i.e., ≥ 20 mg prednisone or equivalent per day), alkylating agents, antimetabolites, transplant-related immunosuppressive drugs, cancer chemotherapeutic agents classified as severely immunosuppressive, TNF blockers, and other biologic agents that are immunosuppressive or immunomodulatory of transplantation or taking immunosuppression therapy)

Casirivimab/Imdevimab POST-EXPOSURE PROPHYLAXIS Dose:

- 600 mg casirivimab / 600 mg imdevimab (1200 mg total) administered together as a single dose **OR**
- For individuals who are not expected to mount an adequate immune response to complete SARS-CoV-2 vaccination where repeat dosing is appropriate in the setting of expected ongoing exposure for > 4 weeks:
 - Initial dose of 600 mg casirivimab / 600 mg imdevimab (1200 mg total) administered together followed by subsequent repeat dosing of 300 mg casirivimab / 300 mg of imdevimab (600 mg total) every 4 weeks for duration of exposure
- *For post-exposure prophylaxis, either IV infusion or subcutaneous x4 syringes can be administered.*

Bamlanivimab/Etesevimab POST-EXPOSURE PROPHYLAXIS Dose:

- Bamlanivimab 700 mg and Etesevimab 1400 mg IV infusion once

Sotrovimab is not permitted for post-exposure prophylaxis at this time

COVID-19 vaccination should be deferred for at least 90 days following COVID-19 monoclonal antibody therapy. This may be an important clinical consideration to weigh in the decision to provide therapy to patients.

Multisystem Inflammatory Syndrome in Children (MIS-C) Associated with SARS-CoV-2 Treatment Algorithm

Refer to BCH MISC working group recommendations for diagnostic evaluation and management ([link](#))

References

Chiotos K, Hayes M, Kimberlin DW, et al. Multicenter interim guidance on use of antivirals for children with coronavirus disease 2019/severe acute respiratory syndrome coronavirus 2. *J Pediatric Infect Dis Soc.* 2021;10(1):34-48. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/32918548>.

Derespina KR, Kaushik S, Plichta A, et al. Clinical manifestations and outcomes of critically ill children and adolescents with coronavirus disease 2019 in New York City. *J Pediatr.* 2020; Published online ahead of print. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/32681989>.

Dulek DE, Fuhlbrigge RC, Tribble AC, et al. Multidisciplinary guidance regarding the use of immunomodulatory therapies for acute coronavirus disease 2019 in pediatric patients. *J Pediatric Infect Dis Soc.* 2020;9(6):716-737. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/32808988>.

Food and Drug Administration. Fact sheet for healthcare providers: emergency use authorization (EUA) of bamlanivimab and etesevimab. 2021. Available at: <https://www.fda.gov/media/145802/download>

Food and Drug Administration. Fact sheet for healthcare providers: emergency use authorization (EUA) of REGEN-COV (casirivimab and imdevimab). 2021. Available at: <https://www.fda.gov/media/145611/download>

Food and Drug Administration. Fact sheet for healthcare providers: emergency use authorization (EUA) of Sotrovimab. 2021. Available at: <https://www.fda.gov/media/149534/download>

Food and Drug Administration. Fact sheet for healthcare providers: emergency use authorization (EUA) of veclury (remdesivir) for hospitalized pediatric patients weighing 3.5 kg to less than 40 kg or hospitalized pediatric patients less than 12 years of age weighing at least 3.5 kg. 2020. Available at: <https://www.fda.gov/media/137566/download>.

Kotch C, Barrett D, Teachey DT. Tocilizumab for the treatment of chimeric antigen receptor T cell-induced cytokine release syndrome. *Expert Rev Clin Immunol.* 2019;15(8):813-822. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/31219357>.

National Institutes of Health Panel on COVID-19 Treatment. COVID-2019 Treatment Guidelines. <https://www.covid19treatmentguidelines.nih.gov/about-the-guidelines/whats-new/> (last updated Oct 7, 2021) <https://www.covid19treatmentguidelines.nih.gov/special-populations/children> (last updated April 21, 2021) <https://www.covid19treatmentguidelines.nih.gov/therapies/anti-sars-cov-2-antibody-products/anti-sars-cov-2-mono-clonal-antibodies/> (last updated Sept 24, 2021)

Ranjbar K, Moghadami, M., Mirahmadizadeh, A. et al. Methylprednisolone or dexamethasone, which one is superior corticosteroid in the treatment of hospitalized COVID-19 patients: a triple-blinded randomized controlled trial. *BMC Infect Dis* 2021;21:337 <https://doi.org/10.1186/s12879-021-06045-3>.

Shekerdeman LS, Mahmood NR, Wolfe KK, et al. Characteristics and outcomes of children with coronavirus disease 2019 (COVID-19) infection admitted to US and Canadian pediatric intensive care units. *JAMA Pediatr.* 2020;174(9):868-873. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/32392288>.

The RECOVERY Collaborative Group. Dexamethasone in Hospitalized Patients with Covid-19 — Preliminary Report. *N Engl J Med.* 2020 Jul 17: NEJMoa2021436. Published online 2020 Jul 17. doi: 10.1056/NEJMoa2021436.

Wolf J, Abzug MJ, Wattier RL, et al. Initial guidance on use of monoclonal antibody therapy for treatment of COVID-19 in children and adolescents. *J Pediatric Infect Dis Soc.* 2021; Published online ahead of print. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/33388760>.

BRONCHODILATOR THERAPY Dosing in Pediatric Patients with confirmed or suspected COVID-19

Nebulized therapies should be avoided in suspected or confirmed COVID-19 patients who are not on closed-circuit mechanical ventilation (hospital ventilators with cuffed endotracheal or trach tubes)

Patients on mechanical ventilation (invasive or non-invasive) should receive nebulized therapy via the Aerogen system.

For bronchodilator guidance, follow algorithm below. Reference for conversion from nebulizers to MDIs:

Nebulizer	MDI
One albuterol neb = 2.5mg albuterol	8 puffs albuterol MDI
One duoneb = 2.5 mg albuterol and 0.5 mg ipratropium	8 puffs albuterol MDI and 8 puffs ipratropium MDI
Continuous albuterol 20 mg/hr	8 puffs MDI q 7-8 minutes (4 rounds of 8 puffs every 30 min)
Continuous albuterol 10 mg/hr	8 puffs MDI q 15 minutes (2 rounds of 8 puffs every 30 min)

- To replace the atrovent given in the first hour of continuous, give atrovent MDI 8 puffs q 20 min X 3 doses
- If administration of dual MDI therapy (albuterol and ipratropium) becomes challenging, consider prioritizing albuterol and limit ipratropium to at least 4 puffs and up to 8 every 20 min x3 doses.

If patient fails MDIs, place patient in negative pressure ventilation room and begin continuous nebulized Albuterol. If patient is not in PICU, contact PICU attending for consideration of urgent transfer to PICU negative pressure room prior to initiation of continuous nebulizer. Also consider early initiation of IV terbutaline (Bolus dose 5 mcg/kg; Starting dose 0.1 mcg/kg/min)

Suspected or Confirmed COVID-19 Patient?

