PURPOSE: To outline consensus recommendations on the management of pediatric patients with suspected or confirmed COVID-19 infections admitted to an inpatient floor or the intensive care unit at CHKD

PATIENT PRESENTATION:
Range from uncomplicated upper respiratory tract viral infection to pneumonia, acute respiratory distress syndrome (ARDS), sepsis, and septic shock (Table 1). No specific data is available establishing risk factors for severe COVID-19 disease in children. A rare but serious inflammatory syndrome in children has been linked to COVID-19. The CDC is calling this condition multisystem inflammatory syndrome in children (MIS-C).

Table 1. Clinical Symptoms Associated with COVID-19:

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uncomplicated Illness</td>
<td>Uncomplicated upper respiratory tract viral infection with nonspecific symptoms including: Fevers, cough, sore throat, nasal congestion, malaise, headache, muscle pain Without signs of dehydration, sepsis, or shortness of breath</td>
</tr>
<tr>
<td>Mild Pneumonia</td>
<td>Non-severe pneumonia presenting with cough or difficulty breathing + tachypnea Without signs of severe pneumonia</td>
</tr>
<tr>
<td>Severe Pneumonia</td>
<td>Adolescent: fever or suspected respiratory infection + one of the below: RR &gt; 30 breaths/min, Severe respiratory distress, SpO₂ &lt; 90% on room air Child: cough or difficulty breathing + one of the below: Central cyanosis, SpO₂ &lt; 90%, Severe respiratory distress, Clinical signs of pneumonia + inability to breast feed or drink, lethargy, convulsions</td>
</tr>
<tr>
<td>ARDS</td>
<td>New or worsening respiratory symptoms within one week of known clinical insult Chest imaging consistent with ARDS Respiratory failure not explained by cardiac failure or fluid overload</td>
</tr>
<tr>
<td>Sepsis/Septic Shock</td>
<td>Diagnosis made clinically</td>
</tr>
</tbody>
</table>

Source: World Health Organization

COVID-19 SPECIFIC THERAPY:

<table>
<thead>
<tr>
<th>Class</th>
<th>Agent</th>
<th>Route</th>
<th>Approval</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antiviral*</td>
<td>Remdesivir (Veklury®)</td>
<td>IV</td>
<td>Inpatients</td>
<td>FDA Approved: ≥ 12 years of age and ≥ 40 kg EUA: &lt; 12 years &amp; ≥ 3.5 kg or &gt; 12 years &amp; &lt; 40 kg Reserved for contraindications to corticosteroid treatment</td>
</tr>
<tr>
<td>JAK-1 Inhibitor*</td>
<td>Baricitinib (Olumiant®)</td>
<td>PO</td>
<td>Inpatients</td>
<td>Not FDA approved for COVID-19 EUA: ≥ 2 years in combo with Remdesivir Reserved for contraindications to corticosteroid treatment</td>
</tr>
<tr>
<td>Monoclonal Antibody*</td>
<td>Casirivimab/Imdevimab</td>
<td>IV</td>
<td>Symptomatic Outpatients</td>
<td>Outpatient use ONLY EUA: ≥ 12 years of age and ≥ 40 kg May be unavailable due to limitations on supply</td>
</tr>
<tr>
<td></td>
<td>Bamlanivimab/Etesevimab</td>
<td>IV</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sorivimab</td>
<td>IV</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Refer to drug specific guidelines, available on kdnnet

Post exposure prophylaxis:
Due to limitations, the use of Casirivimab/Imdevimab post exposure prophylaxis in high-risk individuals will not be utilized at CHKD at this time.
COVID-19 SUPPORTIVE CARE & ANTICOAGULATION:

Supportive Care:
Sufficient fluid and calorie intake, and additional oxygen supplementation should be used in the treatment of children infected with COVID-19. The aim is to prevent ARDS, organ failure, and secondary nosocomial infections. If bacterial infection is suspected, broad-spectrum antibiotics may be used.22

Anticoagulation:
COVID-19 is associated with an increased risk of venous thromboembolism (VTE) in adults. There are no specific recommendations for pediatric patients with COVID-19.15-21 Asymptomatic, mild, or moderate COVID-19 is not an indication for anticoagulant prophylaxis unless the patient qualifies based on risks outlined in Table 2. All hospitalized COVID-19 (+) patients should undergo a risk assessment as outlined in Table 2. & Figure 1.

- Strongly consider Hematology consult to assess risk factors
- If patient qualifies for thromboprophylaxis, obtain D-dimer, fibrinogen, PT/PTT, & Scr, and consult Hematology
- Thromboprophylaxis may be changed to treatment if very high risk for VTE/microvascular thrombosis. Discuss with Hematology
- Patients with decreased renal function should have enoxaparin adjusted or changed to unfractionated heparin, discuss with Hematology
- Length of VTE prophylaxis to be determined by Hematology

Figure 1: Anticoagulation in Pediatric Acute COVID-19

Diagram:
- Hospitalized Acute COVID-19 Patients
- <12 years of age
  - (-) Risk Factors* (Table 2)
  - No known Contraindications
  - Obtain Labs: (D-dimer, fibrinogen, PT/PTT, Scr) + Consult Hematology
- ≥ 12 years of age
  - (-) Risk Factors
  - Reassess q48-72h for duration of the hospitalization
  - Obtain Labs: (D-dimer, fibrinogen, PT/PTT, Scr) + Consult Hematology
  - No known Contraindication
Table 2: Thromboprophylaxis should be considered in patients who meet ≥ 1 of the following Risk Factors for VTE

<table>
<thead>
<tr>
<th>Risk Factors for VTE</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Age ≥12 years or post-pubertal</td>
</tr>
<tr>
<td>• Patients on PICU service</td>
</tr>
<tr>
<td>• Mechanical Ventilation</td>
</tr>
<tr>
<td>• Obesity</td>
</tr>
<tr>
<td>• Central Line(s)</td>
</tr>
<tr>
<td>• Decreased mobility</td>
</tr>
<tr>
<td>• Sickled Cell Disease</td>
</tr>
<tr>
<td>• Autoimmune Disorders</td>
</tr>
<tr>
<td>• Nephrotic Syndrome</td>
</tr>
<tr>
<td>• CF Exacerbation</td>
</tr>
<tr>
<td>• Prolonged Length of Stay (anticipated &gt; 3 days)</td>
</tr>
<tr>
<td>• First degree family history of unprovoked VTE</td>
</tr>
<tr>
<td>• Personal and/or family history of thrombosis/thrombophilia</td>
</tr>
<tr>
<td>• Concomitant estrogen-containing medication</td>
</tr>
<tr>
<td>• Inotropic infusion requirement</td>
</tr>
<tr>
<td>• Any heart rhythm abnormalities</td>
</tr>
<tr>
<td>• Congenital or acquired heart disease with venous stasis or impaired venous return</td>
</tr>
</tbody>
</table>

Table 3. Bleeding Risk Factors:15-22

<table>
<thead>
<tr>
<th>Bleeding Risk Factors</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not Recommended</td>
<td>Intracranial hemorrhage</td>
</tr>
<tr>
<td></td>
<td>Active bleed</td>
</tr>
<tr>
<td>Consider with caution</td>
<td>Intracranial mass</td>
</tr>
<tr>
<td></td>
<td>Lumbar puncture w/in 24 hours</td>
</tr>
<tr>
<td></td>
<td>Coagulopathy</td>
</tr>
<tr>
<td></td>
<td>Neurosurgical procedure w/in 24 hours</td>
</tr>
</tbody>
</table>

MULTISYSTEM INFLAMMATORY SYNDROME-CHILDREN (MIS-C):

Refer to CHKD MIS-C Guideline on kdnet
Figure 2. Treatment Algorithm:
Dosing per (Table 4) or refer to drug specific guideline on kdnet, VTE risk assessment See Figure 1/Table 2

**Symptomatic Outpatients**
COVID-19 (+)
- Low Risk
  - Supportive Care ONLY
- High Risk*
  - Consider €: Casirivimab + Imdevimab

**Inpatient: Mild**
Otherwise healthy child with suspected COVID19 + clinical symptoms including:
- Uncomplicated illness
- Mild Pneumonia
COVID-19 (+)
Assess for VTE Risk Factors
- Respiratory support required
- Supportive Care ONLY

**Inpatient: Moderate**
Clinical symptoms including:
- Mild Pneumonia
- Moderate Pneumonia
- Severe Pneumonia
Consider baseline interleukin levels
COVID-19 (+)
Assess for VTE Risk Factors
- Respiratory support required
- Supportive Care + Steroids + Contact ID€ (Remdesivir)™

**Inpatient: Severe (NICU/PICU)**
Clinical symptoms including:
- Severe Pneumonia
- ARDS
- Sepsis/Shock
Consider baseline interleukin levels
Suspected OR Confirmed COVID-19
AND
Severe disease defined as, ≥ 1 of the below:
- a) SpO2 ≤ 94% on room air
- b) Requiring supplemental oxygen
- c) Requiring mechanical ventilation
- d) Requiring ECMO
Assess for VTE Risk Factors
- Supportive Care + Steroids + Consider Tocilizumab/Sarilumab®

Evaluation of Remdesivir Eligibility:
- Refer to CHKD Remdesivir Guideline

**Remdesivir Approved**
Supportive Care + Steroids + Remdesivir™
Consider Tocilizumab/Sarilumab®

**Remdesivir Exclusion**
Supportive Care + Steroids + Consider Tocilizumab/Sarilumab®

* High Risk- See drug specific guideline on kdnet
€ ID will provide recommendations and/or approval, if indicated
™ Consider Baricitinib if steroids are contraindicated
* Preferred antibody therapy is Casirivimab + Imdevimab at CHKD
Agent based on availability, in patients with signs and symptoms of cytokine storm

Version: 7.0 8/23/2021
Effective Date: 3/20/2020
Page 4 of 9
Table 4. Agents Approved & Under Investigation for Treatment of COVID-19

<table>
<thead>
<tr>
<th>COVID-19 Treatment: Drugs</th>
<th>Dosing &amp; Duration</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Remdesivir*(Veklury®)- (IV only)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Restricted to:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>a) Infectious Disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>b) Patients ≤ 10 days of illness, (ie., do not use in patients with signs and symptoms for &gt; 10 days) unlikely to reap benefits of therapy, risk vs. benefit</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Corticosteroids</strong> (IV/PO)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Dexamethasone-Preferred in adults, no known superior agent in children</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Methylprednisolone is preferred in COVID 19 + asthmatic patients</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Alternatives:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>a) Breastfeeding/Pregnant: Prednisolone or methylprednisolone</td>
<td></td>
<td></td>
</tr>
<tr>
<td>b) Preterm infant: Corrected GA &lt; 40 weeks: Hydrocortisone</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Use in patients with:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>a) Respiratory support: oxygen or invasive mechanical ventilation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>b) Continuation for underlying condition requiring chronic steroid treatment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>c) Additional diagnosis where steroid therapy is appropriate</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Baricitinib</strong> (Olumiant®)-(PO/NG/GT only)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Janus kinase (JAK) inhibitor</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Approved for adult RA treatment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Not FDA approved for COVID-19</td>
<td></td>
<td></td>
</tr>
<tr>
<td>At CHKD, Baricitinib is reserved for patients who meet the stated EUA criteria and have a contraindication to corticosteroid treatment</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Corticosteroids should be 1st line & Baricitinib 2nd line only when steroid use is contraindicated**

CBC, CMP: Required at baseline & daily while on therapy, careful attention to LFTs and Scr/BUN

**Restricted to Infectious Disease**

<table>
<thead>
<tr>
<th>Preferred Drug</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dexamethasone</td>
<td>0.15mg/kg once daily (Max: 6 mg)</td>
</tr>
<tr>
<td>Methylprednisolone</td>
<td>2 mg/kg/day divided q12h (Max: 60 mg/day)</td>
</tr>
</tbody>
</table>

**Alternative Drugs**

<table>
<thead>
<tr>
<th>Preferred Drug</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prednisolone</td>
<td>1 mg/kg once daily (Max: 40 mg)</td>
</tr>
<tr>
<td>Hydrocortisone</td>
<td>0.5 mg/kg q12h X 7 days</td>
</tr>
<tr>
<td>Hydrocortisone</td>
<td>0.5 mg/kg daily X 3 days</td>
</tr>
</tbody>
</table>

**Duration:** up to 10 days

**Dose Adjustments/Contraindications for:**

<table>
<thead>
<tr>
<th>Age</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 2-8 years</td>
<td>2 mg once daily</td>
</tr>
<tr>
<td>≥ 9 years</td>
<td>4 mg once daily</td>
</tr>
</tbody>
</table>

**EUA:** Suspected or confirmed COVID-19 in patients who are:

- Hospitalized AND
- Adults or pediatric patients ≥ 2 years of age AND
- Require supplemental oxygen, invasive mechanical ventilation, or ECMO

**Drug Interactions:**

- Strong OAT3 Inhibitors

**Adverse events:**

- Hypersensitivity-Rare but has been reported

**FDA approved as of 10/22/20**

<table>
<thead>
<tr>
<th>Age / wt (kg)</th>
<th>EUA Needed??</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 12 years* or &lt; 40 kg</td>
<td>YES</td>
</tr>
<tr>
<td>≥ 12 years* &amp; ≥ 40 kg</td>
<td>NO</td>
</tr>
</tbody>
</table>

* must be ≥ 3.5 kg & hospitalized
<table>
<thead>
<tr>
<th>Tocilizumab (TOCI) (IV)</th>
<th>Adult Dosing (≥18 years):</th>
<th>Contraindications:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• IL-6 inhibitor</td>
<td>• 8 mg/kg X 1 (Max 800 mg)</td>
<td>• Avoid in pregnancy/breastfeeding</td>
</tr>
<tr>
<td>• Added to antiviral therapy + steroids in those meeting criteria (Figure 2)</td>
<td>Pediatric Dosing (&lt;18 years):</td>
<td>• Alanine aminotransferase &gt;5 times UNL</td>
</tr>
<tr>
<td></td>
<td>• &lt; 30 kg: 12 mg/kg X 1 (Max 800 mg)</td>
<td>• Absolute neutrophil count &lt;500 cells/µL</td>
</tr>
<tr>
<td></td>
<td>• ≥ 30 kg: 8 mg/kg X 1 (Max 800 mg)</td>
<td>• Platelet count &lt;50,000 cells/µL</td>
</tr>
<tr>
<td></td>
<td>** Round dose to nearest full vial **</td>
<td>Caution:</td>
</tr>
<tr>
<td><strong>Duration:</strong> ONCE</td>
<td></td>
<td>• Avoid live viral vaccines</td>
</tr>
</tbody>
</table>

**Sarilumab (SC or SC given IV)^{23, 35-57}**

- IL-6 inhibitor
- 2nd Line: IL-6 inhibitor, alternative during critical TOCI shortage in those ≥ 40 kg
- Added to antiviral therapy + steroids in those meeting criteria (Figure 2)
- Restricted to Infectious Diseases

Additional Details:
- Should be only utilized in patients ≥ 40 kg, data is limited in children
- Innovative use consent should be completed prior to administration, per CHKD policy

For patient qualifications, refer to drug specific guidelines on kdnet, see Tier 1 and Tier 2

### Monoclonal Antibodies:

<table>
<thead>
<tr>
<th>Bamlanivimab + Etesevimab (BAM-E)</th>
<th>Casirivimab + Imdevimab</th>
<th>Sotrovimab</th>
</tr>
</thead>
</table>
| 49 Bamlanivimab monotherapy is no longer recommended and combination therapy is questionable Casirivimab + Imdevimab 1st line | Dose: (updated 6/3/21)^{52}  
  a) Casirivimab 600 mg  
  b) Imdevimab 600 mg  
  c) =1,200 mg as a single dose | EUA Approved Patients: refer to above |

**EUA Approved Patients:** Confirmed (+) COVID-19 who are:

- a) Outpatients AND  
  ≥ 12 years weighing ≥ 40 kg, AND  
  b) High risk (see CHKD Tier Levels)  

**Excluded Patients:**

- a) Hospitalized  
  b) Require oxygen therapy  
  c) Oxygen dependent with ↑ from baseline oxygen due to COVID-19

Restricted to Infectious Disease

**EUA Approved Patients: refer to above**

Sotrovimab^{38} (IV only)

**EUA Approved Patients:** refer to above

Not currently available at CHKD

\*Pediatric dosing obtained via WHO treatment of pediatric Ebola virus, TdP: Torsade’s de pointes

References:


**Version: 7.0 8/23/2021**

Effective Date: 3/20/2020

Page 6 of 9
9. Michael Cohen-Wolkowiez, MD PhD; Anil Maharaj, PhD; Huali Wu, PhD, et al. Pediatric Trials Network (PTN) Hydroxychloroquine Pediatric Dosing Guidelines to Treat COVID-19 Virus. 20 March, 2020
11. Chen C, Zhang XR, Ju ZY, et al. Advances in the research of cytokine storm mechanism induced by corona virus disease 2019 and the corresponding Go to www.ebmedicine.net/COVID-19 for updates to this article, podcasts and videos, and more immunotherapies. Zhonghua Shao Shang Za Zhi 2020;36:E005-E005 [Basic science review]
25. Multisystem Inflammatory Syndrome in Children (MIS-C) Associated with Coronavirus Disease 2019 (COVID-19). Distributed via the CDC Health Alert Network, May 14, 2020, 4:45 PM ET, CDCHAN-00432
27. Royal College of Paediatrics and Child Health Guidance: Paediatric multisystem inflammatory syndrome temporally associated with COVID-19

Version: 7.0 8/23/2021
Effective Date: 3/20/2020
Page 7 of 9


37. Baricitinib [EUA Fact Sheet]. Copyright © 2020, Eli Lilly and Company. All rights reserved, issued 11/19/2020

38. Bamlanivimab [EUA Fact Sheet]. Copyright © 2020, Eli Lilly and Company. All rights reserved, issued 11/9/2020

39. OWS Therapeutics Pre-EUA Playbook – Monoclonal Antibodies, Outpatient administration playbook, 02 Nov 2020; version 1.0


52. FDA Authorizes Lower 1,200 mg Intravenous and Subcutaneous Dose of REGEN-COV™ (casirivimab and imdevimab) Antibody Cocktail to Treat Patients with COVID-19. Regeneron Pharmaceuticals, Inc. Jun 04, 2021


Author/Owner(s):

- **Sarah Parsons**, Pharm D, BCPPS, Infectious Diseases, Antimicrobial Stewardship Co-Lead
- **Laura Sass MD**, Pediatric Infectious Disease

Reviewers: Chris Foley MD; Michael Chicella Pharm. D., BCPPS, FPPAG; MD, Melissa Mark, MD & William Owen, MD, Pediatric Hematology/Oncology, Jessica Price Pharm. D. Pediatric Hematology/Oncology Pharmacy Specialist; Brittany Asaban Pharm. D., BCPP Pharmacy Specialist, Tina Hellauer Pharm. D., Pharmacy Specialist

Originated: 03/20/2020
Last Revised: 8/23/2021

Revision History:

8/23/21: remdesivir restriction added
8/20/21: clarified recommendations for dexamethasone and Remdesivir in algorithm added, sarilumab added w/ innovative use guidance, C/I ppx comment added
7/23/21: updated steroid recommendations
6/2/21: conv plasma removed, monoclonal antibodies updated to reflect variant changes, C/I recommended agent, dosing for Sotrovimab added with note to used C/I as preferred, flow diagram updated
3/24/21: Anticoagulation lab recommendations, Bamlanivimab monotherapy removed.
2/26/21: MIS-C guideline separation, update treatment to include anticoagulation recommendations and risk assessment. Added BAM-E to guideline and recommended using BAM containing first over C/I.
1/28/21: added heme-one consult and removed ASA as initial therapy without consult. Add dosing recommendations and caveat in dosing table.
1/20/21: updated MIS-C guideline, steroids and anakinra dosing, Remdesivir ALT recommendations
12/15/20: updated Baricitinib recommendations from 12/14 NIH
11/24/20: added Bamlanivimab & Casirivimab and Imdevimab, and Baricitinib, removed nebulized recommendations, added covid specific therapy chart, removed
10/23/20: Updated MIS-C management and FDA Remdesivir approval
8/7/20: clarified recommendations for dexamethasone and Remdesivir in algorithm
7/22/20: updated Remdesivir use of CHKD product under EUA
7/17/20: updated anakinra dosing and tocilizumab information
6/24/20: added nebulized therapy guideline, renumbered tables
6/17/20: Hydroxychloroquine and azithromycin removed from guideline
6/1/20: ID consult added to MIS-C and moderate-severe criteria combine
5/29/20: Hydroxychloroquine removed from algorithm and ID will recommend as a 2nd line therapy if indicated, and moved to 2nd line in table 4. ID consult added to algorithm. Reformating of table 4
5/22/20: addition of definition and review of treatment for MIS-C, Remdesivir EUA update, addition of chart with known indication in COVID-19 and unclear, anakinra added to list, cytokine storm table moved to tocilizumab dosing table, QTC chart updated. MIS-C severity table, guideline for MIS-C treatment and dosing. MIS-C flow diagram, Simplified tocilizumab dosing
5/4/20: Updated information on disease process in children, added EUA to Remdesivir, changed to consider Hydroxychloroquine to the treatment algorithm. Added new references. Removed Lopinavir-Ritonavir
4/9/20: NG administration for hydroxychloroquine, Remdesivir added to figure 1, azithromycin changed to (+/-) in figure 1. Tables renumbered for organization, VTE prophylaxis guidance-Reviewed by Eric Lowe MD & Jessica Price PharmD
4/3/20: Remdesivir reference to guideline, included reference for cytokine storm
3/30/20: updated Lopinavir/ritonavir dosing and duration, remove azithromycin from combination early initiation, added QT monitoring recommendations and risks, NSAID statement

The recommendations in this guide are meant to serve as treatment guidelines for use at The Children’s Hospital of The King’s Daughters. As a result of ongoing research, practice guidelines may from time to time change. The authors of these guidelines have made all attempts to ensure the accuracy based on current information, however, due to ongoing research, users of these guidelines are strongly encouraged to confirm the information through an independent source.

This policy is in effect for Children’s Hospital of The King’s Daughters Health System (CHKDHS) to include the following subsidiaries: Children’s Hospital of The King’s Daughters, Incorporated (CHKD), Children’s Medical Group, Inc., and CMG of North Carolina, Inc. (CMG), and Children’s Surgical Specialty Group, Inc. (CSSG).

**Version: 7.0 8/23/2021**
Effective Date: 3/20/2020

Page 9 of 9