Antimicrobial Stewardship Guidelines

Guidance for the Management of Acute COVID-19 in Children

I. General Principles:

- This guidance is specific to acute infection with SARS-CoV-2. For evaluation and management of multisystem inflammatory syndrome in children, please refer to Guidelines for the Evaluation and Management of MIS-C.
- There are no data available from comparative studies evaluating therapies for COVID-19 in pediatric patients.
- The majority of children with SARS-CoV-2 infection have mild or moderate disease and recover with supportive care alone. Therefore, the risks of therapies must be carefully weighed against unclear benefit.
- Whether or not to initiate therapy is at prescriber's discretion. Prior to treatment, the risks, benefits, and alternatives should be discussed with the patient and documented in the medical record.
- Antibiotics should only be used for confirmed or strong suspicion of a co-existing bacterial infection or sepsis. Re-evaluate antibiotics daily and de-escalate or discontinue if there is no evidence of bacterial infection.
- Infectious Diseases (ID) consultation should be considered for children hospitalized with severe SARS-CoV-2 infection, especially because treatment options are changing rapidly. ID consultation is recommended if considering use of immunomodulators (i.e. baricitinib or tocilizumab).
- Additional BJC COVID resources:
  - General information, including recommendations for SARS-CoV-2 in adults: https://covid19.bjc.org/Resources
  - Outpatient management of SARS-CoV-2, including a decision-making algorithm for outpatient therapeutics and ordering information: www.bjc.org/for-physicians/covid
  - Monoclonal Antibody Therapy: https://www.bjc.org/For-Physicians/Monoclonal-Antibody-Therapy
  - Tixagevimab/cilgavimab (Evusheld) for pre-exposure prophylaxis is no longer authorized in the U.S. as of 1/26/2023. The EUA has been revised to limit its use to when combined resistant SARS-CoV-2 variants are ≤ 90%. All regions in the U.S. are currently above this 90% threshold of resistant variants and Evusheld is unlikely to be effective.

II. SARS-CoV-2 Treatment Recommendations:

Disease severity	Respiratory support requirement	Management
Not Hospitalized Mild/Moderate	No increase in oxygen requirement. Symptoms may be limited to the upper respiratory tract, or may include X-ray changes	• Supportive care alone is appropriate for most • For patients at high risk of severe disease who meet eligibility criteria (see table below for details), consider ○ **Nirmatrelvir/ritonavir (Paxlovid) PO** (preferred for those ≥12 years & ≥ 40 kg) or ○ **Remdesivir IV** (≥ 28 days old & ≥ 3 kg, at highest risk [see criteria in table below]) ○ **Molnupiravir PO** (≥18 years, if other options unavailable, and patient agrees to contraception requirements)
Hospitalized Mild/Moderate	No increase in oxygen requirement. Symptoms may be limited to the upper respiratory tract, or may include X-ray changes	• Supportive care alone is appropriate for most • Consider **remdesivir IV 3-day course** for patients at high risk of severe disease who meet eligibility criteria (see table below for details) • mAbs and oral agents are **not** authorized for patients hospitalized for COVID-19
Severe	New or increase from baseline supplemental oxygen requirement **without** need for new or increase in baseline non-invasive[1]/invasive mechanical ventilation.	• Supportive care • Consider **dexamethasone**[2] • Consider **remdesivir IV 5-day course**[2]
Critical	New or increased requirement for invasive or non-invasive[1] mechanical ventilation, sepsis, or multi-organ failure.	• Supportive care • Recommend **dexamethasone** • Consider **remdesivir IV 5-day course**[3] • Consider **tocilizumab IV** or **baricitinib PO**[4]

[1]Non-invasive mechanical ventilation includes high-flow nasal cannula, continuous positive airway pressure (CPAP), or bilevel positive airway pressure (BiPAP).
[2]Especially for otherwise healthy children with minimal oxygen requirement, supportive care alone may be appropriate.
[3]Benefit of remdesivir in patients requiring invasive mechanical ventilation or ECMO is not clear and may be marginal
[4]Especially for patients with rapidly increasing oxygen needs and systemic inflammation

III. Risk Factors for Severe Disease

The majority of children who develop severe COVID-19 have underlying medical problems. There are limited data about which medical conditions increase the risk of severe disease and hospitalization in children. Eligibility criteria for most therapeutics focus on risk factors identified in adults. The following medical conditions have been associated with higher risk of hospitalization and more severe disease in children in some studies:

- Medical complexity (e.g. neurologic impairment, developmental delay, genetic syndromes including trisomy 21)
- Obesity, especially in teenagers
- Asthma and chronic lung disease
- Congenital heart disease
- Diabetes mellitus
- Sickle cell disease
- Immunosuppression

Hospitalization and death rates are higher in nonwhite children compared to white children.

Unvaccinated status is the greatest risk factor for hospitalization in both children and adults.

IV. Detailed Information Regarding SARS-CoV-2 Directed Therapeutics

High-Quality Evidence Supporting Efficacy and Safety

Outpatient Therapeutics

- For additional information on outpatient management of SARS-CoV-2 at BJC, including a decision-making algorithm for outpatient therapeutics and ordering information: https://www.bjc.org/for-physicians/covid
- Outpatient therapies are currently allocated to the states by the US Department of Health and Human Services and then distributed by the state to healthcare systems.
- Due to supply and capacity constraints, it is not possible to provide outpatient therapeutics to all eligible patients. The NIH has provided a tiered prioritization system when there are logistical or supply constraints.
- The primary goal of prioritization of these agents is to prevent progression to severe disease and hospitalization and protect our strained and overburdened healthcare system.
- **Most children do not require any treatment for mild COVID-19.** Outpatient therapies for mild COVID-19 may be considered, especially for patients who are at highest risk of hospitalization: patients who are **moderately to severely immunocompromised** OR **not fully vaccinated* with at least one risk factor for progression to severe disease.** Fully vaccinated patients with at least one risk factor for progression to severe disease can be considered for these therapies on a case-by-case basis.
    - **Fully vaccinated = 2 doses mRNA vaccine or 1 dose of J&J vaccine*

Nirmatrelvir/ritonavir (Paxlovid) **CRITERIA FOR USE:** • ≥12 years of age and ≥40 kg • COVID-19 positive • Mild-moderate symptoms • High risk for progression to severe illness • Must be started within 5 days of symptom onset	**Mechanism:** inhibitor of SARS-CoV-2 main protease (Mpro), preventing viral replication **Relevant Literature:** • EPIC-HR: RCT of 2,246 non-hospitalized patients with COVID-19 at high risk for disease progression treated within 3 days of symptom onset. Pfizer's press release of the interim analysis showed 89% risk reduction of hospitalization or death from any cause at Day 28 compared to placebo (6.5% vs. 0.8%). All-cause mortality through Day 28 was 0% in the Paxlovid arm and 1.1% in the placebo arm (n=12). **Use in Children:** No data in children. **Availability and Use:** • Available via EUA at all BJC retail pharmacies. Current regulations require that Missouri providers send prescription to Missouri pharmacies and Illinois providers to send prescription to Illinois pharmacies. These across-state regulations do not apply to non-BJC retail pharmacies, where Paxlovid may be stocked. • Indicated for use in patients at high risk for disease progression. See CDC website for full list of risk factors. **Most common side effects:** dysgeusia, diarrhea, hypertension, myalgia **Warnings:** • **Always check drug-drug interactions. Ritonavir is a potent CYP3A4 inhibitor.** See BJC website for guidance on how to manage certain interactions, and for additional considerations with Paxlovid and other outpatient therapies. • Hepatotoxicity • Embryo-fetal toxicity. There is no data in pregnancy and breastfeeding. Consultation with clinical expert recommended. 2nd line in pregnancy after mAbs. • Caution should be taken in patients with uncontrolled HIV, as use of Paxlovid may increase risk of developing HIV resistance to protease inhibitors

	Dose/Duration: • **eGFR ≥ 60 ml/min**: 300mg nirmatrelvir + 100mg ritonavir (3 pills total: #2 150mg nirmatrelvir tabs + #1 100mg ritonavir tab) BID x5 days • **eGFR ≥ 30 to < 60 ml/min**: #1 150mg tab of nirmatrelvir + #1 100mg tab of ritonavir BID x5 days • eGFR < 30 ml/min: Use not recommended • Avoid use in severe hepatic impairment (Child-Pugh Class C)
Monoclonal Antibody Therapy Specific product will be based on availability and CDC/State recommendations for circulating variants **Current mAb: NONE**	
Molnupiravir **CRITERIA FOR USE:** • ≥18 years old • COVID-19 positive • Mild-moderate symptoms • High risk for progression to severe illness • Other preferred FDA-authorized therapies are not clinically appropriate or accessible • Not pregnant and agrees to contraceptive requirements • Must be started within 5 days of symptom onset **Molnupiravir (continued)**	**Mechanism:** Oral prodrug of ribonucleoside that is incorporated into SARS-CoV-2 RNA by RNA polymerase, resulting in accumulation of errors in the viral genome leading to inhibition of replication (viral lethal mutagenesis). **Relevant Literature:** • MOVe-OUT: RCT of 1,433 high-risk non-hospitalized adults with mild-moderate COVID-19. All-cause hospitalization 24 hours or more or death at Day 29 was 6.8% for molnupiravir (n=48) and 9.7% for placebo (n=68), with a relative risk reduction of 30%. Mortality at Day 29 was 0.1% for molnupiravir (n=1) and 1.3% for placebo (n=9). **Use in Children:** No data available. Only authorized for use in adults ≥18 years old **Availability and Use:** • Available via EUA at all BJC retail pharmacies. Current regulations require that Missouri providers send prescription to Missouri pharmacies and Illinois providers to send prescription to Illinois pharmacies. These across-state regulations do not apply to non-BJC retail pharmacies, where molnupiravir may be stocked. • Indicated for use in patients at high risk for disease progression when other preferred treatments are not clinically appropriate or accessible. See CDC website for full list of risk factors. **Most common side effects:** diarrhea, nausea, dizziness **Warnings/Contraindications:** • Bone and cartilage toxicity • Embryo-fetal toxicity **Exclusions:** • Pregnancy • Breastfeeding and unable to pump/discard during therapy and 4 days after last dose • Individuals of childbearing potential unable to use effective contraception correctly and consistently during therapy and 4 days after the last dose • Males of reproductive potential sexually activity with females of childbearing potential who are not using a reliable method of contraception correctly and consistently during treatment and for at least 3 months after the last dose. **Dose/Duration:** 800mg every 12 hours (4 pills per dose) x5 days

Outpatient/Inpatient Therapeutics	
Remdesivir **CRITERIA FOR USE:** **Outpatient** **Must meet all of the following:** • Symptomatic, laboratory-confirmed COVID-19 • Therapy can be initiated within 7 days of symptom onset • ≥ 3 kg AND ≥ 28 days old • Unable to receive nirmatrelvir/ritonavir (Paxlovid) due to age/weight restrictions, severe drug-drug interactions, etc. AND **Must meet 1 of the following:** • Moderately to severely immunocompromised, regardless of vaccination status OR • Unvaccinated with one or more risk factor(s) for severe disease	**Mechanism:** Inhibits RNA-dependent RNA polymerase in SARS-CoV-2 **Relevant Literature:** • ACTT-1: In an RCT of 1,059 adults hospitalized with COVID-19, time to recovery was significantly faster in those randomized to remdesivir vs. placebo (11 vs. 15 days). Greatest benefit in patients receiving supplemental oxygen (Beigel, NEJM 2020). • SOLIDARITY: Multinational study by the World Health Organization included 11,266 adults in 30 countries randomized to local standard of care vs. one of four different repurposed antivirals, 2750 were randomized to remdesivir. Compared to standard of care, there was no reduction in mortality, initiation of mechanical ventilation, or duration of hospitalization (WHO Solidarity Trial Consortium, NEJM 2020). • No clear benefit demonstrated in patients requiring invasive mechanical ventilation or ECMO. In ACTT-1, remdesivir did not improve recovery or survival in this subgroup. • PINETREE: 562 non-hospitalized patients ≥18 years with mild-moderate COVID-19 at high risk of severe disease randomized within 7d of symptom onset to 3d of remdesivir vs. placebo. 87% relative reduction in risk of hospitalization or death at day 28 compared to placebo (Gottlieb, NEJM 2021). **Outpatient** **Availability and Use:** • FDA approved for patients ≥ 28 days old AND ≥ 3 kg for a 3-day course **Ordering and Administration:** • Refer to Epic Tip Sheet for ordering instructions. Providers must complete 2 steps: 1) Appointment Request order to notify appropriate infusion location to schedule, 2) Order the Therapy Plan • Infusions will be scheduled at the SLCH 9S infusion clinic on 3 consecutive days. Infusion series must be started Monday, Tuesday, or Wednesday. **Monitoring:** • Obtain serum creatinine to determine eGFR, prothrombin time, AST, and ALT during first infusion visit. These do not have to result prior to giving the first infusion. • Provider will be contacted for AST/ALT ≥ 3x ULN or CrCl < 30 ml/min to consider risks vs benefit of proceeding with subsequent doses of remdesivir. **Patient Education:** • See Appendix I below for talking points to review with patients. This addresses financial questions and other logistics. **Dosing (3-day regimen):** • ≥ 40 kg: 200 mg IV on day 1, then 100 mg IV q24h × 2 days • 3 - < 40 kg: 5 mg/kg IV on day 1, then 2.5 mg/kg IV q24 × 2 days
Remdesivir, continued **CRITERIA FOR USE:** **Inpatient** **Must meet all of the following:** • Symptomatic, laboratory-confirmed COVID-19 • Hospitalized for < 14 days AND **Must meet at least 1 of the following:** • Severe and/or critical illness defined by:	**Inpatient** **Availability and Use:** • FDA approved for patients hospitalized due to COVID-19 who are ≥ 28 days old AND ≥ 3 kg for a 5-day course • Off-label for 5-day course in patients hospitalized with COVID-19 who are either < 28 days old or < 3 kg. Consult Infectious Diseases. • Off-label for 3-day course in hospitalized patients with mild/moderate COVID-19 at high risk of severe disease weighing ≥ 3 kg.

○ Oxygen saturation (SpO2) of ≤ 94% on room air, or ○ Requiring supplemental oxygen, or ○ Requiring invasive mechanical ventilation, or ○ Requiring ECMO • Symptomatic COVID-19 disease of any severity with one or more risk factors for progression to severe disease (see Fact Sheet for full list of qualifying risk factors).	**Monitoring**: • Obtain eGFR, prothrombin time, and LFTs prior to administration. Depending on baseline results and patient-specific considerations, repeat labs throughout treatment as indicated. **Dosing:** Severe COVID-19 in patients who are hypoxic/require supplemental O_2 (5-day regimen): • ≥ 40 kg: 200 mg IV on day 1, then 100 mg IV q24h × 4 days, or until hospital discharge, whichever comes first • 3 - < 40 kg: 5 mg/kg IV on day 1, then 2.5 mg/kg IV q24 × 4 days, or until hospital discharge, whichever comes first • < 3 kg: Optimal dosing not known. **Consult Infectious Diseases** to determine dosing recommendations if remdesivir is indicated. For mild/moderate COVID-19 in patients at high risk of severe disease (3-day regimen based on PINETREE study): • ≥ 40 kg: 200 mg IV on day 1, then 100 mg IV q24h × 2 days • 3 - < 40 kg: 5 mg/kg IV on day 1, then 2.5 mg/kg IV q24 × 2 days
Inpatient Therapeutics	
Dexamethasone **CRITERIA FOR USE:** • Symptomatic, laboratory-confirmed COVID-19 AND • Severe and/or critical illness requiring supplemental oxygen, non-invasive or invasive mechanical ventilation, or ECMO.	**Mechanism:** Glucocorticoid **Relevant Literature:** • In the RECOVERY trial, a multicenter randomized open-label trial of hospitalized patients, adults who were randomized to dexamethasone had lower 28-day mortality than those who received standard of care. Benefit was most significant for patients who were mechanically ventilated (29% mortality in dexamethasone arm compared to 40.7% in control arm). There was also benefit for those requiring supplemental oxygen who were not mechanically ventilated (21.5% vs. 25%). There was no benefit for those who did not require supplemental oxygen (Horby, NEJM 2020). **Use in Children:** Results from pediatric arm of RECOVERY have not yet been reported **Dosing:** 0.15 mg/kg (max 6 mg) daily for up to 10 days or until hospital discharge, whichever comes first
Tocilizumab **CRITERIA FOR USE:** **Must meet <u>all of the following</u>:** • Laboratory-confirmed COVID-19 • Critical illness requiring supplemental oxygen via non-invasive or invasive mechanical ventilation, or ECMO • 2 years of age or older • Receiving systemic corticosteroids	**Mechanism:** Anti-IL-6 receptor monoclonal antibody proposed as treatment for inflammatory syndrome similar to cytokine release syndrome (CRS). **Relevant Literature:** • Multiple early RCTs, including an industry-sponsored trial (COVACTA), of hospitalized adults with COVID-19 pneumonia failed to demonstrate clinical improvement or reduction in overall mortality (Rosas, NEJM 2021). • REMAP-CAP trial of 803 critically ill adults requiring respiratory support in an ICU showed that tocilizumab reduced in-hospital mortality and increased the number of organ support-free days (REMAP-CAP, NEJM 2021). • RECOVERY: Open label RCT of 4116 adults with COVID-19 pneumonia with hypoxia and C-reactive protein ≥75 mg/L. Patients who received tocilizumab demonstrated improved survival at 28 days and were less likely to progress to mechanical ventilation or death (RECOVERY, Lancet 2021). • In the trials reporting benefit, tocilizumab was initiated early (within 3 days of hospitalization or within 24 hours of ICU admission). Tocilizumab may be more beneficial in patients with early rapidly progressing disease. **Use in Children:** No data exist for patients < 18 years old.

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<td>There is a critical nationwide shortage of Tocilizumab. It is currently restricted to patients meeting one of these criteria:
• GFR< 30 ml/min in children 2-8 years old, GFR< 15 ml/min in patients > 8 years old, receiving renal replacement therapy, or non-resolving AKI
• Pregnant
• Unable to obtain enteral access, OR
• Within 24 hours of ICU admission and rapid progression of respiratory failure</td>
<td>Availability and Use:
• via EUA
• ID consult recommended.
• EUA order available in Epic. Prescriber must attest the patient meets all EUA requirements, Fact Sheet has been communicated and given to patient/caregiver.
Exclusions:
• >48 hours of ICU admission at BJC hospital
• >10 days of invasive mechanical ventilation
Potential Adverse Effects: gastrointestinal perforation, anemia, neutropenia, secondary infections, hepatitis, and infusion reactions
Dosing: (Patients should NOT receive more than one dose)
• <30 kg: 12 mg/kg IV x 1
• ≥30 kg: 8 mg/kg IV x 1 (max 800 mg)</td>
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<td>Baricitinib

Baricitinib may be considered as an alternative to tocilizumab due to national shortage

CRITERIA FOR USE:
<u>Must meet all of the following</u>:
• Symptomatic, laboratory-confirmed COVID-19
• Critical illness requiring supplemental oxygen via non-invasive or invasive mechanical ventilation, or ECMO
• 2 years of age or older
• Receiving systemic corticosteroids

Baricitinib, continued</td>
<td>Mechanism: Janus kinase (JAK) inhibitor that may prevent cellular immune activation and inflammation in COVID-19. Approved by FDA for severe rheumatoid arthritis.
Relevant Literature:
• ACTT-2: multinational, randomized, placebo-controlled trial in 1,033 hospitalized patients with COVID-19 pneumonia found median time to recovery was shorter in baricitinib plus remdesivir group (7 days) than in the remdesivir only group (8 days) (Kalil, NEJM 2020). Trial was done before dexamethasone established as standard of care with mortality benefit and dexamethasone was not included in either arm.
• COV-BARRIER: multinational RCT in 1,525 hospitalized adults with pneumonia and elevation in >1 inflammatory marker. No significant difference in progression to high-flow oxygen, non-invasive ventilation, invasive mechanism ventilation, or 28-day mortality. 60-day all-cause mortality was lower in baricitinib group (10.3%) vs. placebo (15.2%) (Marconi, Lancet Respir Med 2021).

Availability:
• via EUA
• ID consult recommended.
• EUA order available in Epic. Prescriber must attest the patient meets all EUA requirements, Fact Sheet has been communicated and given to patient/caregiver.
Use in Children: No data exist for patients < 18 years old.
Exclusions:
• >48 hours of ICU admission at BJC hospital
• >10 days of invasive mechanical ventilation
• GFR< 30 ml/min in pediatric patients 2-8 years old, GFR< 15 ml/min in all other patients, or receiving renal replacement therapy or non-resolving acute kidney injury.
Consider holding or interrupting therapy if:
• ALC <200 cell/µL
• ANC <500 cell/µL
• Suspected drug-related liver injury
Potential Adverse Effects: thrombosis, gastrointestinal perforation, anemia, neutropenia, secondary infections, hepatitis, infusion reactions</td>
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Dosing:

Indication	CrCl (mL/min) ≥ 60	30-59	15-29	< 15 or IHD	CRRT/SLED
Adult and pediatric patients 9 years of age and older	4 mg daily	2 mg daily	1 mg daily	Not recommended	Not recommended
Pediatric patients 2 years to less than 9 years of age	2 mg daily	1 mg daily	Not recommended	Not recommended	Not recommended

Duration: 14 days or until hospital discharge, whichever comes first

Not Recommended	
Hydroxychloroquine **Azithromycin** **Lopinavir/ritonavir** **Colchicine**	All of these therapies have been proposed for SARS-CoV-2 due to evidence of in vitro efficacy. For each therapy, multiple studies have shown no clinical benefit in patients with infection due to SARS-CoV-2. Due to lack of clinical efficacy, these therapies should not be used for management of SARS-CoV-2 infection.

V. Resources and Fact Sheets for Therapeutics

Convalescent Plasma Fact Sheets
Convalescent Plasma Fact Sheet for Health Care Providers
Convalescent Plasma Fact Sheet for Patients/Caregivers

Tocilizumab Fact Sheets
Tocilizumab EUA Fact Sheet for Health Care Providers
Tocilizumab EUA Fact Sheet for Patients, Parents, and Caregivers

Baricitinib Fact Sheets
Baricitinib EUA Fact Sheet for Health Care Providers
Baricitinib EUA Fact Sheet for Patients

Monoclonal Antibody Fact Sheets
Bebtelovimab Fact Sheet for Health Care Providers
Bebtelovimab Fact Sheet for Patients/Caregivers (English)
Bebtelovimab Fact Sheet for Patients/Caregivers (Spanish)

Molnupiravir
Molnupiravir Fact Sheet for Health Care Providers
Molnupiravir Fact sheet for Patients/Caregivers (English)
Molnupiravir Fact Sheet for Patients/Caregivers (Spanish)

Paxlovid (nirmatrelvir/ritonavir)
Paxlovid Fact Sheet for Health Care Providers
Paxlovid Fact Sheet for Patients/Caregivers (English)
Paxlovid Fact Sheet for Patients/Caregivers (Spanish)

VI: Pediatric Thromboprophylaxis Guidelines for Acute COVID-19

These are general guidelines on initiation of *prophylactic anticoagulation* in children admitted to St. Louis Children's Hospital with confirmed SARS-CoV-2 infection. This does not replace formal recommendations by the consulting hematology team who will formulate an individualized plan for each patient. These guidelines are subject to change given rapidly evolving data. *This guideline is not applicable to patients who develop thrombosis where standard treatment is recommended.*

Background:

- SARS-CoV-2 infection in adults is associated with an increased risk of coagulopathy.
- The *International Society on Thrombosis and Hemostasis* [ISTH] and *Anticoagulation Forum* have recommended prophylactic anticoagulation for all adult inpatients with SARS-CoV-2 infection.
- There is a paucity of pediatric studies investigating the impact of SARS-CoV-2 infection on both coagulopathy and thrombosis.
- Venous thrombo-embolism in rare in children (1:100,000/yr) compared to adults (1:1000/yr), though the incidence in hospitalized children in the US in increasing. Thrombosis in children tends to be multi-factorial; >85% of children with VTE have multiple risk factors for thrombosis.

Recommendations:

- We suggest obtaining the following labs for all patients admitted with confirmed SARS-CoV-2 infection (i) on admission and (ii) change in clinical status or level of care (i.e. transfer to ICU/ need for supplemental oxygen etc)
    - Platelet count
    - PT/aPTT
    - Fibrinogen
    - D-dimer
    - BUN/creatinine
- General recommendations for anticoagulation are in Table 1.
- Indications for thromboprophylaxis should be reviewed daily; thromboprophylaxis should be discontinued once criteria are not met, including change in the level of care

Table 1. Recommendations for anticoagulation in patients with Acute COVID-19

	Mild/Moderate	Severe	Critical
Anticoagulation	<12 years: early ambulation & SCDs if tolerated	<12 years: Consider prophylactic enoxaparin per VTE order set in patients with **2** or more additional VTE risk factors[1,2]	Prophylactic anticoagulation per VTE order set, in the absence of increased risk of bleeding[2]
	≥12 years: Consider prophylactic enoxaparin per VTE order set for patients with **2** or more additional VTE risk factors[1,2]	≥12 years: Consider prophylactic enoxaparin per VTE orderset for patients with **1** or more additional VTE risk factors[1]	

[1]VTE risk factors: obesity, presence of central venous catheter, chronic inflammatory illness, use of estrogen-containing contraception, personal history of VTE or thrombophilia trait, family history of VTE in 1st-degree relative, altered mobility 30 days prior to admission (major surgery, significant trauma)

[2]Consider withholding VTE prophylaxis in the presence of bleeding risk factors: platelets <50 k/mm^3, fibrinogen <100 mg/dL, elevated PT/aPTT, hepatic or renal failure, recent or ongoing bleeding, recent surgery. Discuss net clinical benefit on a case-by-case basis. May consider low-dose unfractionated heparin (10 units/kg/hr) for high risk of bleeding and thrombosis. Anti-Xa goal 0.1-0.3 units/mL. PTT goal 60-75 sec.

Appendix 1: Talking Points Regarding Outpatient Remdesivir in Pediatric Patients

- The U.S. Food and Drug Administration recently expanded the use of the antiviral drug VEKLURY (more commonly known as remdesivir (rem-des-uh-veer)) to certain non-hospitalized adults and pediatric patients. It was previously only available to hospitalized patients.
- It is used for the treatment of mild-to-moderate COVID-19 to reduce the risk of hospitalization in high-risk patients.
- It isn't a substitute for being vaccinated.

Requirements for pediatric patients

- It is approved for use in pediatric patients 28 days old or older who weigh at least 3 kilograms (about 7 pounds).
- Patients must have a positive COVID test with mild-to-moderate symptoms and be at a high risk for progression to severe COVID-19.
- The drug should be administered within 7 days of symptoms appearing.

How is remdesivir administered?

- This antiviral drug is administered through a vein with daily IV infusions for 3 consecutive days in an outpatient setting at Children's Hospital.
- On the day of the first infusion, lab tests will be sent before infusion is started. The infusion can be administered prior to those labs resulting.
- Patients are monitored during the infusion and observed for at least 1 hour after the infusion.
- The amount of the dose is adjusted for the child's body weight.

What is the cost?

- There are costs for the drug itself, for the infusion used to deliver the drug, and for lab tests.
- The cost of the antiviral drug will vary depending upon the child's weight and how much of the drug is used.

Weight	Total number of vials for 3 days of therapy based on PINETREE	Cost of Drug
20 kg (44 pounds) or less	3	Up to $7,020 Up to $4,212 with 40% self-pay discount
21 kg (46.2 pounds) or more	4	Up to $9,360 Up to $5,615 with 40% self-pay discount

- Costs will vary depending on whether the patient has insurance. We expect patients with insurance to have much less out-of-pocket costs.
- Most insurance plans will cover the cost of the infusion so parents should check with their insurance provider to see if they are covered.
    - Medicare and MO Medicaid provide coverage for this service.
- Lab tests that are included with the infusion treatment will total $327 for four different tests. For those who are self-pay, the discounted cost will be $196.20.
- Some patients with commercial insurance plans may have out-of-pocket costs for the infusion or lab tests. Check with your insurance provider. Parents may call the BJC Price Estimate line for specific questions about their potential costs at 314.747.8845 or toll-free 1.844.747.8845.