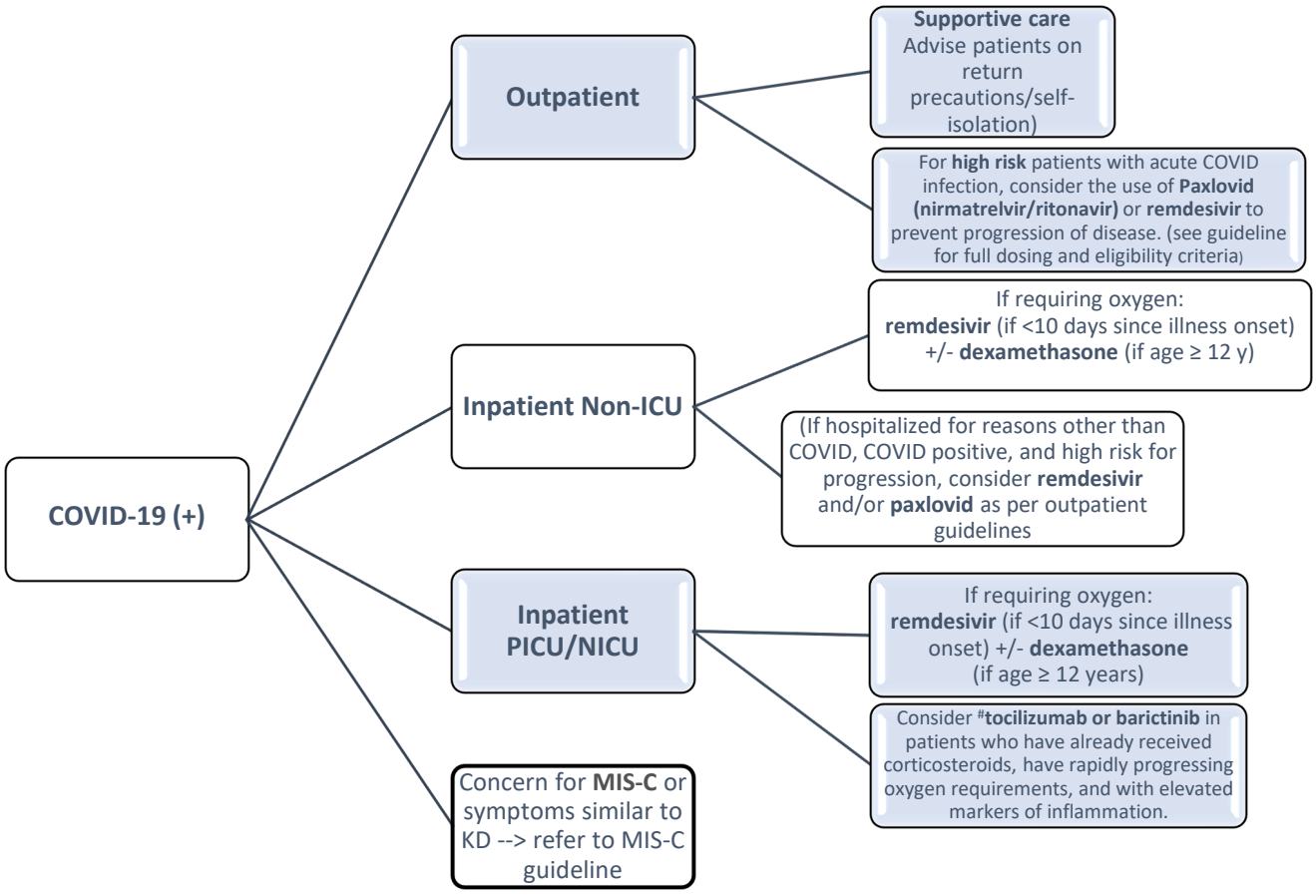
UC DAVIS HEALTH | CHILDREN'S HOSPITAL

COVID Pediatric Treatment Guidelines

Below are recommendations for management of pediatric patients with suspected or documented COVID-19.

These guidelines will be updated periodically.



Prioritization of High-risk pediatric patients	
Tier 1 (Highest risk)	Immunocompromised individuals not expected to mount an adequate immune response to COVID vaccination, regardless of vaccine status (Highest priority are severely immunosuppressed, including: patients receiving B-cell depleting therapies such as rituximab, patients receiving Bruton tyrosine kinase inhibitors, CAR-T recipients, post stem cell transplant <2 years or on immunosuppressive therapy, hematologic or solid tumor malignancies on active therapy, solid organ therapy on immunosuppression, moderate to severe primary immunodeficiency (e.g., SCID, DiGeorge, CVID, Wiskott Aldrich), patients with advanced HIV (CD4 T cell count <200 or other manifestations of advanced HIV), on high dose corticosteroids for ≥2 weeks (defined as 20mg prednisone or equivalent per day)
Tier 2	Multiple risk factors and no immunity (vaccination not up to date, no recent infection: defined as in the last 4 months) **Definite high risk conditions:** Severely immunocompromised, chronic lung disease excluding asthma, chronic cardiac condition, prematurity, neurologic disease, obesity, diabetes mellitus, medical technology dependence (i.e., tracheostomy, ventilator usage) **Probable high risk conditions**: sickle cell disease, mild-moderate immunocompromised, neuro-disabilities, chronic kidney, GI or liver disease.
Tier 3 See risk factors in Tier 2	Multiple risk factors and prior immunity (vaccination up to date or recent infection: defined as in the last 4 months)
Tier 4 See risk factors in Tier 2	Single risk factor and no immunity (vaccination not up to date, no recent infection: defined as in the last 4 months)
Tier 5 See risk factors in Tier 2	Single risk factor and prior immunity (vaccination up to date or recent infection: defined as in the last 4 months)

Definite high risk conditions: Severely immunocompromised, chronic lung disease excluding asthma, chronic cardiac condition, prematurity, neurologic disease, obesity, diabetes mellitus

Probable high risk conditions: sickle cell disease, mild-moderate immunocompromised, neuro-disabilities, chronic kidney, GI or liver disease.

Outpatient Therapeutic Agents

<table>
<tr><th>Agents</th><th>Criteria for use</th><th>Drug Information and Dosing</th></tr>
<tr>
<td>Remdesivir (IV only)</td>
<td>Eligibility:
-Pediatric patients weighing ≥ 1.5kg with mild-moderate COVID who are not requiring hospitalization for COVID-19 and are at high risk for progression of disease
-Onset of disease within 7 days
-Recommended for high risk patients (as defined above), with most benefit likely to be seen in children aged <1 year or 12-17 years but can be considered in 1-12 years</td>
<td>
<table>
<tr><th>Body Weight</th><th>Loading dose
(Day 1)</th><th>Maintenance dose
(from Day 2)</th></tr>
<tr><td>1.5 to <3 kg</td><td>2.5mg/kg x 1</td><td>1.25mg/kg/dose on days 2-3</td></tr>
<tr><td>3 to < 40 kg</td><td>5mg/kg IV x1</td><td>2.5mg/kg IV daily on days 2-3</td></tr>
<tr><td>≥ 40 kg and adults</td><td>200mg IV x1</td><td>100mg IV daily on days 2-3</td></tr>
</table>
Important notes:
• A 3 day duration is recommended for patients who are not hospitalized or hospitalized for reasons other than COVID-19.
• Must be administered in a setting where patients can be observed for at least 1 hour after infusion
• Use caution in patients with eGFR <30mL/minute
• Baseline LFTs, creatinine are recommended prior to initiation of treatment
</td>
</tr>
<tr>
<td>Paxlovid (combination of Nirmatrelvir and Ritonavir)</td>
<td>Eligibility:
-Pediatric patients ≥12 years old and weighing ≥ 40kg with mild-moderate COVID (through EUA) who are not requiring hospitalization for COVID-19 and are at high risk for</td>
<td>
<table>
<tr><th>Agent</th><th>Dosing</th><th>Duration</th></tr>
<tr><td>Nirmatrelvir
Ritonavir
(They are provided together within a 5 day dose pack)</td><td>2 tablets PO twice a day
1 tablet PO twice a day
Both medications should be taken at the same time</td><td>5 days</td></tr>
</table>
Important notes:
• Please provide the Fact Sheet for Patients, Parents, and Caregivers to the family and document in the chart https://www.fda.gov/media/155051/download
• Drug-drug interactions are common due to ritonavir being a P450 3A4 inhibitor, so other medications should be reviewed closely for possible interactions
• Patients with moderate renal impairment may need dosing adjustment
</td>
</tr>
</table>

	progression of disease -Onset of disease within **5 days** -Recommended for **high risk** patients (as defined above) **-**Contraindicated in patients with severe renal impairment (eGFR of <30 mL/min or severe hepatic impairment)	• Common side effects: dysgeusia, diarrhea, hypertension, myalgia • May take with or without food; tablets need to be swallowed whole (cannot be crushed)
Monoclonal antibodies (IV only)	**NO CURRENT MONOCLONAL ANTIBODIES RECOMMENDED**	

Inpatient Treatment of Patients with Symptomatic COVID-19 infection

(For patients with acute COVID infection that are hospitalized for other reasons but are at high risk of progression, consider the use of one of the outpatient therapies as listed above)

<table>
<tr><th>Agents</th><th>Criteria for use</th><th>Drug Information and Dosing</th></tr>
<tr><td>Remdesivir (IV only)</td><td>Eligibility:
-Hospitalized children with symptomatic COVID-19 requiring any supplemental oxygen and weighing ≥ 1.5kg

-Highest benefit in patients aged ≥12 yrs, onset of disease ≤10 days prior, and at risk for progression to critical COVID-19

-Unlikely to be helpful for infants with bronchiolitis or croup due to COVID-19</td><td>
<table>
<tr><th>Body Weight</th><th>Loading dose
(Day 1)</th><th>Maintenance dose
(from Day 2)</th></tr>
<tr><td>1.5 to <3 kg</td><td>2.5mg/kg x 1</td><td>1.25mg/kg/dose on days 2-5</td></tr>
<tr><td>3kg to < 40 kg</td><td>5mg/kg IV x1</td><td>2.5mg/kg IV daily for days 2-5</td></tr>
<tr><td>≥ 40 kg and adults</td><td>200mg IV x1</td><td>100mg IV daily for days 2-5</td></tr>
</table>

Duration of therapy: 5 days or until patient is discharged. For patients otherwise ready to discharge, do not delay discharge to complete remdesivir course.
Can consider extending treatment to 10 days in patients who are immuncompromised or severely ill
Use caution in patients with eGFR <30mL/minute
Baseline LFTs, creatinine, and coags are recommended prior to initiation of treatment; follow LFTs while on treatment

</td></tr>
<tr><td>Corticosteroids</td><td>Eligibility:
-Hospitalized children with COVID-19 who are requiring oxygen through high-flow device, non-invasive or invasive ventilation

-Most likely to benefit patients ≥12 years</td><td>
<table>
<tr><th>Agent</th><th>Dosing</th><th>Maximum Dose</th></tr>
<tr><td>Dexamethasone
(preferred)</td><td>0.15m/kg IV/PO daily</td><td>6mg</td></tr>
<tr><td>Alternatives with glucocorticoid equivalency to dexamethasone</td><td>Prednisolone/Prednisone
1mg/kg PO/NG daily

Methylprednisolone
0.8mg/kg IV daily</td><td>32 mg</td></tr>
<tr><td>Preterm infants with corrected gestational age of < 40 weeks</td><td>Hydrocortisone 0.5mg/kg every 12 hours for 7 days then 0.5mg/kg daily for 3 days</td><td>-</td></tr>
</table>
Duration of treatment: 10 days or until patent is discharged
</td></tr>
</table>

<table>
<tr><td></td><td></td><td></td></tr>
<tr><td>Tocilizumab

Drug class: IL-6 receptor inhibitor</td><td>Eligibility:
-Available for children ≥2 years old through EUA to treat COVID-19

- Used for patients with acute COVID infection within 24 hours of ICU admission or exhibiting respiratory deterioration with elevated CRP (>7.5mg/dL) and receiving oxygen through high flow nasal cannula or non-invasive or invasive ventilation

-Should be used <u>in combination with steroids</u>

<u>-Needs ID approval</u></td><td><table><tr><th>Body Weight</th><th>Dose</th></tr><tr><td>< 30 kg</td><td>12mg/kg IV x 1</td></tr><tr><td>≥ 30 kg</td><td>8mg/kg IV x 1 (max 800mg)</td></tr></table>
Important notes:
Please provide the Fact Sheet for Patients, Parents, and Caregivers to the family and document in the chart https://www.gene.com/download/pdf/actemra_eua_patient_fact_sheet.pdf
Send quantiferon Gold and Hepatitis B serologies (unless vaccinated previously) prior to initiation of treatment (do not need to wait for results before starting)
Daily CBC, CMP recommended while receiving this treatment
Should not administer this treatment if any live attenuated vaccine given within the last 2 weeks
See table below for adverse reactions</td></tr>
<tr><td>Baricitinib

Drug class: Janus Kinase (JAK) inhibitor</td><td>Eligibility:
-Available for children ≥2 years old through EUA to treat COVID-19

- Used for patients with acute COVID infection within 24 hours of ICU admission or exhibiting respiratory deterioration with elevated CRP (>7.5mg/dL) and receiving oxygen through high flow nasal cannula or non-invasive or invasive ventilation

-Should be used <u>in combination with steroids</u>

- <u>Needs ID approval</u></td><td><table><tr><th>Age</th><th>Dosing</th><th>Duration</th></tr><tr><td>2 yo to <9yo</td><td>2 mg by mouth once daily</td><td>14 days or until hospital discharge (whichever comes first)</td></tr><tr><td>Adults and pediatric patients ≥ 9yo</td><td>4 mg by mouth once daily</td><td>14 days or until hospital discharge (whichever comes first)</td></tr></table>
Important notes:
Please provide the Fact Sheet for Patients, Parents, and Caregivers to the family and document in the chart https://www.fda.gov/media/143824/download
Send quantiferon Gold and Hepatitis B serologies (unless vaccinated previously) prior to initiation of treatment (do not need to wait for results before starting)
Daily CBC, CMP recommended while receiving this treatment (discuss with ID if lymphopenic, neutropenic, elevated LFTs, liver synthetic dysfunction, or renal dysfunction)
Should not administer this treatment if any live attenuated vaccine given within the last 2 weeks
See table below for adverse reactions (NOTE: Increased risk of thrombosis)
Available as tablets but can be manipulated (dispersed in water)</td></tr>
</table>

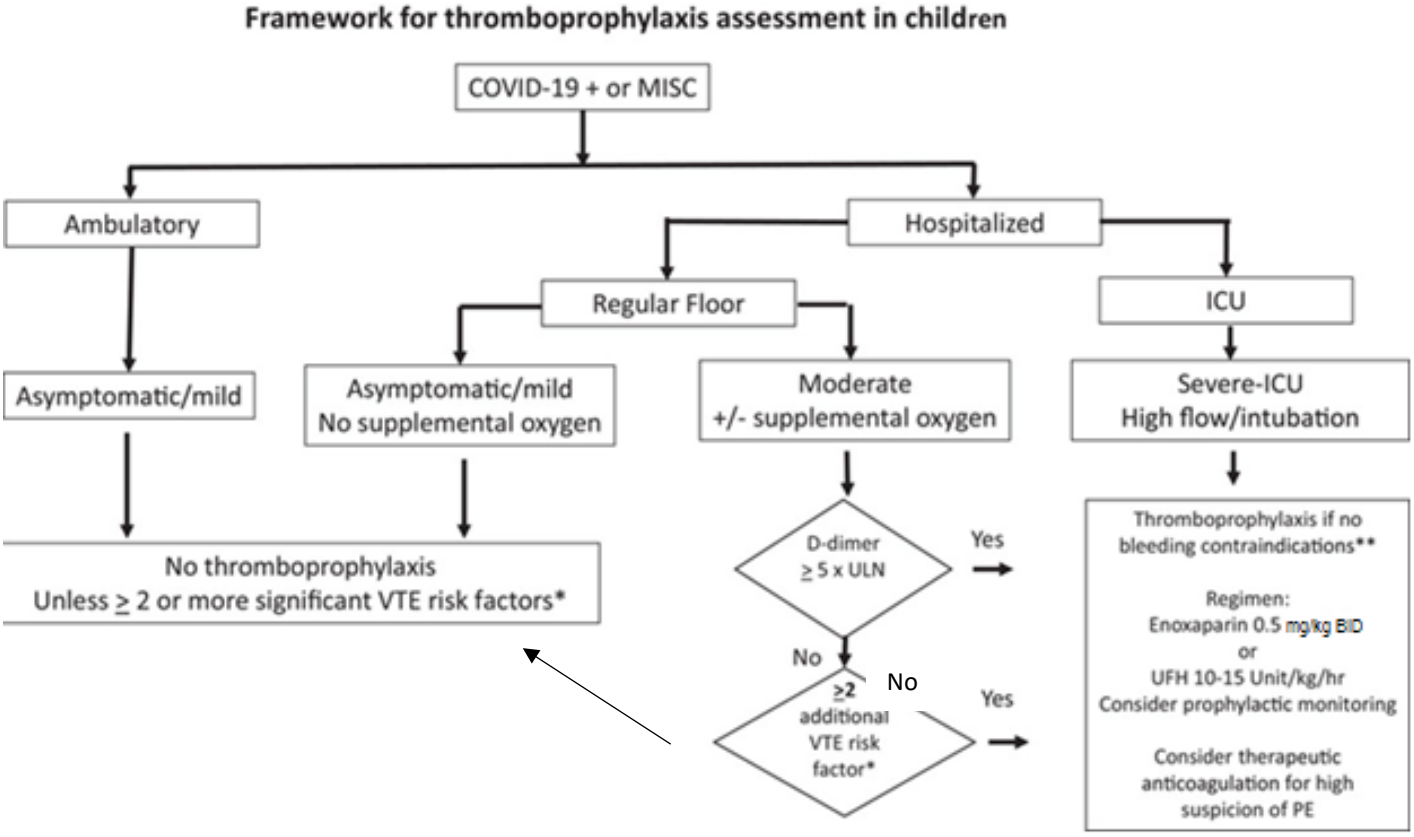
Anticoagulation

Recommended

- refer to treating provider to assess for therapeutic appropriateness and safety of anticoagulation
- COVID-19 (+) patients should routinely be monitored for risk of thrombosis

Anticoagulation guidelines for COVID-19 and MIS-C.

Adapted from Sharathkumar et al. Pediatr Blood Cancer. 2021 Jul; 68(7).



Recommendations for anticoagulation:	
Non-PICU admission	Recommend no thromboprophylaxis unless: 1. Patient requiring oxygen AND D dimer ≥ 5 times the upper limit of normal OR 2. ≥2 additional venous thromboembolism (VTE) risk factors: MIS-C, age ≥12 years, obesity, complete immobilization, central line, estrogen therapy, family history of VTE In which case **prophylactic** management with **enoxaparin or unfractionated heparin** (UH) should be used.
PICU admission	Recommend **prophylactic** management with **enoxaparin or unfractionated heparin** for all COVID-19 patients unless otherwise contraindicated (platelet count <50,000, fibrinogen <100mg/dL, major bleeding). Consider hematology consult but do not delay initiation of anticoagulation. • Once patient is stable for transfer to ward, can usually be discontinued unless they meet any of the criteria listed above (for non-PICU admission).

Hematology consult	• Rapidly increasing D-dimers • History of VTE • Patients with significant underlying medical conditions (i.e., malignancy, sickle cell disease or other hemoglobinopathy, cardiac disease, nephrotic syndrome, CF, autoimmune disease)Patients with suspected or confirmed venous thrombo-embolism or pulmonary embolus
Discharge recommendations	• Consider stopping anticoagulation at time of discharge unless patient has known thrombus, central line, D dimer remains ≥ 5 times the upper limit of normal, or other medical conditions. In those situations, **please consult with pediatric hematology and arrange for outpatient follow up if recommended**. May need an additional 1-2 week course of anticoagulation, or until risk factors no longer present.
* For patients who do not meet requirements or are contraindicated for use with enoxaparin or UH, consider early ambulation and/or the use of sequential compression devices. *If patients were previously on prophylactic dosing of enoxaparin or UH, they should be increased to treatment dosing *For initiation of heparin in COVID-19 patients, consult hematology and pharmacy to dose.	

Enoxaparin (Lovenox)	
Prophylactic Dosing	• 1 to < 2 months: 0.75mg/kg SQ every 12 hours • ³ 2 months: 0.5mg/kg SQ every 12 hours • Crcl < 30ml/min: 0.5mg/kg SQ every 24 hours or consider using heparin
Monitoring	CBC, serum creatinine, LMWH Anti-xa assay Enoxaparin target peak levels (drawn 4-6 hours post second dose): • Prophylaxis: 0.1 - 0.3 units/mL (Treatment: 0.5 to 1 units/mL)
Caution/contraindications	• Hypersensitivity to enoxaparin • Active bleeding, major surgery, trauma • History of heparin Induced Thrombocytopenia/Thrombosis (HITT)
Black Box Warning	• Spinal/epidural hematoma may occur in patients receiving enoxaparin and neuraxial anesthesia or undergoing spinal puncture

Anti-infective Agent	Monitoring parameters & clinical pearls
Remdesivir	Adverse Events: • **Hepatic function:** Self-limiting, reversible hepatotoxicity has been observed, which resolved after therapy cessation. Hepatic laboratory testing should be performed in all patients at baseline and routinely. No dose adjustments are provided. Discontinue therapy if ALT increases > 10x ULN. May resume therapy when ALT is < 5x ULN. • **Renal function:** Remdesivir is not recommended in adult and pediatric patients (greater than 28 days old) with eGFR less than 30 mL/min or in full-term neonates (at least 7 days to less than or equal to 28 days old) with serum creatinine greater than or equal to 1 mg/dL unless the potential benefit outweighs the potential risk. Remdesivir contains excipient sulfobutylether-beta-cyclodextrin sodium salt (SBECD) which may accumulate in renal impairment. However, SBECD is readily removed by hemodialysis and renal replacement therapies. Remdesivir should not be withheld in renal impairment given the clinical insignificance of SBECD in a short course of therapy. Metabolism: Remdesivir is a prodrug metabolized via CYP3A4, concomitant CYP3A4 inhibitors should be avoided if possible.
Corticosteroids	Adverse Events: • Hyperglycemia • Secondary infections • Reactivation of latent infections • Psychiatric disturbances • Adrenal insufficiency • Increased blood pressure • Peripheral edema Monitoring: Blood glucose, blood pressure, signs and symptoms of new infection
Monoclonal antibodies	Adverse Events/Monitoring: • Potential for severe hypersensitivity reaction including **anaphylaxis.** Discontinue medication immediately and provide supportive medications. • Infusion related reactions fever, chills, nausea, hypotension, angioedema, pruritus, rash, myalgia can occur. • If a patient experiences an adverse effect, please report to FDA Medwatch, instructions for doing so can be found at the following link.
Baricitinib	Black box warning: Serious infections, malignancy, thrombosis Adverse Events/Monitoring: • GI perforations • Hematologic toxicity, do not initiate in patients with an absolute lymphocyte count < 500 cells/mm^3, ANC < 1000 cells/mm^3, or hemoglobin < 8 g/dL • Hepatic effects – elevated liver enzymes. Monitor LFTs at baseline and periodically • Hypersensitivity • Lipid abnormalities
Tocilizumab	Black box warning: serious infections (ex. tuberculosis, invasive fungal infections, opportunistic pathogens) Adverse events/monitoring: • GI perforation • Malignancy • Hematologic effects (neutropenia, thrombocytopenia) • Hepatic injury (use with caution in pateints with hepatic impairment) • Hyperlipidemia • Hypersensitivity

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