

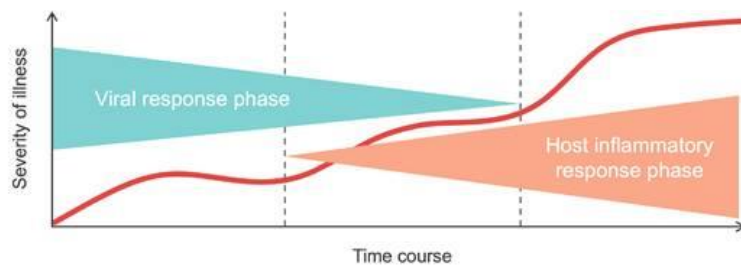
# COVID-19 Pathway v12.0: Table of Contents

**Stop and Review**

## Inclusion Criteria

- Suspected COVID-19 acute infection
- OR
- Fever AND critically ill
- OR
- Persistent fever  $\geq 3$ d AND ill-appearing AND concern for MIS-C
- OR
- Persistent unexplained fever  $\geq 5$  days

## COVID-19 (Acute COVID and MIS-C) Care



The features of acute COVID infection complicated by hyperinflammation and MIS-C may overlap; consider time course and clinical scenario and refer to both MIS-C and acute COVID algorithm as needed  
Adapted from Siddiqi, H.K. and Mehra, M.R. 2020.

**Vaccination**

**Acute COVID**

**MIS-C**

**Anticoagulation in COVID-19 and MIS-C**

**Differential Diagnoses**

**Definitions of Organ System Involvement**

**Resources**

## Appendix

**Version Changes**

**Approval & Citation**

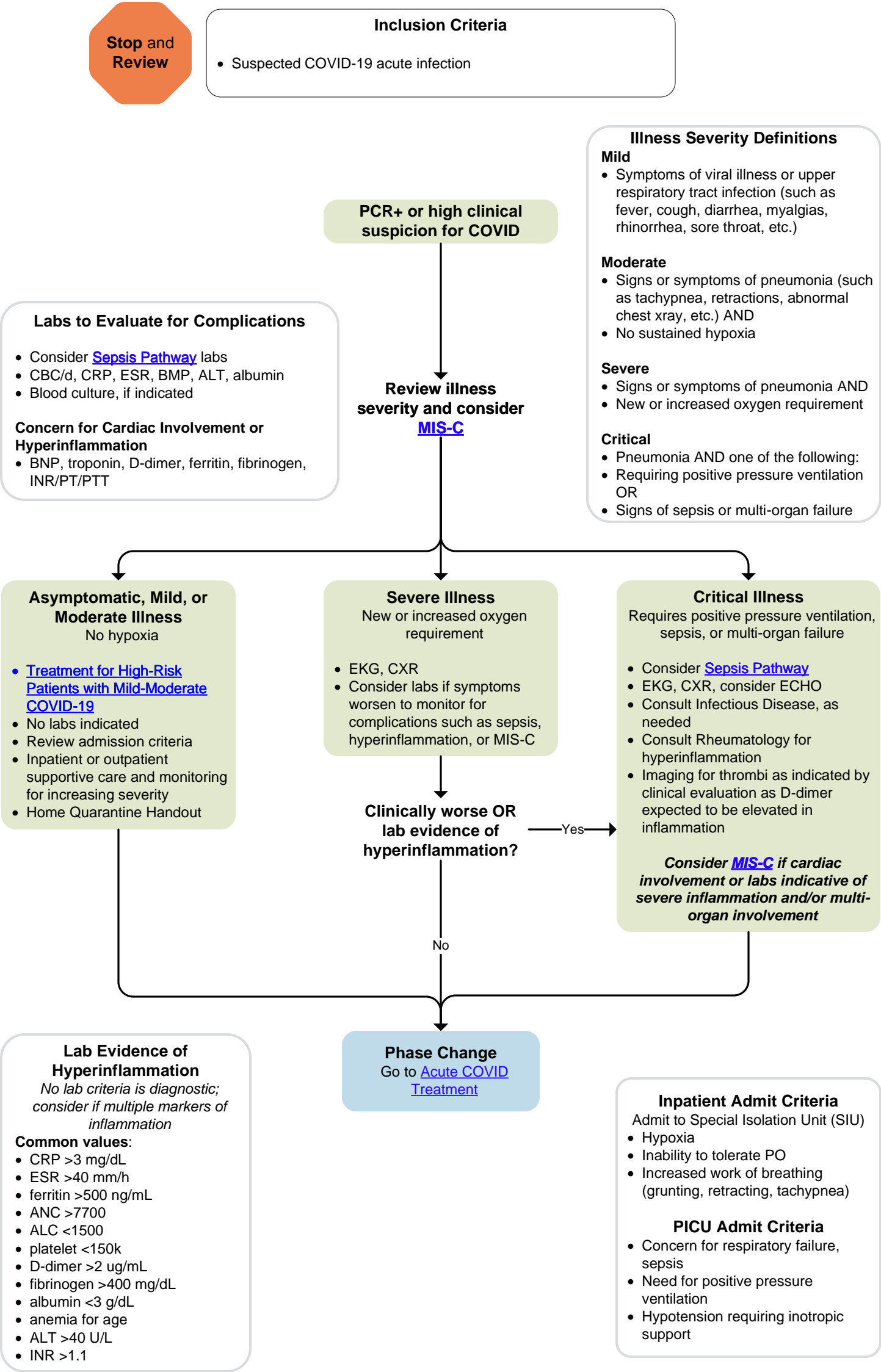
**Evidence Ratings**

**Bibliography**

# COVID-19 Pathway v12.0: Vaccination

- COVID-19 vaccination is recommended for all patients and family members. Contraindications include age <6 months, current COVID-19 infection or MIS-C, severe allergy to vaccine component, or receipt of COVID-19 monoclonal antibody product within 90 days.
- Outpatients or family members may schedule now through the [Seattle Children's public portal](#).
- Inpatient care teams may email [PatientCOVIDVaccine@seattlechildrens.org](mailto:PatientCOVIDVaccine@seattlechildrens.org) with the subject line: Inpatient Vaccination Request.
- Vaccine post-MIS-C: CDC and AAP recommend patients with a history of MIS-C should consider delaying vaccination until after they have recovered from illness (including return to normal cardiac function) and for at least 90 days following their diagnosis of MIS-C. Currently, there are limited data about the safety and efficacy of COVID-19 vaccine in patients with a history of MIS-C. Pediatricians and patients/families should participate in shared decision making in weighing risks and benefits of COVID-19 vaccination for each individual patient.

# COVID-19 Pathway v12.0: Acute COVID



# COVID-19 Pathway v12.0: Acute COVID Treatment

Acute COVID illness severity	Antiviral Medications	Immunomodulator Medications	Anticoagulation
<b>Mild disease attributable to COVID-19 with no new/increased O2 required (either outpatient or hospitalized for other cause)</b>	Low risk patients: none. Severe immunocompromise or high-risk condition (link to mild mod page): <ul style="list-style-type: none"> <li>≥ 12 years and ≥ 40 kg, consider nirmatrelvir-ritonavir (Paxlovid™)</li> <li>Unable to receive Paxlovid: consider IV <a href="#">remdesivir</a> (3-day course)</li> <li>Outpatients requesting remdesivir or <a href="#">monoclonal abs</a> need to submit intake form</li> </ul>	None (unless indicated for another condition)	None (unless indicated for another condition)
<b>On low-flow oxygen (or increased supplemental oxygen) attributable to COVID-19 lower respiratory tract disease (excluding bronchiolitis or asthma)</b>	Recommend <a href="#">remdesivir</a> , especially for adolescents or with symptom onset <7 days	Consider dexamethasone for patients with increasing oxygen needs, particularly adolescents	SCDs and low-dose LMWH for age ≥12 or any other risk factors (link) if no contraindications
<b>Requires NIV or HFNC attributable to COVID-19 lower respiratory tract disease</b>	Consider <a href="#">remdesivir</a> , especially for adolescents or with symptom onset <7 days	Dexamethasone recommended. Consider baricitinib or tocilizumab* for children who do not have rapid (e.g., within 24 hours) improvement in oxygenation after initiation of dexamethasone, consider baricitinib or tocilizumab*	SCDs and low-dose LMWH for age ≥12 or any other risk factors (link) if no contraindications
<b>Requires invasive mechanical ventilation or ECMO attributable to COVID-19 lower respiratory tract disease</b>	<a href="#">Remdesivir</a> not routinely recommended; may be considered case-by-case	Dexamethasone recommended. Consider baricitinib or tocilizumab* for children who do not have rapid (e.g., within 24 hours) improvement in oxygenation after initiation of dexamethasone, consider baricitinib or tocilizumab*	SCDs and low-dose LMWH (link) if no contraindications

Adapted from NIH COVID Guidelines Recommendations for the Therapeutic Management of Children. Accessed April 10, 2023.

\*Baricitinib or Tocilizumab use is based on recommendations from NIH, WHO, and Australian COVID taskforce. Studies showed a reduction in mortality in critically ill adults; there have been no randomized trials including pediatric patients with COVID. These medications may be difficult to obtain at SCH; discuss with pharmacist as soon as possible.

# COVID-19 Pathway v12.0: Acute COVID Discharge Instructions

## Discharge Instructions

### Isolation:

- Determine length of isolation and need for repeat testing based on severity of illness, first positive PCR or onset of illness, and immunosuppression (patients receiving steroids are considered immunosuppressed by IP) using Infection Prevention Guidance document (*for SCH only*).
- Advise family, PCP, and followup providers of end date of isolation and, if immunosuppressed, that repeat PCR x2 after 20 days of isolation is needed to end healthcare facility-based isolation (it should not be needed to end home isolation).
- Please obtain repeat PCR if result may clear patient from healthcare facility-based isolation (ex: if immunosuppressed and 20 days have passed since first positive PCR).

### Return to sports or exercise:

- **Children with asymptomatic/mild illness:** PCP evaluation after isolation period.
- **Children with moderate/severe illness (prolonged fever or hospitalized):** PCP evaluation and an ECG after symptom resolution and after isolation.
- **Children with critical illness/MIS-C:** No strenuous exercise for least three to six months and obtain cardiology clearance prior to resuming training or competition (refer prior to discharge).

# COVID-19 Pathway v12.0: Early Treatment for high-risk patients with mild-moderate COVID-19: Antiviral Medications and Monoclonal Antibodies, page 1

**Background:** FDA Emergency Use Authorizations (EUA) allow for the use of monoclonal antibody products and oral antivirals for early treatment of mild-moderate COVID-19 in high-risk patients  $\geq 12$  years of age and 40 kg. Efficacy of monoclonal antibodies varies with current circulating SARS-CoV-2 variants. In addition, the FDA has approved IV remdesivir x 3 daily doses for high-risk children of all ages for this indication. Oral antivirals are now readily available at SCH as well as at community pharmacies.

**Guidance statement:** Based on accumulated evidence, we suggest against routine administration of these treatments for COVID-19 in most children or adolescents. Rather, their use should be considered on a case-by-case basis for patients at high risk of progression to severe disease. Oral antiviral therapy (nirmatrelvir/ritonavir) is preferred option for high-risk patients who are able to receive it (see criteria below).

**Rationale:** There are limited safety or efficacy data for these products in children. Based on our experience both internally and around the globe, children in general have lower risk of progression to severe disease and poor outcomes. In addition, clear risk factor stratification data is limited. Finally, supplies of these products or infusion capacity are often limited.

## Eligibility criteria:

1. Severe immunocompromise, severe obesity (BMI  $\geq 35$  or 95<sup>th</sup>ile), medical complexity WITH respiratory technology dependence OR.
2. MULTIPLE moderate risk factors (diabetes, other immunocompromise, sickle cell disease, obesity (BMI  $\geq 25$  or 85<sup>th</sup>ile), other medical complexity, chronic cardiac, respiratory or kidney disease).
3. All currently available products except remdesivir require children to be at least 12 years of age and weigh at least 40 kg.

## Exclusion criteria:

Hospitalization for COVID-19, supplemental O2 requirements for COVID-19, infection  $>7$  days.

[Return to Acute COVID](#)

# COVID-19 Pathway v12.0: Early Treatment for high-risk patients with mild-moderate COVID-19: Antiviral Medications and Monoclonal Antibodies, page 2

## Procedure for obtaining therapy:

1. Oral Paxlovid (nirmatrelvir/ritonavir): for patients  $\geq 12$  years AND 40 kg: COVID Therapeutics Committee approval is NOT required for high-risk outpatients who meet eligibility criteria above and are within 5 days from beginning of infection (first symptoms or positive test). Paxlovid can be prescribed at SCH or at community pharmacies. Please refer to SCH formulary and [FDA EUA provider fact sheet](#) for prescribing information.
  - a. Providers should verify possible drug interactions before prescribing Paxlovid on this site or with a pharmacist: <https://www.covid19-druginteractions.org/checker>.
  - b. Paxlovid availability in the community can be checked on this site: <https://covid-19-therapeutics-locator-dhhs.hub.arcgis.com/>
2. IV remdesivir (3 day course):
  - a. For outpatients: Please submit the Intake form for approval for remdesivir therapy for outpatients including ED patients who will be discharged. Referring providers will be responsible for arranging with assistance from Infusion Center APP team.
  - b. For inpatients (including ED patients who are likely to be admitted): Committee approval is NOT required for high-risk patients who meet eligibility criteria above and have no exclusion criteria. Please follow dosing per Seattle Children's Hospital formulary.
3. Monoclonal antibody therapy (when available): COVID Therapeutics Committee approval is required. Please submit Intake form for patients who meet eligibility criteria. In times of limited availability, monoclonal antibody therapy will be prioritized for those who are incompletely vaccinated or unlikely to respond to vaccination. Referring providers will be responsible for arranging infusion with assistance from Infusion Center APP team.

SCH Providers who would like their patient considered for Monoclonal Antibody therapy or outpatient IV remdesivir should submit Intake form.

Community providers can call SCH Infectious Disease on call or email:  
[COVIDmab@seattlechildrens.org](mailto:COVIDmab@seattlechildrens.org)

[Return to Acute COVID](#)



# COVID-19 Pathway v12.0: MIS-C

**Stop and Review**

!

Consider differential diagnosis including acute COVID

## Inclusion Criteria

- Fever AND critically ill
- OR
- Persistent fever  $\geq 3$ d AND ill-appearing AND concern for MIS-C
- OR
- Persistent unexplained fever  $\geq 5$  days

## MIS-C Case Definitions

- [CDC](#)
- [WHO](#)

## Clinical Features/Evidence of MIS-C

- Most patients have  $\geq 4$  organ system involvement;  $\geq 2$  required for diagnosis
- Involvement of following systems (percent of patients in case series):
  - Gastrointestinal (92%)
  - Cardiovascular (80%)
  - Hematologic (76%)
  - Mucocutaneous (74%, 59% had rash)
  - Respiratory (70%)
  - Musculoskeletal (23%)
  - Renal (8%)
  - Neurologic (6%)
  - See [definitions](#) of organ system involvement
- Recent COVID illness OR exposure (note: not necessary to suspect MIS-C)

## Lab Evidence of MIS-C

No lab criteria is diagnostic; most patients have 4 or more markers of inflammation

- **Evidence of inflammation, common values:** CRP  $>3$  mg/dL, ESR  $>40$  mm/h, ferritin  $>500$  ng/mL, ANC  $>7700$ , ALC  $<1500$ , platelet  $<150k$ , D-dimer  $>2$  ug/mL, fibrinogen  $>400$  mg/dL, albumin  $<3$  g/dL, anemia, ALT  $>40$  U/L, INR  $>1.1$
- **Other:** AKI, hyponatremia, high LDH, high troponin, BNP  $>400$  pg/mL, prolonged PT or PTT; If ESR low but high ferritin and CRP, consider MAS

Percentages and values adapted from NEJM Feldstein et al. June 2020.

## Signs of Shock?

Yes

No

- Obtain **Initial Labs**  
If high clinical suspicion, add **Additional Labs**
- CXR (if resp sx)

- Obtain **Initial and Additional Labs**, EKG, CXR
- ECHO (early if signs of cardiac dysfunction)
- Consider [Sepsis Pathway](#)  
Caution with boluses; monitor for cardiac dysfunction

## Lab Evidence of MIS-C?

Yes

No

- Consider alternate diagnoses
- Consider discharge with close follow-up

- Obtain **Additional Labs**
- EKG
- Contact Cardiology to discuss necessity/timing of Echo

## Complete or Incomplete Kawasaki?

Yes

No

- Follow [Kawasaki Disease Pathway](#) if COVID testing negative or while pending
- Monitor closely for signs of shock

## Evidence of MIS-C without alternate diagnosis?

Yes

PCR or IgG+ with recent exposure/ infection OR cardiac dysfunction

**Phase Change**  
Go to [MIS-C Treatment](#)

## Inpatient Admit Criteria

- Admit to Special Isolation Unit (SIU)
- Suspected MIS-C (review case definition "clinically severe illness")

## PICU Admit Criteria

- Altered mental status
- Concern for respiratory failure, sepsis
- Need for positive pressure ventilation
- Hypotension or shock

!

**Patients with MIS-C have significant risk for developing shock**



# COVID-19 Pathway v12.0: MIS-C Treatment

**Review case definition:** age <21, >24h fever, lab evidence of inflammation (most patients have 4 or more markers), multi-system involvement, and clinically seriously ill, without alternative diagnosis (review [differential diagnosis](#)) plus confirmed recent SARS-CoV-2 or known exposure within 6 weeks. (For age >21 see NIH Guidelines for adults)

- ECHO if not already done; repeat as indicated
- Antibiotics per Sepsis Pathway only if and while bacterial infection suspected
- Consider supportive care only for patients who have mild\* illness; monitor for increasing severity until clearly improving
- Consult Infectious Disease, Cardiology, and Rheumatology as needed to support primary team diagnostic or therapeutic decision making

## First-line treatment for all seriously\*\* ill patients with MIS-C:

- IVIG 2 g/kg (use ideal body weight, max dose 100g) over 12 hours
- Anti-platelet: ASA 3-5 mg/kg (max of 81 mg) due to risk of developing coronary aneurysms, hold ASA if Plt <50 k
- Mechanical thromboprophylaxis with SCDs if possible
- Anticoagulation prophylaxis is usually indicated: see [anticoagulation page](#)
- Steroids are indicated for most seriously ill patients with MIS-C; consider short course (3-5 days) for patients who are not critically ill and improve rapidly, or wean over 2-3 weeks
  - Methylprednisolone 1-2 mg/kg/day divided BID (max dose 30mg BID for low/mod dose), PO route when tolerating diet
  - Consider higher dose steroids (methylprednisolone 10mg/kg/day) for patients who are worsening despite treatment, or with moderately or severely depressed cardiac function, in consultation with Heart Failure team and Rheumatology
  - Start H2 blocker for GI ulcer prophylaxis while on both steroids and ASA

**Second-line:** Anakinra if not improving post steroid initiation or if labs suggestive of MAS

- 4 mg/kg/dose q6 hours (or frequency per Rheumatology), max dose 100 mg/dose

Trend CBCd, CRP, LDH, ALT, Albumin, Ferritin, Creatinine, Lytes, D-Dimer, Fibrinogen and BNP (frequency dependent on clinical status and medication weaning; post-discharge labs per consultants)

*Classification of illness severity is not well defined. Consider:*

*\*Mild: Normal vital signs apart from fever, does not meet inpatient criteria other than poor PO, mild dehydration, or monitoring for worsening.*

*\*\*Serious: Definitively meets case definition and any of: ill-appearing, evidence of organ dysfunction/injury, require for respiratory or cardiovascular support.*

## Discharge Instructions

### Isolation

- Determine length of isolation and need for repeat testing based on severity of illness, first positive PCR or onset of illness, and immunosuppression (patients receiving steroids are considered immunosuppressed by IP) using Infection Prevention Guidance document (*for SCH only*).
- Advise family, PCP, and followup providers of end date of isolation and, if immunosuppressed, that repeat PCR x2 after 20 days of isolation is needed to end healthcare facility-based isolation (it should not be needed to end home isolation).
- Please obtain repeat PCR if result may clear patient from healthcare facility-based isolation (ex: if immunosuppressed and 20 days have passed since first positive PCR).
- Avoid NSAIDs while on aspirin.

### Return to sports or exercise

- **Children with asymptomatic/mild illness:** PCP evaluation after isolation period.
- **Children with moderate/severe illness (prolonged fever or hospitalized):** PCP evaluation and an ECG after symptom resolution and after isolation.
- **Children with critical illness/MIS-C:** No strenuous exercise for least three to six months and obtain cardiology clearance prior to resuming training or competition (refer prior to discharge).

## Treatment of Mild-Moderate COVID-19 References

FDA EUA for nirmatrelvir/ritonavir (Paxlovid) (28 June 2022): [Paxlovid HCP FS 06282022 \(fda.gov\)](#)

FDA EUA for bebtelovimab (17 May 2022): [Bebtelovimab Patient Fact Sheet \(fda.gov\)](#) Gottlieb RL, Vaca CE, Paredes R et al. Early Remdesivir to Prevent Progression to Severe Covid-19 in Outpatients. NEJM 2022 Jan 27. 386(4);305-315

NIH COVID-19 Treatment Guidelines (8 April 2022): [Nonhospitalized Adults: Therapeutic Management | COVID-19 Treatment Guidelines \(nih.gov\)](#)

NIH COVID-19 Guidelines (13 May 2022): [Prioritization of Therapeutics | COVID-19 Treatment Guidelines \(nih.gov\)](#)

NIH Pediatric specific guidance (24 Feb 2022): [Children | COVID-19 Treatment Guidelines \(nih.gov\)](#)

Wolf, J., Abzug, M., Anosike, B., Vora, S., et al. J Pediatric Infect Dis Soc. 2022 February 2, piab124: [Updated Guidance on Use of Monoclonal Antibody Therapy for Treatment of COVID-19 Adolescents](#)

**Return to Acute COVID  
Treatment**

# Remdesivir Evidence Summary

**Remdesivir evidence summary adapted from NIH COVID treatment guidelines. Accessed April 2023.**

Remdesivir is approved by the Food and Drug Administration (FDA) for hospitalized and non-hospitalized pediatric patients aged  $\geq 28$  days and weighing  $\geq 3$  kg. If decision is made to treat, remdesivir should be administered for 5 days or until the patient is ready for discharge, whichever comes first. Treatment may be extended to 10 days for severely ill patients who have not clinically improved or for patients who are severely immunocompromised. When used as early treatment to prevent severe disease in high-risk patients, it is given for a 3-day course.

The efficacy of remdesivir has not been evaluated in clinical trials of hospitalized children with COVID-19. The level of evidence for the recommendation to use remdesivir in pediatric patients is all expert opinion, based on evidence in adult patients and safety and tolerability studies in children. There have been multiple trials evaluating the efficacy in adults, summarized below.

- In the ACTT-1 RCT for hospitalized adults with COVID-19 the remdesivir arm had a shorter time to clinical recovery than the placebo arm (10 days vs. 15 days) for adult patients who required oxygen therapy.
- The World Health Organization's Solidarity trial reported for adult patients receiving supplemental oxygen but not NIV or mechanical ventilation, remdesivir significantly reduced the risk of in-hospital mortality by 13% (14.6% vs. 16.3%).
- The CATCO study demonstrated remdesivir reduced the need for mechanical ventilation in hospitalized adults with COVID-19 (8% vs. 15%; relative risk 0.53; 95% CI, 0.38–0.75).
- In contrast to these 2 studies, the DisCoVeRy trial demonstrated no difference for any clinical outcome when the use of remdesivir plus usual care was compared to usual care alone.

**Return to Acute COVID  
Treatment**

# Anticoagulation in COVID-19 and MIS-C

Patients with severe or critical acute COVID infection or MIS-C are likely at higher risk for thrombosis and therefore should be considered for anticoagulation; review criteria to determine if they require low dose or therapeutic dosing. Also use mechanical thromboprophylaxis with SCDs if possible.

- Relative contraindications to anticoagulation include active major bleeding, platelet level <50,000, and fibrinogen <100mg/dL.
- Discontinue prophylactic anticoagulation at discharge or earlier if patients are improved and risk factors resolved; consider continuation post-discharge for ongoing severe inflammation with other risk factors.
- Consult Hematology for documented thrombosis or as indicated for recommendations in unusual circumstances.
- Asymptomatic, mild, or moderate COVID is not an indication for anticoagulation, use standard indications.

## Indications for low dose anticoagulation (LMWH goal=0.2-0.4units/mL or UFH goal=0.1-0.3units/mL):

Hospitalized with MIS-C or severe/critical COVID-19

AND one or more of the following risk factors:

- D-dimer >2.5 mcg/mL
- Age >12 years or post-pubertal
- Obesity (>95th %ile)
- Concomitant estrogen-containing oral contraceptive use
- First degree family history of unprovoked VTE
- History of thrombosis or acquired or inherited thrombophilia
- Central venous catheter
- Any rhythm abnormalities: heart block, etc.
- Inotropic infusion requirement
- Sedated and muscle-relaxed or complete immobility
- Active malignancy, nephrotic syndrome, flare of underlying inflammatory disease state, sickle cell VOC
- Congenital or acquired heart disease with venous stasis or impaired venous return

## Indications for therapeutic anticoagulation (LMWH goal=0.5-1units/mL or UFH goal=0.3-0.6units/mL):

Hospitalized with MIS-C or severe/critical COVID-19

AND One or more of the following:

- Documented thrombosis (also consult Hematology)
- Moderate to severe ventricular dysfunction per Cardiology
- Coronary aneurysm Z score >10
- **Consider therapeutic anticoagulation for active malignancy, nephrotic syndrome, flare of underlying inflammatory disease state, heart disease with venous stasis or impaired venous return, personal history of thrombosis, or multiple risk factors – discuss indications with specialist managing underlying condition and/or hematology**

Continue therapeutic dosing while indicated and formulate outpatient plan with consultants

Adapted from Goldenberg et al. 2020

[Return to MIS-C Treatment](#)

## Differential Diagnoses

### Kawasaki Disease

- More common in younger children, if COVID testing negative, and without shock/cardiac dysfunction
- SARS-CoV-2 antibody can remain positive for months after infection and does not necessarily indicate recent infection

### Bacterial Infections/Sepsis

- Obtain cultures and evaluate for source
- Consider meningitis

### Staph/Strep Toxin-Mediated or Post-Infectious

- Consider Toxic Shock or Acute Rheumatic Fever
- Obtain cultures and evaluate for source including gynecologic or scarlet fever

### Staph Scalded Skin Syndrome (SSSS)

- Increasing erythema and bullae
- Younger children
- Obtain cultures

### Tick-Borne Illnesses

- With epidemiologic risk factors
- Rocky Mountain Spotted Fever or Leptospirosis

### Viral Infections

- Measles, adenovirus, enterovirus, active COVID infection

### Myocarditis

- May overlap with MIS-C or have alternate cause

### Drug Hypersensitivity Reactions

- Consider SJS, DRESS, or serum sickness like reaction
- History of recent or semi-recent exposure to drug; consider with arthralgias and diffuse mucositis

[Return to MIS-C](#)

[Return to MIS-C  
Treatment](#)

# Definitions of Organ System Involvement

## Gastrointestinal 92%

- Nausea/vomiting
- Diarrhea
- Abdominal pain
- Appendicitis
- Pancreatitis
- Hepatitis
- Gallbladder hydrops or edema

## Cardiovascular 80%

- Hypotension or shock
- Cardiac dysrhythmia or arrhythmia
- Ejection fraction <55%
- Pulmonary edema due to left heart failure
- Coronary artery z score  $\geq 2.5$
- Pericarditis or pericardial effusion or valvulitis
- B-type natriuretic peptide (BNP) >400 pg/mL
- Elevated troponin
- Receipt of vasopressor or vasoactive support
- Receipt of cardiopulmonary resuscitation (CPR)

## Hematologic 76%

- Total white blood cell <4k
- Anemia for age
- Platelet count <150,000 / $\mu$ L
- Deep vein thrombosis
- Pulmonary embolism
- Hemolysis
- Bleeding or prolonged PT/PTT
- Ischemia of an extremity

## Mucocutaneous 74%

- Bilateral conjunctival injection
- Oral mucosal changes
- Rash or skin ulcers
- 'COVID' toes
- Swollen red cracked lips
- Erythema of palms or soles
- Edema of hands or feet
- Periungual (nails) desquamation

## Respiratory 70% (more frequent in teens)

- Receipt of mechanical ventilation or any type of supplemental oxygen (or increased support for patients receiving respiratory support at baseline)
- Severe bronchospasm requiring continuous bronchodilators or
- Pulmonary infiltrates on chest radiograph
- Lower respiratory infection
- Pleural effusion
- Pneumothorax or other signs of barotrauma
- Pulmonary hemorrhage
- Chest-tube or drainage required

## Musculoskeletal 23% (more frequent in teens)

- Arthritis or arthralgia
- Myositis or myalgia

## Renal 8%

- Acute kidney injury with or without dialysis

## Neurologic 6%

- Stroke or acute intracranial hemorrhage
- Seizures
- Encephalitis, aseptic meningitis, or demyelinating disorder
- Altered mental status
- Suspected meningitis with negative culture

Adapted from Feldstein et al. NEJM June 2020

[Return to MIS-C](#)

## Resources (All Languages)

### Information for Parents on Child's Illness and Home Care:

[For parents and guardians: what to do when you or your child gets COVID-19 - King County](#)

[How to care for yourself or others with COVID-19 - King County](#)

### Isolation/Quarantine/Testing:

Isolation vs Quarantine: [Isolation and Quarantine for COVID-19: WA Department of Health](#)

Testing: [COVID-19 testing in King County](#)

### Financial and Other Assistance:

In King County to stay home from work: [Household Assistance Request program – King County](#)

In other counties in WA: [Care Connect Washington: WA Department of Health](#)

### WA State Resources:

List of COVID resources and vaccine locator: [WA State Coronavirus Response \(COVID-19\)](#)

### Vaccine Information:

CDC information: [Key things to Know About COVID-19 Vaccines](#)

Vaccine locator above under WA State Resources



## Summary of Version Changes

- **Version 1.0 (7/9/2020):** Go live.
- **Version 2.0 (8/13/2020):** Removed CK and triglycerides from Labs. Added consult with Cardiology with Echo and added Indications for therapeutic dosing of anticoagulation to Treatment page.
- **Version 3.0 (9/17/2020):** Added Acute COVID algorithm and treatment pages.
- **Version 4.0 (12/21/2020):** Changes include
  - Updated document to the new CSW algorithm template (incl. a Table of Contents)
  - Added illustration of time course highlighting overlap between viral phase and inflammatory phase
  - Acute COVID Tier 1 labs edited to remove D-dimer, LDH, and ferritin; those were moved to Tier 2 due to concern for overuse, guidance added on getting Tier 2 labs for “worsening” cases
  - Added advice on interpreting D-dimer
  - Monoclonal antibody guidance added
  - Updated anticoagulation information: indications for prophylactic and therapeutic dosing as well as contraindications were edited based on Goldenberg et al. 2020.
  - Inpatient and PICU admit criteria added to MIS-C algorithm
  - Steroid wean over “2-3” weeks changed from “minimum 3 weeks” based on ACR guidelines
  - Discharge isolation guidance box added
  - SIU Policies and Guidance page added
  - Bibliography edited to reflect current references
- **Version 5.0 (5/11/2021):** Updated verbiage to reflect appropriate consultation for Acute COVID treatment, updated policy and job aid links, and added appropriate citations to Monoclonal Antibody Products page and Bibliography.
- **Version 6.0 (7/8/2021):** Changed wording to encourage steroid treatment for critically ill patients with MIS-C and added recommendation for post-discharge sports clearance.
- **Version 7.0 (11/4/2021):** Changes include
  - Added Vaccination tab with information and resources
  - Updated language for Acute COVID Treatment Remdesivir guidance
  - Added NSAID recommendation to MIS-C Treatment Discharge Instructions
  - Updated language and added current FDA EUA references to Monoclonal Antibody Products for Mild-Moderate COVID-19 page
  - Updated the COVID-19 mAb Intake Form
  - Updated Resources page (formerly titled SIU Policies and Guidance) to include Patient and Family Handouts and Website COVID Resources
- **Version 8.0 (12/22/2021):** Changes include
  - Updated language on Monoclonal Antibody Products for Mild-Moderate COVID-19 page
  - Updated references on Monoclonal Antibody Products for Mild-Moderate COVID-19 References page
- **Version 9.0 (1/4/2022):** Changes include
  - Updated language on Monoclonal Antibodies and Antiviral Medications for Mild-Moderate COVID-19 page per new guidelines
  - Updated references on Monoclonal Antibody Products for Mild-Moderate COVID-19 References page

## Summary of Version Changes

- **Version 9.1 (1/25/2022):** Updated link to COVID-19 Monoclonal Antibody and Antiviral Intake Form.
- **Version 10.0 (3/15/2022):** Changes include
  - Added information regarding vaccines post-MIS-C
  - Updated MIS-C treatment consultation recommendation
  - Updated MIS-C first line treatment, adding steroids to first line for most seriously ill patients and including greater specificity for steroid use
  - Updated Monoclonal Antibody Products for Mild-Moderate COVID-19 References with current guidance
  - Added information to Differential Diagnoses page under Kawasaki Disease
- **Version 11.0 (7/20/2022):** Changes include
  - Updated Vaccination guidance to reflect current CDC recommendations
  - Updated Acute COVID-19 Treatment to reflect FDA approval of remdesivir
  - Modified consult recommendations for Acute COVID
  - Changed recommendations and procedures on Early Treatment for High-Risk Patients and integrated them into algorithm format (formerly Monoclonal Antibodies and Antiviral Medications for Mild-Moderate COVID-19)
  - Updated references for Early Treatment for High-Risk Patients
  - Updated links to resources
- **Version 12.0 (7/7/2023):** Changes include
  - Updated labs recommended for Acute COVID
  - Updated Acute COVID Treatment guidance
  - Added evidence summary for remdesivir

## Approval & Citation

Approved by the CSW COVID-19 Pathway team for December 21, 2020, go-live

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GME (Resident), Stakeholder	Sarah Nutman, MD
Cardiology, Stakeholder	Michael Portman, MD
Urgent Care, Stakeholder	Denise Shushan, MD
PICU, Stakeholder	Hector Valdivia, MN, ARNP, ACCNS-P, CCRN
Infectious Disease, Stakeholder	Surabhi (Sara) Vora, MD, MPH
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Librarian	Peggy Cruse, MLIS, Library
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### Clinical Effectiveness Leadership:

Medical Director	Darren Migita, MD
Operations Director	Jaleh Shafii, RN, MS

Retrieval Website: <https://www.seattlechildrens.org/pdf/covid-19-pathway.pdf>

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# Evidence Ratings

This pathway was developed through local consensus based on published evidence and expert opinion as part of Clinical Standard Work at Seattle Children's. Pathway teams include representatives from Medical, Subspecialty, and/or Surgical Services, Nursing, Pharmacy, Clinical Effectiveness, and other services as appropriate.

When possible, we used the GRADE method of rating evidence quality. Evidence is first assessed as to whether it is from randomized trial or cohort studies. The rating is then adjusted in the following manner (from: Guyatt G et al. J Clin Epidemiol. 2011;4:383-94, Hultcrantz M et al. J Clin Epidemiol. 2017;87:4-13.):

Quality ratings are *downgraded* if studies:

- Have serious limitations
- Have inconsistent results
- If evidence does not directly address clinical questions
- If estimates are imprecise OR
- If it is felt that there is substantial publication bias

Quality ratings are *upgraded* if it is felt that:

- The effect size is large
- If studies are designed in a way that confounding would likely underreport the magnitude of the effect OR
- If a dose-response gradient is evident

## Certainty of Evidence

★★★★ High: The authors have a lot of confidence that the true effect is similar to the estimated effect

★★★○ Moderate: The authors believe that the true effect is probably close to the estimated effect

★★○○ Low: The true effect might be markedly different from the estimated effect

★○○○ Very low: The true effect is probably markedly different from the estimated effect

Guideline: Recommendation is from a published guideline that used methodology deemed acceptable by the team

Expert Opinion: Based on available evidence that does not meet GRADE criteria (for example, case-control studies)

# Bibliography

## Literature Search Methods

Both CDC and WHO case definitions were utilized in the development of this pathway. The articles cited are a representation of local and international experts' and national societies' resources that were being shared widely, some pre-publication and many that were published by the centers that were diagnosing and treating this new syndrome as the pandemic swept across the globe.

Due to the rapidly evolving literature and the need for urgent guidance, a non-systematic review was used to guide the development of the initial version of this algorithm.

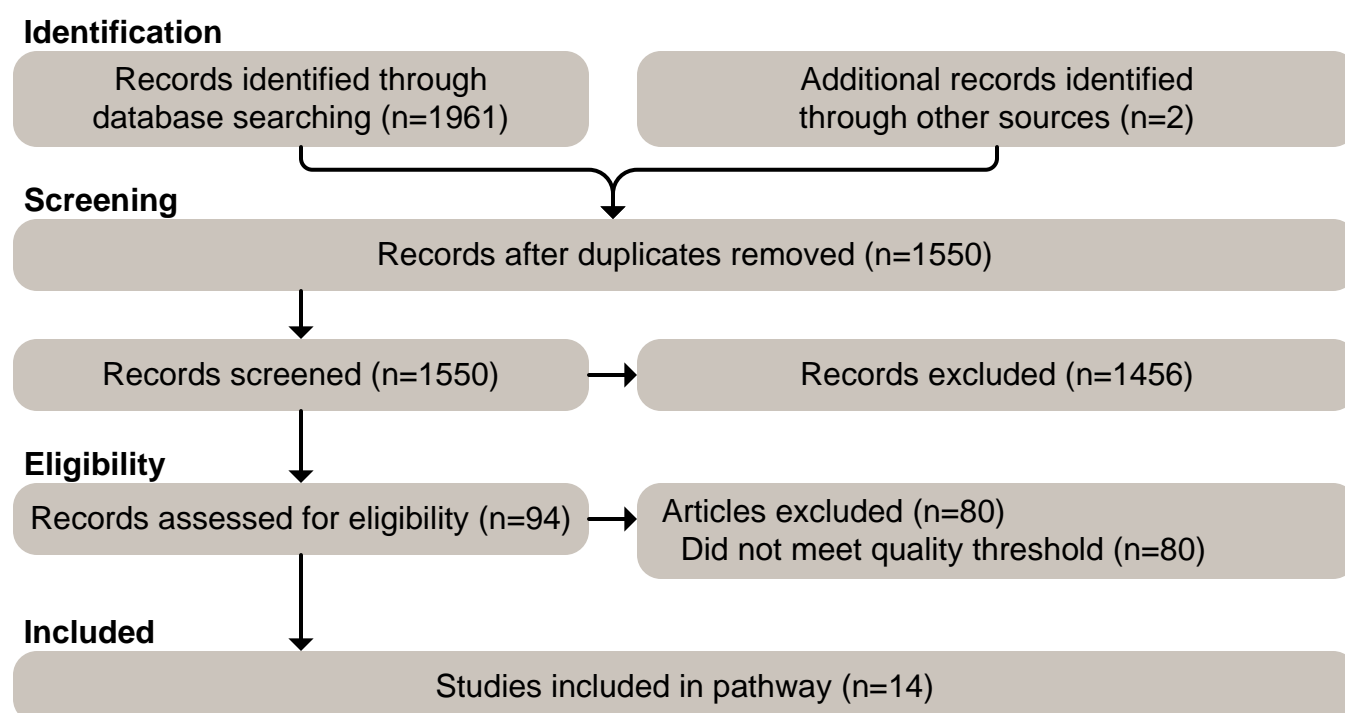
Literature searches were conducted on June 8, 2020 in Ovid Medline, Embase, Cochrane Database of Systematic Review (CDSR), and Turning Research into Practice database (TRIP). The search captured results on COVID-19 or Multisystem Inflammatory Syndrome in Children (MIS-C) or Pediatric Inflammatory Multisystem Syndrome (PIMS). The COVID-19 concept was limited to Synthesis or Expanded study-types, pediatrics, and January 2020 to current. MIS-C/PIMS concept was not limited by study-type but results were limited to April 2020 to current. All items were limited to English language.

Two reviewers independently screened abstracts and included guidelines and systematic reviews that addressed MIS-C and Acute Covid of patients who meet pathway inclusion/exclusion criteria]. One reviewer screened full text and extracted data and a second reviewer quality checked the results. Differences were resolved by consensus.

## Literature Search Results

The search retrieved 1961 records. Once duplicates had been removed, we had a total of 1550 records. We excluded 1173 records based on titles and abstracts. We obtained the full text of the remaining 94 records and excluded 80. We included 14 studies. The flow diagram summarizes the study selection process.

December 2020



Flow diagram adapted from Moher D et al. BMJ 2009;339:bmj.b2535

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## Medical Disclaimer

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The authors have checked with sources believed to be reliable in their efforts to provide information that is complete and generally in accord with the standards accepted at the time of publication.

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