Cincinnati Children's Hospital Medical Center

COVID-19 TREATMENT MANAGEMENT GUIDELINES

Updated May 2023

Origin and Purpose of this Guideline

To assemble experts from within CCHMC to design algorithm(s) to treat patients with COVID-19 based on our current knowledge of the infection. The guidance is designed to facilitate logical decisions regarding all the treatment options in this rapidly evolving epidemic and to offer standardized management. The recommendations in this guidance, however, do not indicate an exclusive course of treatment or serve as a standard of medical care. Variations, considering individual circumstances, may be appropriate.

The FDA continues to update their approvals and recommendations for available therapy. This document outlines the use of treatments approved for COVID-19, approved for other indications (off-label), and treatments that have not been approved for any indication. We anticipate that this document will continue to evolve as new evidence is available supporting the therapies below, or as new therapeutic interventions are identified.

This guideline does not specifically address ICU-based supportive care such as cardio-pulmonary support, renal replacement therapy or fluid therapy. This guideline does not address prevention of COVID-19 in immunocompromised patients with Evusheld (tixagevimab co-packaged with cilgavimab).

Step 1: Assess your patient's risk of progression to severe COVID-19 disease

Table 3b. The Panel's Framework for Assessing the Risk of Progression to Severe COVID-19 Based on Patient Conditions and COVID-19 Vaccination Status

Last Updated: August 8, 2022

Conditions	Risk Level by Vaccination Status[a]		
	Unvaccinated	Primary Series	Up to Date
Strong or Consistent Association With Progression to Severe COVID-19			
• Moderately or severely immunocompromised (see Special Considerations in People Who Are Immunocompromised)	High		
• Obesity (BMI ≥95th percentile for age), especially severe obesity (BMI ≥120% of 95th percentile for age)[b] • Medical complexity with dependence on respiratory technology[c] • Severe neurologic, genetic, metabolic, or other disability that results in impaired airway clearance or limitations in self care or activities of daily living • Severe asthma or other severe chronic lung disease requiring ≥2 inhaled or ≥1 systemic medications daily • Severe congenital or acquired cardiac disease • Multiple moderate to severe chronic diseases	High	Intermediate	
Moderate or Inconsistent Association With Progression to Severe COVID-19			
• Aged <1 year • Prematurity in children aged ≤2 years • Sickle cell disease • Diabetes mellitus (poorly controlled) • Nonsevere cardiac, neurologic, or metabolic disease[d]	Intermediate		
Weak or Unknown Association With Progression to Severe COVID-19			
• Mild asthma • Overweight • Diabetes mellitus (well controlled)	Low		

[a] **Unvaccinated** = individuals who are not eligible for COVID-19 vaccination or are <2 weeks from the final dose of the primary series. **Vaccinated with primary series** = individuals who completed the primary series of 2 or 3 doses (the current CDC term is "fully vaccinated") and are >2 weeks after the final dose of the primary series but have not received a booster, if they are eligible for a booster. Children aged <5 years are not currently eligible for booster doses. **Vaccinated and up to date** = individuals who received the recommended booster dose(s) if eligible or have completed the primary series but are not yet eligible for a booster. See the CDC for more information.

[b] The degree of risk conferred by obesity in younger children is less clear than it is in older adolescents.

[c] Includes tracheostomy or NIV.

[d] Data for this group are particularly limited.

Key: BMI = body mass index; CDC = Centers for Disease Control and Prevention; NIV = noninvasive ventilation; the Panel = the COVID-19 Treatment Guidelines Panel

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• Medical complexity with dependence on respiratory technology[c]	
• Severe neurologic, genetic, metabolic, or other disability that results in impaired airway clearance or limitatio	
• Severe asthma or other severe chronic lung disease requiring ≥2 inhaled or ≥1 systemic medications daily	…mediate
• Severe congenital or acquired cardiac disease	
• Multiple moderate to severe chronic diseases	
Moderate or Inconsistent Association With Progression to Severe COVID-19	
• Aged <1 year	
• Prematurity in children aged ≤2 years	
• Sickle cell disease	
• Diabetes mellitus (poorly controlled)	
• Nonsevere cardiac, neurologic, or metabolic disease[d]	
Weak or Unknown Association With Progression to Severe COVID-19	
• Mild asthma	
• Overweight	
• Diabetes mellitus (well controlled)	

[a] **Unvaccinated** = individuals who are not eligible for COVID-19 vaccination or are <2 weeks from the final dose of… …cinated") and are >2 weeks after the final dose of the primary series but have not received a booster, if they are eligible for a booster. Children aged <5 years are not cu… …ed the primary series but are not yet eligible for a booster. See the CDC for more information.

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Key: BMI = body mass index; CDC = Centers for Disease Control and Prevention; NIV = noninvasive ventilation; the Panel = the COVID-19 Treatment Guidelines Panel

Patients who are moderately-severely immunocompromised:

- Have a hematologic malignancy, regardless of treatment status
- Received a solid-organ or an islet transplant and are receiving immunosuppressive therapy
- Are receiving active treatment for a hematologic malignancy or solid tumor
- Received chimeric antigen receptor T cell (CAT T-cell) therapy or a hematopoietic stem cell transplant (HCT) and are within 2 years of transplantation or are receiving immunosuppressive therapy
- Have a moderate or severe primary immunodeficiency (e.g. SCID, DiGeorge syndrome, Wiskott-Aldrich syndrome, CVID)
- Have advanced or untreated HIV infection with CD4 T lymphocyte cell counts <200 cell/mm^3, a history of an AIDS-defining illness without immune reconstitution, or clinical manifestations of symptomatic HIV
- Are receiving active treatment with high-dose corticosteroids (i.e. ≥20 mg prednisone or equivalent per day when administered for ≥2 weeks), alkylating agents, antimetabolites, transplant-related immunosuppressive drugs, cancer chemotherapeutic agents classified as severely immunosuppressive, and biologic agents that are immunosuppressive or immunomodulatory

Step 2: Determine the appropriate management. If your patient is and will not be hospitalized due to COVID-19, please see “Outpatient” section. If your patient is or will be hospitalized due to COVID-19, please see “Inpatient” section.

OUTPATIENT: Treatment Options

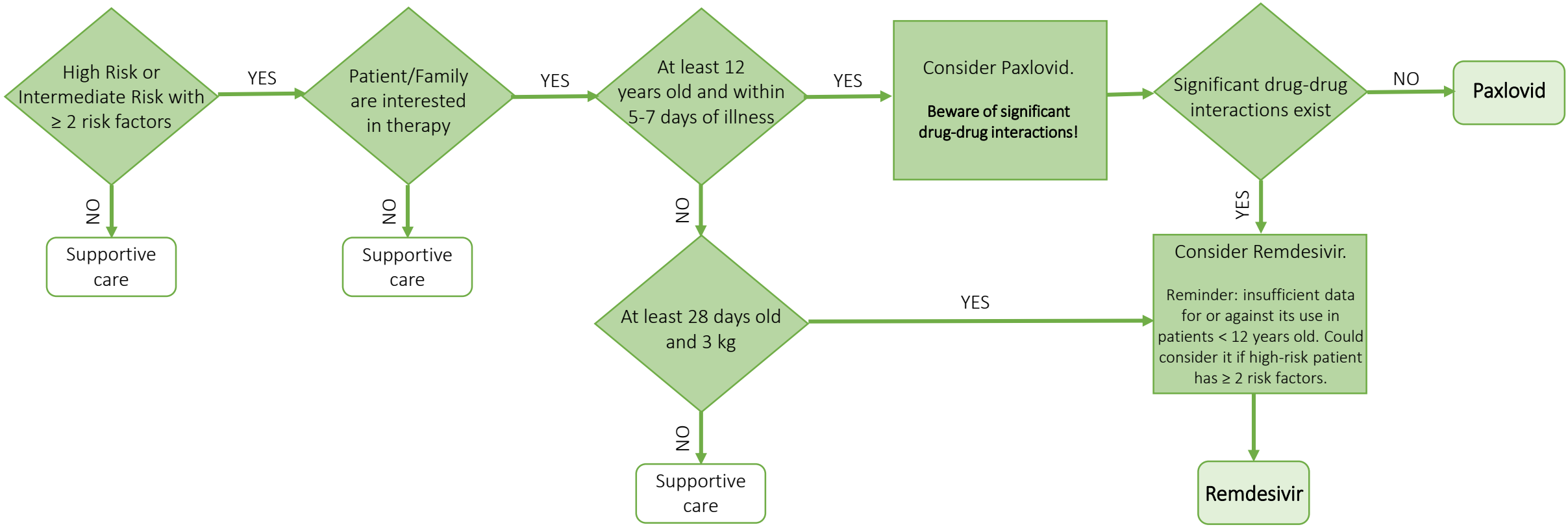
Clinical Situation	Risk Category	Treatment Options and Details				
Asymptomatic patients or **patients with mild disease**. Of note, patients with mild disease are not requiring any additional respiratory support.	Low	Only supportive care recommended.				
	Intermediate	Insufficient evidence for or against any therapy. Could consider it if patient has ≥ 2 risk factors.				
	High	**Class**	**Medication**	**Patient**	**Dosing**	**Note**
		Antivirals	**Ritonavir-boosted Nirmatrelvir** or **"Paxlovid"** is an oral antiviral permitted for emergency use under EUA issued by FDA.	Patient must be at least 12 years old, at least 40 kg, and within 5 days of symptom onset. It is a first-line agent.	Nirmatrelvir 300 mg and Ritonavir 100 mg q12h x 5 days **Paxlovid has several dosing considerations for renal impairment and significant drug-drug interactions, like JAK inhibitors, for instance. The Provider Fact Sheet MUST be evaluated by providers to check for drug-drug interactions prior to Paxlovid prescription and can be found at:** https://www.covid19oralrx-patient.com/files/Final-Emergency-Use-Full-Prescribing-Info-HCP-Fact-Sheet-COVID-19-Oral-Antiviral.pdf.	Paxlovid is available at CCHMC base ED outpatient pharmacy. It should be ordered in EPIC or by phone at (513) 517-8358. The Patient Fact Sheet MUST be given to patients/families and can be found at: https://labeling.pfizer.com/ShowLabeling.aspx?id=16473&format=pdf. Paxlovid is also available at many local pharmacies. https://covid-19-therapeutics-locator-dhhs.hub.arcgis.com/

OUTPATIENT: Treatment Options

Clinical Situation	Risk Category	Treatment Options and Details				
		Class	Medication	Patient	Dosing/Pharmacy	Note
Asymptomatic patients or **patients with mild disease**. Of note, patients with mild disease are not requiring any additional respiratory support.	High	Antivirals	**Remdesivir** or **"Veklury"** is an intravenous antiviral approved for use by the FDA. It is no longer under EUA.	Patient must be at least 28 days old, at least 3kg, and within 7 days of symptom onset. • For patients <12 years old, there is insufficient evidence for or against use of Remdesivir. Could consider it if patient has ≥ 2 risk factors. It is a second-line agent.	3-day course: • 5 mg/kg (max 200 mg) on day 1 • 2.5 mg/kg (max 100 mg) as a single dose daily on days 2 and 3	Remdesivir infusions may be given at CCHMC's Infusion Center. Please go to: https://centerlink.cchmc.org/managers/co-v. Under "Clinician Resources" click "General" and then "Scheduling Process: COVID-19 Outpatient Infusion Therapy" to make arrangements.
			Molnupiravir or **"Lagevrio"** is an oral antiviral permitted for emergency use under EUA issued by the FDA.	Patient must be at least 18 years old and within 5 days of symptom onset. It is a third-line agent.	800 mg q12h x 5 days	Molnupiravir is not currently available at CCHMC.

Of note, as of December 2022, there are no monoclonal antibody therapies used for treatment with adequate activity against currently circulating SARS-CoV-2 variants. Bebtelovimab, Casirivimab and imdevimab, Bamlanivimab and etesevimab, and Sotrovimab should no longer be used per FDA.

OUTPATIENT: Algorithm



For dosing/duration and administration information, please see pages 6-7.

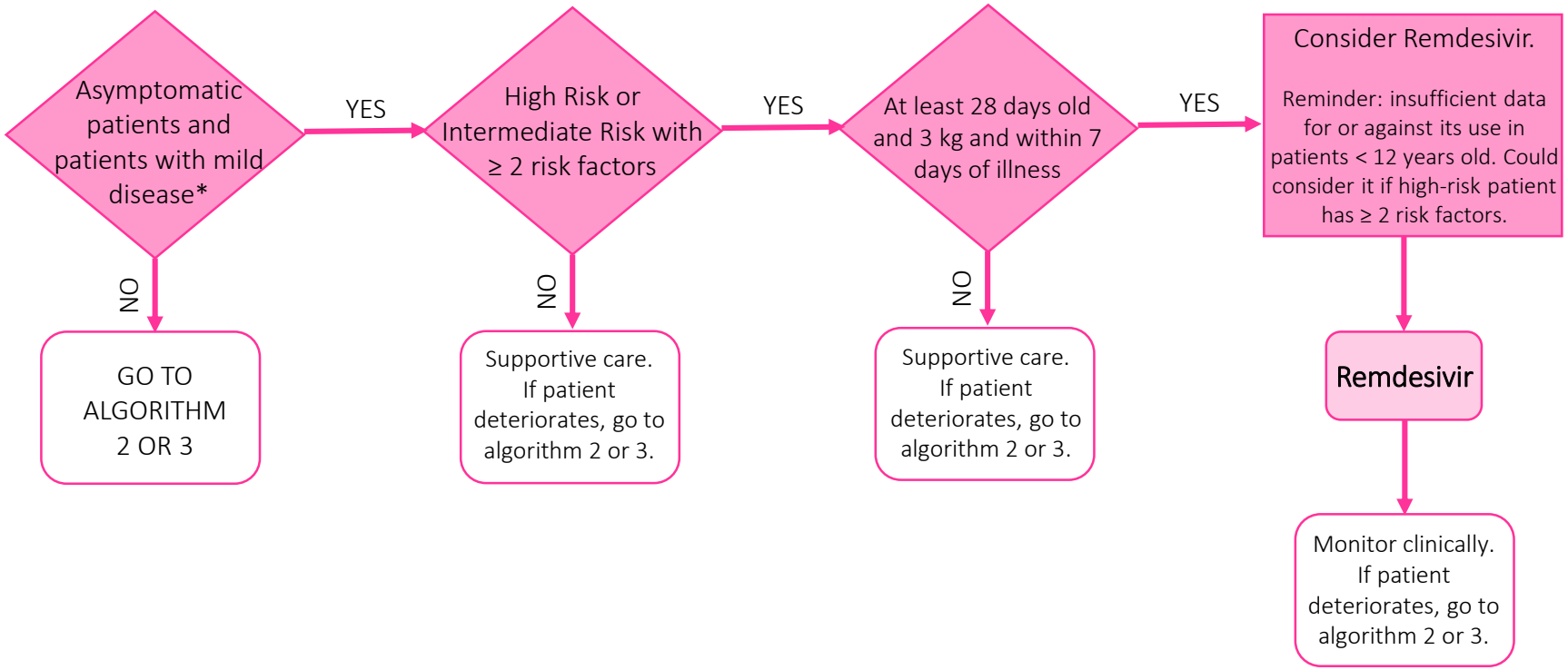
INPATIENT: Treatment Options

Clinical Situation	Risk Category	Treatment options and details		
Asymptomatic patients or **patients with mild disease**. Of note, patients with mild disease are not requiring any additional respiratory support.	Low	Only supportive care recommended.		
	Intermediate	Insufficient evidence for or against any therapy. Could consider Remdesivir if patient has ≥ 2 risk factors.		
	High	**Medication**	**Patient**	**Dosing**
		Remdesivir	Patient must be at least 28 days old, at least 3kg, and within 7 days of symptom onset. • For patients <12 years old, there is insufficient evidence for or against use of Remdesivir. Could consider it if patient has ≥ 2 risk factors.	3-day course: • 5 mg/kg (max 200 mg) as a single dose daily on day 1 • 2.5 mg/kg (max 100 mg) as a single dose daily on days 2 and 3
Patients with moderate disease. That is, they are requiring new or increased from baseline conventional O^2 (not high-flow, NIV, MV, or ECMO).	All	**Remdesivir**	Patient must be at least 28 days old, at least 3kg, and within 10 days of symptom onset.	5-day course (or until hospital discharge, whichever comes first): • 5 mg/kg (max 200 mg) as a single dose daily on day 1 • 2.5 mg/kg (max 100 mg) as a single dose daily on days 2-5 *Course may be extended to 10 days
		Dexamethasone	All	0.3 mg/kg (max 6 mg) x 10 days (or until hospital discharge, whichever comes first)

INPATIENT: Treatment Options

Clinical Situation	Risk Category	Treatment options and details		
		Medication	Patient	Dosing
Patients with severe disease. That is, they are requiring new or increased from baseline O^2 through high-flow, NIV, MV, or ECMO.	All	**Remdesivir**	Patient must be at least 28 days old, at least 3kg, and within 10 days of symptom onset.	5-day course (or until hospital discharge, whichever comes first): • 5 mg/kg (max 200 mg) as a single dose daily on day 1 • 2.5 mg/kg (max 100 mg) as a single dose daily on days 2-5 *Course may be extended to 10 days
		Dexamethasone	All	0.3 mg/kg (max 6 mg) x 10 days (or until hospital discharge, whichever comes first)
		Tocilizumab may be considered for children who do not have rapid (i.e. within 24 hrs) improvement in oxygenation after initiation of Dexamethasone.	Patients at least 2 years old.	
			Patients < 30 kg.	12 mg/kg as a single dose
			Patients at least 30 kg.	8 mg/kg as a single dose
		Baricitinib may be considered for children who do not have rapid (i.e. within 24 hrs) improvement in oxygenation after initiation of Dexamethasone.	Patients 2 – < 9 years old.	
			eGFR ≥ 60 mL /min /1.73 m^2	2 mg as a single dose daily x 14 days
			eGFR 30 – < 60 mL /min/1.73 m^2	1 mg as a single dose daily x 14 days
			eGFR < 30 mL /min/1.73m^2	Not recommended
			Patients at least 9 years old.	
			eGFR ≥ 60 mL /min /1.73 m^2	4 mg as a single dose daily x 14 days
			eGFR 30 – < 60 mL /min/1.73 m^2	2 mg as a single dose daily x 14 days
			eGFR < 30 mL /min/1.73m^2	1 mg as a single dose daily x 14 days

INPATIENT: Algorithm 1 / MILD

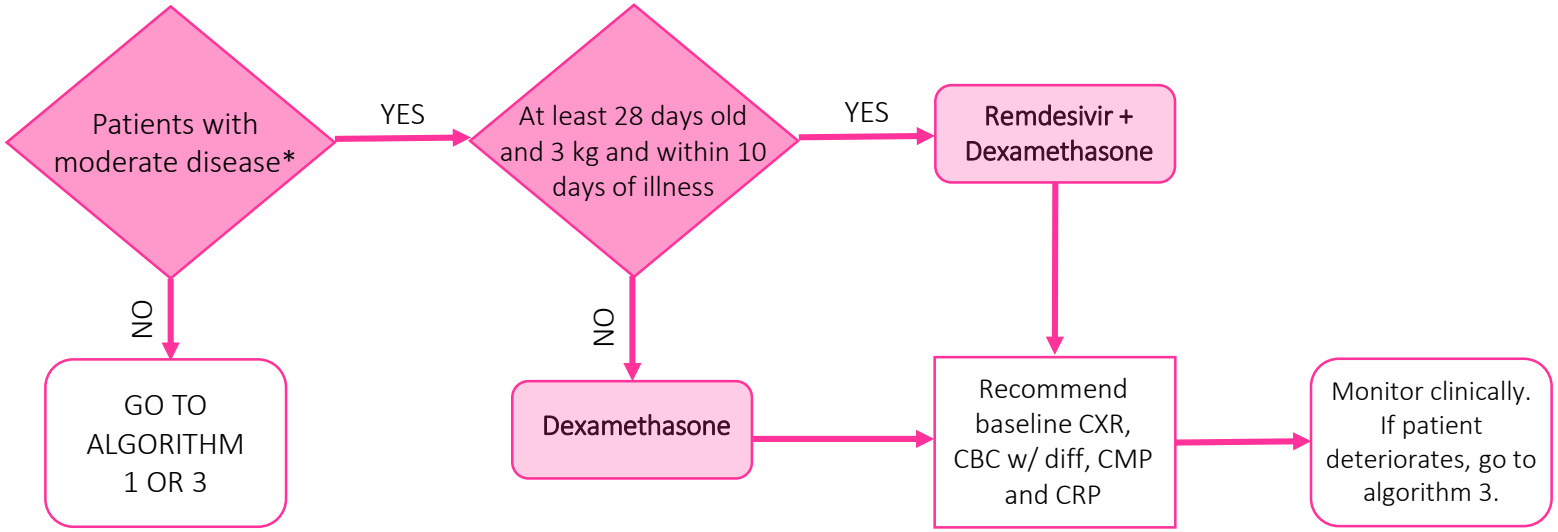


*Patients with mild disease are not requiring any additional respiratory support.

For dosing/duration information, please see page 9.

OF NOTE, ID's involvement in these decisions is not required. However, ID will certainly provide advice as needed, if needed.

INPATIENT: Algorithm 2 / MODERATE

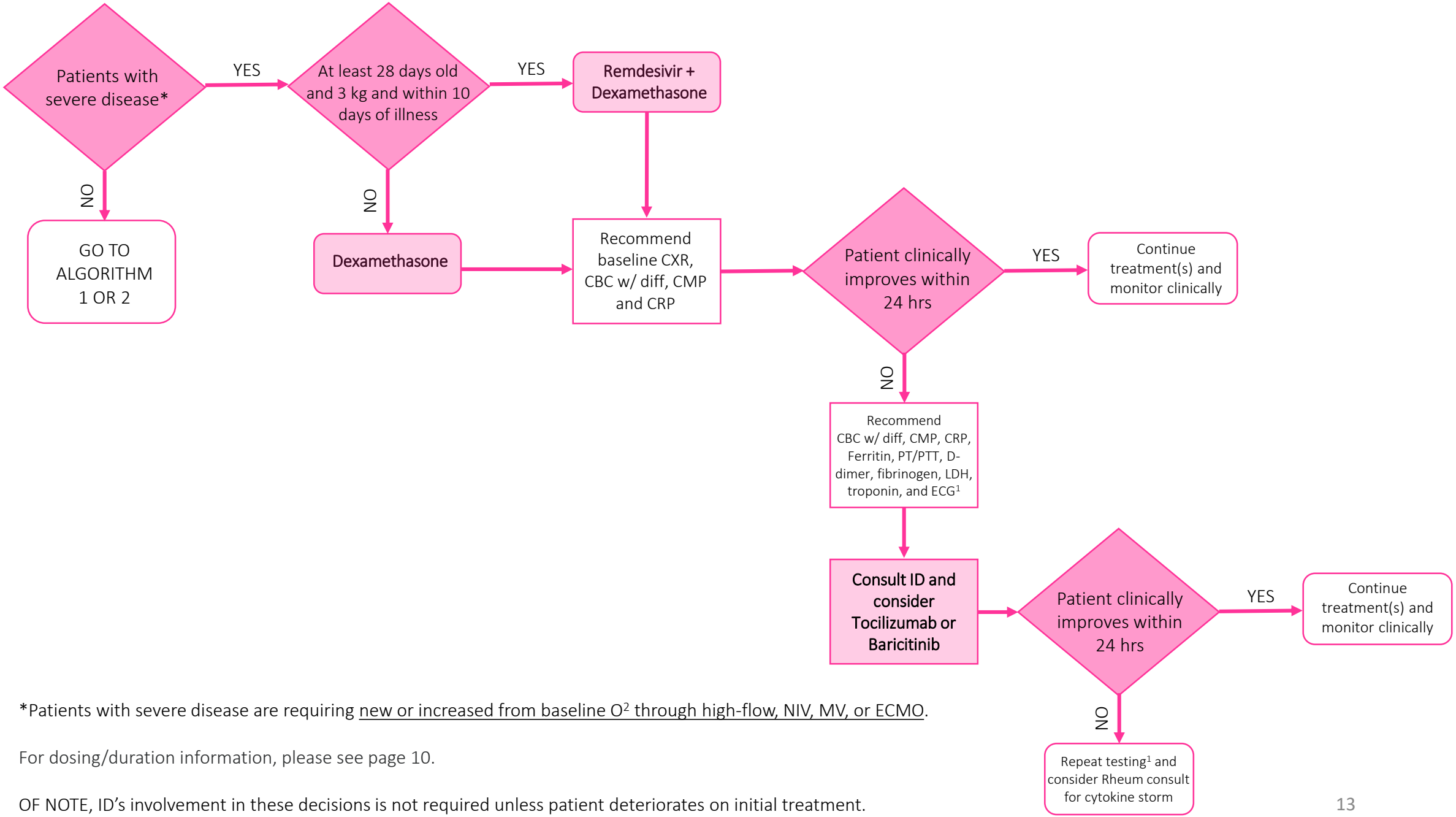


*Patients with moderate disease are requiring <u>new or increased from baseline conventional O^2</u> (not high-flow, NIV, MV, or ECMO).

For dosing/duration information, please see page 9.

OF NOTE, ID's involvement in these decisions is not required. However, ID will certainly provide advice as needed, if needed.

INPATIENT: Algorithm 3 / SEVERE



*Patients with severe disease are requiring new or increased from baseline O^2 through high-flow, NIV, MV, or ECMO.

For dosing/duration information, please see page 10.

OF NOTE, ID's involvement in these decisions is not required unless patient deteriorates on initial treatment.

Re: Thromboprophylaxis guidelines, which are produced and maintained by Hematology. Questions on these should be directed to their service.

Clinician Resources

Expand All

General

- Algorithm: COVID-19 Treatment
  Updated 12/5/22
- Algorithm: Mask Refusal
- Algorithm: MIS-C (Multi-system Inflammatory Syndrome in Children)
  Updated 2/7/22
- Algorithm: Return to Sports after COVID-19
  Updated 8/23/21
- Exposed Patient: Notification Script for Exposure to a COVID-19 Positive Employee
- Epic: Resources for COVID-19 Reassignments
- Patient Care: Aerosol-Generating Procedures & PPE Guidelines
  Updated 3/22/21
- Patient Care: Inpatient COVID-19 Care Guide
  Updated 5/18/22
- Patient Care: Thromboprophylaxis Diagram
- Patient Care: Thrombosis COVID-19 Guidelines
- Patient Testing: Adding COVID Results from External Lab
  New 9/2/21
- Patient Testing: Inpatient Caregivers
  10/12/21
- PPE: Donning and Doffing Resources
- Scheduling Process: COVID-19 Outpatient Infusion Therapy
  Updated 5/24/22