(Age <25 years)



Patient with COVID-19 (confirmed or presumed)

Appropriate PPE, rooming and staffing.
Educate family on positive test and isolation.

Aim: To provide guidance for management of COVID-19.

Assess COVID-19 Illness Level.

Ask family/patient if any history of abnormal immunity or if patient has been evaluated by Immunology or Rheumatology in the past. Discuss with Children's Immunology if concerns.

**←----**>

## Asymptomatic

Tested for reasons other than symptoms (e.g., pre-op, behavioral health admission).

- No additional tests/ treatments needed.
- See "behavioral health" order set for guidance on retesting in behavioral health patients.

### Mild

Uncomplicated URT viral infection, non-specific symptoms (e.g. fever, fatigue, cough, anorexia, muscle pain, sore throat, nasal congestion, headache). No respiratory distress or O<sub>2</sub> requirement; able to self-hydrate (may be after initial fluid support). Suitable for outpatient care.

Supportive care (note 1) in clinic or ED and recommendations for home.

### **COVID-19 Therapeutics**

Assess eligibility for Paxlovid™ or remdesivir if high-risk factors for progression to severe COVID-19. See p.2-4 for more detail.

#### Moderate

Requiring close inpatient monitoring for potential of worsening respiratory status or ongoing IVF support. Not on HFNC or LFNC.

- Supportive care (note 1)
- Consults: none
- · Labs: As clinically indicated.
- Consider CXR
- VTE prophylaxis: per VTE guideline

# **COVID-19 Therapeutics**

Assess eligibility for remdesivir if highrisk factors for progression to severe COVID-19. See p.2-4 for more detail.

#### Severe

Respiratory symptoms requiring admission to med-surg unit for LFNC or HFNC based on following:

- Pediatric patients: SpO<sub>2</sub>< 90% or acute respiratory distress (e.g. grunting, retractions, tachypnea)</li>
- · Adolescent and adult patients: one of the following:
  - Respiratory rate > 30 breaths/min
  - $SpO_2 < 94\%$  on room air
  - Severe respiratory distress (e.g. dyspnea, retractions)
- Supportive care (note 1)
- Consults: Optional discussion with Infectious Disease
- Labs: As clinically indicated (page 5)
  - If starting remdesivir, obtain ALT, AST, PT/INR before initiation and AST/ALT q48 hours.
- CXR as clinically indicated
- VTE prophylaxis: per <u>VTE guideline</u>

# COVID-19 Therapeutics: see PIDS guidance and page 5

- <12 years and low risk with supplemental O2 above baseline\*:</li>
  - · LFNC: consider remdesivir and dexamethasone
  - · HFNC: consider remdesivir; give dexamethasone
- >=12 years or <12 years and moderate/high risk with O2 above baseline: remdesivir and dexamethasone
- Any age and rapidly increasing O2 need\*: remdesivir and dexamethasone
- If not showing improvement in oxygenation within 24 hours of steroid initiation, consult ID/immunology to discuss other therapies

### Critical

Critically ill, requiring ICU
level of care for respiratory support, sepsis, or
septic shock.

- Supportive care (note 1)
- Consults: Infectious Disease, Immunology, Pulmonology, and other specialists as needed.
- Labs: CBC+diff, CRP, CMP, blood culture, serum to save (≥ 3 mL).
- CXR
- VTE prophylaxis: per VTE guideline

COVID-19 Therapeutics: see Pediatric Infectious Diseases Society (PIDS) Guidance on Covid and page 6

\*It is not known if remdesivir offers an additional clinical benefit to standard care in younger children with SARS-CoV-2 infection who are receiving respiratory support for bronchiolitis, asthma, or croup.<sup>2</sup> Utilize shared decision making with family. Consider viral co-infections in your decision management.

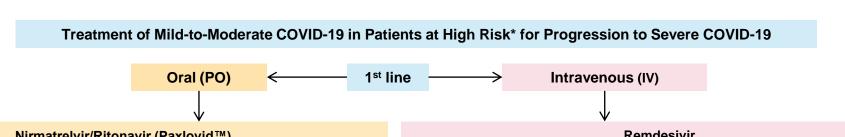
(Age <25 years)



\*Moderate risk patients may be considered on a case by

case basis per PIDS Covid-19 Guidance

Aim: To provide guidance for management of COVID-19.



### Remdesivir

#### Must meet all criteria below:

- > 37 weeks gestational age and weighing > 1.5 kg
- Presence of high-risk factors for progression to severe COVID-19
  - · High-risk factors in pediatric patients
  - · High-risk factors in adult patients
- · Within 7 days of symptom onset
- Outpatient or inpatient mild-to-moderate COVID-19
- Infectious Disease approval needed for outpatient remdesivir (Contact Children's Physician Access at 612-343-2121 to discuss with the ID provider on call for the St. Paul campus.) Prescribing process linked here.

### Nirmatrelvir/Ritonavir (Paxlovid™) Must meet all criteria below:

- ≥ 18 years of age **OR** 12-17 years of age and weighing ≥ 40 kg
- Presence of high-risk factors for progression to severe COVID-19
  - High-risk factors in pediatric patients
  - High-risk factors in <u>adult patients</u>
- · Within 5 days of symptom onset
- Ability to swallow pills
- eGFR ≥ 30 mL/min
- No severe hepatic impairment (Child-Pugh Class C)
- No contraindicated <u>drug interactions</u>
- Outpatient or inpatient mild-to-moderate COVID-19

Prescribers should refer to the **Paxlovid™** prescribing process for complete guidance.

(Age <25 years)



Aim: To provide guidance for management of COVID-19.

# **Comparison of Outpatient Therapeutics for Mild-to-Moderate COVID-19**

	Nirmatrelvir/ritonavir (Paxlovid™)	Remdesivir	
Administration route	Oral	IV	
Age and weight requirements	≥ 18 years of age regardless of weight 12-17 years of age AND ≥ 40 kg	> 37 weeks gestational age and ≥ 1.5 kg	
Initiate within # days of symptom onset	5 days	7 days	
Duration of therapy	5 days	3 days	
Clinical efficacy (Reduction in hospitalization or death vs. placebo in high-risk adults)	Absolute risk reduction: 6.3% → 0.8% Relative risk reduction: 88% NNT: 18	Absolute risk reduction: 5.3% → 0.7% Relative risk reduction: 87% NNT: 22	
Renal function requirements	eGFR ≥ 30 mL/min	None	
Hepatic function requirements	No severe hepatic impairment (Child-Pugh Class C)	Perform hepatic laboratory testing in all patients before and during treatment as clinically appropriate	
Advantages	Highly efficacious Oral Safe in pregnancy	Highly efficacious Few known drug interactions Safe in pregnancy	
Disadvantages	Drug interactions	IV infusion on 3 consecutive days (Infectious disease consult required to set up)	
Side effects	Dysgeusia (6%), diarrhea (3%), hypertension (1%), myalgia (1%)	Nausea (6%), transaminase elevation (~2% of hospitalized patients with moderate COVID-19), constipation (17%)	

NNT: Number needed to treat

(Age <25 years)



Aim: To provide guidance for management of COVID-19.

CLINICAL SEVERITY	THERAPEUTIC AGENTS	COMMENTS	MONITORING
Mild Illness	Consider Nirmatrelvir/Ritonavir (Paxlovid™) or Remdesivir in patients at high-risk for progression to severe COVID-19  Assess eligibility criteria (see p. 2)  Refer to Paxlovid™ prescribing process for guidance on Paxlovid™.  Outpatient remdesivir requires ID approval. Call Children's Physician Access 612-343-2121 to discuss with ID provider on-call for St. Paul campus. Prescribing process linked here.  Dosing Paxlovid™:  Paxlovid™ is FDA-approved in adults but under an EUA for pediatric patients 12-17 years of age weighing ≥ 40 kg. See Note 2 (Paxlovid™) on p.7 for EUA documentation/reporting requirements. More information in next column.  Dose:  • eGFR ≥ 60 mL/min: Nirmatrelvir 300 mg (2 x 150 mg tablets) and ritonavir 100 mg (1 x 100 mg tablet) twice daily x 5 days.  • eGFR 30 to < 60 mL/min: Nirmatrelvir 150 mg (1 x 150 mg tablet) and 100 mg ritonavir (1 x 100 mg tablet) twice daily x 5 days.  Dosing Remdesivir:  FDA approval applies to pediatric patients >37 weeks gestational age and ≥1.5 kg, and to all adult patients  Dose:  Adults (regardless of weight) and pediatric patients weighing ≥40 kg: 200 mg IV × 1, followed by 100 mg IV q24h × 2 days (3-day course)  Pediatric patients  ○ {<28 days of age and ≥ 1.5 kg} OR {≥ 28 days of age and ≥ 1.5 kg to <3kg}: 2.5 mg/kg IV × 1, followed by 1.25 mg/kg q24h × 2 days (3-day course)	Provider Tools for Paxlovid™  • Paxlovid™ package insert (approved indication)  • FDA EUA Paxlovid™ Fact Sheet for Healthcare Providers  • FDA EUA Paxlovid™ Fact Sheet for Patients and Caregivers  • FDA EUA Paxlovid™ FAQs  • Paxlovid™ prescribing process  • Paxlovid™ drug interaction checker  Provider Tools for Remdesivir  • FDA remdesivir package insert  EUA: Emergency Use Authorization	Patients on remdesivir:  If starting remdesivir, obtain ALT, AST, PT/INR before initiation  Consider discontinuation if ALT > 10 × ULN during treatment  Discontinue if ALT elevation is accompanied by s/s of liver inflammation
Moderate Illness	Consider Nirmatrelvir/Ritonavir (Paxlovid™) or Remdesivir in patients at high-risk for progression to severe COVID-19  • Prefer remdesivir if eligible and patient is inpatient  • Assess eligibility criteria (see p. 2)  • Refer to Paxlovid™ prescribing process for guidance on Paxlovid™.  • Outpatient remdesivir requires ID approval. Call Children's Physician Access 612-343-2121 to discuss with ID provider on-call for St. Paul campus.  Dosing Paxlovid™:  Paxlovid™:  Paxlovid™ is FDA-approved in adults but under an EUA for pediatric patients 12-17 years of age weighing ≥ 40 kg. See Note 2 (Paxlovid™) on p.7 for EUA documentation/reporting requirements. More information in next column.  • Dose:  • eGFR ≥ 60 mL/min: Nirmatrelvir 300 mg (2 x 150 mg tablets) and ritonavir 100 mg (1 x 100 mg tablet) twice daily x 5 days.  • eGFR 30 to < 60 mL/min: Nirmatrelvir 150 mg (1 x 150 mg tablet) and 100 mg ritonavir (1 x 100 mg tablet) twice daily x 5 days.  Dosing Remdesivir:  • FDA approval applies to pediatric patients >37 weeks gestational age and ≥1.5 kg, and to all adult patients  Dose:  • Adults (regardless of weight) and pediatric patients weighing ≥40 kg: 200 mg IV × 1, followed by 100 mg IV q24h × 2 days (3-day course)  • Pediatric patients  • {28 days of age and ≥ 1.5 kg} OR {≥ 28 days of age and ≥ 1.5 kg to < 3kg}: 2.5 mg/kg IV x 1, followed by 1.25 mg/kg q24h x 2 days (3-day course)  • ≥ 28 days of age weighing ≥ 3 kg to < 40 kg: 5 mg/kg IV × 1, followed by 2.5 mg/kg q24h x 2 days (3-day course)	Provider Tools for Paxlovid™  Paxlovid™ package insert (approved indication)  FDA EUA Paxlovid™ Fact Sheet for Healthcare Providers  FDA EUA Paxlovid™ Fact Sheet for Patients and Caregivers  FDA EUA Paxlovid™ FAQs  Paxlovid™ prescribing process  Paxlovid™ drug interaction checker  Provider Tools for Remdesivir  FDA remdesivir package insert  EUA: Emergency Use Authorization	Lab monitoring as clinically relevant. If symptom progression, refer to severe/critical pathway.  Patients on remdesivir:  If starting remdesivir, obtain ALT, AST, PT/INR before initiation and AST/ALT q48 hours.  Consider discontinuation if ALT > 10 × ULN during treatment  Discontinue if ALT elevation is accompanied by s/s of liver inflammation

(Age <25 years)



Aim: To provide guidance for management of COVID-19.

CLINICAL SEVERITY	THERAPEUTIC AGENTS DOSING/PRESCRIBING INFORMATION	COMMENTS	MONITORING
Severe	Refer to Pediatric Infectious Diseases Society Covid-19 guidance when making choices regarding therapeutic agents. Dosing and prescribing information for the agents that MAY be used per PIDS guidance are as follows:  Systemic Corticosteroids:  Dexamethasone 0.15 mg/kg (max 6 mg/dose) PO/NG/IV q24h for up to 10 days; discontinue at discharge unless required for another indication (i.e. asthma)  Recommend against use in patients not requiring supplemental oxygen (unless required for another indication such as croup/asthma)  In preterm reconates, risks vs. benefits should be considered based on gestational age, postnatal age, and illness severity  Remdesivir (clinical benefit of remdesivir is greatest if it is initiated within 10 days of symptom onset).  FDA approval applies to pediatric patients of gestational age greater than 37 weeks and weighing at least 1.5 kg, and to all adult patients to sto known if remdesivir offers an additional clinical benefit to standard care in younger children with SARS-CoV-2 infection who are receiving respiratory support for bronchiolitis, asthma, or croup. Publize shared decision making with family. Consider viral co-infections in your decision management.  Dose:  Adults (regardless of weight) and pediatric patients weighing ≥40 kg: 200 mg IV × 1, followed by 100 mg IV q24h × 4 days (5-day course). If no clinical improvement after a total of 5 days of treatment, treatment can be extended to up to a total of 10 days. Discontinue when meets discharge criteria.  Pediatric patients (<28 days of age and ≥ 1.5 kg) OR (≥ 28 days of age and ≥ 1.5 kg to < 3kg): 2.5 mg/kg IV × 1, followed by 1.25 mg/kg q24h × 4 days (5-day course) If no clinical improvement after a total of 5 days of treatment, treatment can be extended to up to a total of 10 days. Discontinue when meets discharge criteria.  Pediatric patients ≥ 28 days of age weighing 3 kg to < 40 kg: 5 mg/kg IV × 1, followed by 2.5 mg/kg q24h × 4 days (5-day course) If no clinical improvement after a total of 5 days of treatment, treatm	Systemic Corticosteroids Recommend gastric ulcer prophylaxis  Systemic Corticosteroid Alternatives (If dexamethasone is not available)  • Prednisolone 1 mg/kg (max 40 mg/dose) PO/NG q24h for up to 10 days  • Methylprednisolone 0.8 mg/kg (max 32 mg/dose) IV q24h for up to 10 days  Provider Tools for Remdesivir  • FDA remdesivir package insert	All hospitalized patients  As clinically indicated: Consider CBC+diff, CRP, CMP, blood culture, serum to save (≥ 3 mL). Labs per COVID VTE guideline if starting prophylaxis  If transfer to ICU, review if needs critical labs on page 1.  Patients on Remdesivir If starting remdesivir, obtain ALT, AST, PT/INR before initiation and AST/ALT q48 hours.  Consider discontinuation if ALT > 10 × ULN during treatment  Discontinue if ALT elevation is accompanied by s/s of liver inflammation  Patients on Empiric Antibiotics Need, duration, and spectrum of antibiotics should be assessed daily based on microbiology results and clinical status  Useful websites  PIDS Covid-19 Guidance COVID-19 drug interactions http://www.covid19-druginteractions.org/

(Age <25 years)



Aim: To provide guidance for management of Covid-19

CLINICAL SEVERITY	THERAPEUTIC AGENTS DOSING/PRESCRIBING INFORMATION	COMMENTS	
Critical	Refer to Pediatric Infectious Diseases Society Covid-19 guidance when making choices regarding therapeutic agents. Dosing and prescribing information for the agents that MAY be used per PIDS guidance are as follows: Systemic Corticosteroids.  Dexamethasone 0.15 mg/kg (max 6 mg/dose) PO/NG/IV q24h for up to 10 days; discontinue at discharge unless required for another indication (i.e. asthma) Recommend against use in patients not requiring supplemental oxygen (unless required for another indication such as croup/asthma) In preterm neonates, risks vs. benefits should be considered based on gestational age, postnatal age, and these severity Remdesivir (clinical benefit of remdesivir is greatest if it is initiated within 10 days of symptom onset) FDA approval applies to pediatric patients of gestational age greater than 37 weeks and weighing at least 1.5 kg, and to all adult patients Dose:  Adults (regardless of weight) and pediatric patients weighting 240 kg; 200 mg IV × 1, followed by 100 mg IV q24h Pediatric patients <28 days of age weighting ≥ 3 kg to < 40 kg: 200 mg IV × 1, followed by 1.05 mg/kg q24h Pediatric patients ≥ 28 days of age weighting ≥ 3 kg to < 40 kg: 5 mg/kg IV × 1, followed by 2.5 mg/kg q24h Pediatric patients ≥ 28 days of age weighting ≥ 3 kg to < 40 kg: 5 mg/kg IV × 1, followed by 2.5 mg/kg q24h Pediatric patients ≥ 28 days of age weighting ≥ 3 kg to < 40 kg: 5 mg/kg IV × 1, followed by 2.5 mg/kg q24h Pediatric patients ≥ 28 days of age weighting ≥ 3 kg to < 40 kg: 5 mg/kg IV × 1, followed by 1.5 mg/kg q24h Pediatric patients ≥ 28 days of age weighting ≥ 3 kg to < 40 kg: 5 mg/kg IV × 1, followed by 1.5 mg/kg q24h Pediatric patients ≥ 28 days of age weighting ≥ 3 kg to < 40 kg: 5 mg/kg IV × 1, followed by 1.5 mg/kg q24h Pediatric patients ≥ 28 days of age weighting ≥ 3 kg to < 40 kg: 5 mg/kg IV × 1, followed by 1.5 mg/kg q24h Pediatric patients ≥ 28 days of age weighting ≥ 3 kg kg to < 40 kg: 5 mg/kg kg kg vg × 1 kg	Systemic Corticosteroids Recommend gastric ulcer prophylaxis  Systemic Corticosteroid Alternatives (If dexamethasone is unavailable)  • Prednisolone 1 mg/kg (max 40 mg/dose) PO/NG q24h for up to 10 days  • Methylprednisolone 0.8 mg/kg (max 32 mg/dose) IV q24h for up to 10 days  • Provider Tools for Tocilizumab  • FDA Tocilizumab package insert (approved indication)  • FDA EUA Tocilizumab Fact Sheet for Providers  • FDA EUA Tocilizumab Fact Sheet for Patients  • FDA EUA Tocilizumab FAQs  Tocilizumab should be avoided or benefit/risk assessed if any of the following:  • Active concurrent non-SARS-CoV-2 infection, including localized infection; High risk for GI perforation; Preexisting or recent onset demyelinating disorders; ALT or AST 10 × ULN; ANC <1000 cells/µL; Platelet count <50,000 cells/µL  • Consider prophylactic Ivermectin for patients from areas where Strongyloides is endemic (e.g. SE Asia, sub-Saharan Africa)  Provider Tools for Baricitinib  • FDA Baricitinib package insert (approved indication)  • FDA EUA Baricitinib Fact Sheet for Providers  • FDA EUA Baricitinib Fact Sheet for Patients  • FDA EUA Baricitinib Fact Sheet for	All have C (2)  Patie If A A  C C > D are in  Patie Need antibi basee clinica  Patie Monit neutr HSV, perfor Patie Lal eG Re inte her  Mon DV  Useft 1. 1

#### All hospitalized patients

On admission: CBC+diff, CRP, CMP,-blood culture, serum to save (≥ 3 mL). Labs per COVID VTE quideline if starting prophylaxis

MONITORING

#### Patients on Remdesivir

- If starting remdesivir, obtain ALT, AST, PT/INR before initiation and AST/ALT q48 hours.
- Consider discontinuation if ALT
   > 10 × ULN during treatment
- Discontinue if ALT elevation is accompanied by s/s of liver inflammation

#### **Patients on Empiric Antibiotics**

Need, duration, and spectrum of antibiotics should be assessed daily based on microbiology results and clinical status

#### Patients on Tocilizumab

Monitor for hepatotoxicity, leukopenia, neutropenia, infection reactivation (e.g. HSV, VZV, TB, Strongyloides), GI perforation

#### Patients on Baricitinib

- Labs prior to initiation and daily: eGFR, aminotransferases, CBC+diff
- Requires dose adjustments for drug interactions and if abnormal renal, hematological and hepatic labs.
- Monitor for thromboembolism (PE, DVT), GI perforation

#### Useful websites

- 1. PIDS Covid-19 Guidance
  - COVID-19 drug interactions http://www.covid19-druginteractions

(Age <25 years)



Aim: To provide guidance for management of COVID-19.

# **NOTE 1: Supportive Care**

• Systemic corticosteroids may be used for asthma/croup indications in patient with COVID-19.

NOTE 2: Nirmatrelvir/Ritonavir (Paxlovid™) FDA EUA Documentation and Reporting Requirements. Despite recent FDA approval of Paxlovid™ in adults (5/25/23), due to insufficient Paxlovid™ supply, the EUA continues to include the patient population now approved by the FDA. The following EUA requirements apply to all patients until further guidance is provided by the HSS.

- Providers must document in EMR that they:
- 1) Communicated to the patient/caregiver information consistent with the <u>FDA EUA Paxlovid™ Fact Sheet for Healthcare Providers</u> and provided them with the <u>FDA EUA Paxlovid™ Fact Sheet for Healthcare Providers</u>; prior to administration of Paxlovid™.

Providers must **report** all medication errors and serious adverse events potentially related to Paxlovid™ within 7 calendar days from the event by:

- 1) Submitting a MedWatch Report, and
- 2) Faxing the completed MedWatch form to Pfizer at 1-866-635-8337

#### NOTE 3: Antibiotic recommendations for suspected or proven bacterial coinfection (community-acquired)

- For infants <60 days: If applicable, refer to Febrile Infant 1-60 Days without a source or Bronchiolitis guideline. Consider ID consult. Consider neonatology consult if infant 1-7 days old or are premature <37 weeks and PMA <44 weeks
- For patients > 60 days old to 17 years of age, see the Community Acquired Pneumonia treatment guideline.
- For patients 18 to < 25 years of age, see the Empiric Recommendations for Treatment of Common Infections in Adults.

### NOTE 4: Tocilizumab FDA EUA Counseling and Reporting Requirements (Applies to patients ≥ 2 years old to < 18 years of age.)

- Providers must **communicate** to patients/caregivers information consistent with the <u>Tocilizumab EUA Fact Sheet for Patients and Caregivers</u> and **provide** them with a copy of the Fact Sheet prior to administration of tocilizumab. If providing this information will delay administration of tocilizumab to a degree that would endanger the life of the patient, the information must be provided to the parent/caregiver as soon as feasible after administration of tocilizumab.
- Providers must report all medication errors and serious adverse events potentially related to tocilizumab within 7 calendar days from the event by:
- 1) Submitting a MedWatch Report, and
- 2) Emailing a copy of the submitted MedWatch Report to Genentech <u>us\_drug.safety@gene.com</u>

## NOTE 5: Baricitinib FDA EUA Documentation and Reporting Requirements (Applies to patients ≥ 2 years old to < 18 years of age.)

- Providers must document in EMR that patient/caregiver was:
- 1) Given the Baricitinib Fact Sheet for Patients and Caregivers;
- 2) Informed of alternatives to baricitinib, and
- 3) Informed that baricitinib is an approved drug that is authorized for this unapproved use
- Providers must report all medication errors and serious adverse events potentially related to baricitinib within 7 calendar days from the event by:
- 1) Submitting a MedWatch Report, and
- 2) Emailing a copy of the submitted MedWatch Report to Eli Lilly mailindata gsmtindy@lilly.com

## Discharge Criteria

- · Routine medical criteria
- · Encourage virtual or in-clinic follow-up with PCP

(Age <25 years)



Aim: To provide guidance for management of COVID-19.

## REFERENCES

#### **Guidelines, Expert Reviews, Evidence Summaries**

- 1. Retired: National Institutes of Health COVID-19: Clinical Management of Adults. <a href="https://www.covid19treatmentguidelines.nih.gov/management/clinical-management-of-adults/clinical-management-of-adults/clinical-management-of-adults-summary/">https://www.covid19treatmentguidelines.nih.gov/management/clinical-management-of-adults/clinical-management-of-adults/clinical-management-of-adults-summary/</a>
- 2. Retired: National Institutes of Health COVID-19: Clinical Management of Children. https://www.covid19treatmentguidelines.nih.gov/management-of-children/clinical-management-of-children/clinical-management-of-children.
- 3. Bhimraj A et al. Infectious Diseases Society of America Guidelines on the Treatment and Management of Patients with COVID-19 https://www.idsociety.org/practice-guideline/covid-19-guideline-treatment-and-management/
- 4. Henderson LA, Canna SW, Friedman KG, Gorelik M, Lapidus SK, Bassiri H, et al. American College of Rheumatology Clinical Guidance for Pediatric Patients with Multisystem Inflammatory Syndrome in Children (MIS-C) Associated with SARS-CoV-2 and Hyperinflammation in COVID-19. Version 3. Arthritis Rheumatol. doi: https://onlinelibrary.wiley.com/doi/10.1002/art.42062
- 5. CDC. Underlying Medical Conditions Associated with Higher Risk for Severe COVID-19. https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-care/underlyingconditions.html
- 6. Willis ZI, et al. Guidance for prevention and management of COVID-19 in children and adolescents: A consensus statement from the Pediatric Infectious Diseases Society Pediatric COVID-19 Therapies Taskforce. J Pediatric Infect Dis Soc. 2024; 13(3):159 185.

### **Drug Interactions**

7. COVID-19 drug interactions, University of Liverpool http://www.covid19-druginteractions.org/

#### Nirmatrelvir/Ritonavir (Paxlovid™)

- 8. Nirmatrelvir/Ritonavir (Paxlovid™) Prescribing Information: Paxlovid™ package insert (approved indication), Paxlovid™ prescribing process, Paxlovid™ drug interaction checker
- 9. FDA Fact Sheet for Healthcare Providers for Emergency Use Authorization (EUA) of Nirmatrelvir/Ritonavir https://www.fda.gov/media/155050/download
- 10. FDA Fact Sheet for Patients And Parent/Caregivers for Emergency Use Authorization (EUA) of Nirmatrelvir/Ritonavir https://www.fda.gov/media/155051/download
- 11. FDA Frequently Asked Questions on the Emergency Use Authorization of Nirmatrelvir/Ritonavir. https://www.fda.gov/media/155052/download

### Remdesivir

- 12. Remdesivir (Veklury) Prescribing Information: https://www.gilead.com/-/media/files/pdfs/medicines/covid-19/veklury/veklury\_pi.pdf
- 13. Gottlieb RL and PINETREE Investigators. Early Remdesivir to Prevent Progression to Severe Covid-19 in Outpatients. N Engl J Med. 2022 Jan 27;386(4):305-315.
- 14. Beigel JH et al. Remdesivir for the treatment of Covid-19 Final report. N Engl J Med. 2020;383(19):1813-1826.
- 15. Spinner CD et al. Effect of remdesivir vs standard care on clinical status at 11 days in patients with moderate COVID-19: A randomized clinical trial. JAMA. 2020;324(11):1048-1057.
- 16. Goldman JD et al. Remdesivir for 5 or 10 days in patients with severe COVID-19. Published online May 27, 2020. N Engl J Med. 2020;383(19):1827-1837.
- 17. WHO Solidarity Trial Consortium. Repurposed Antiviral Drugs for Covid-19 Interim WHO Solidarity Trial Results. N Engl J Med. 2021; 384(6):497-511.
- 18. Ader F et al. Remdesivir plus standard of care versus standard of care alone for the treatment of patients admitted to hospital with COVID-19 (DisCoVeRy): a phase 3, randomised, controlled, open-label trial. Lancet Infect Dis. 2022 Feb;22(2):209-221.
- 19. Ahmed A. et al. Remdesivir for COVID-19 in Hospitalized Children: A Phase 2/3 Study. Pediatrics. 2024; 153(3):e2023063775.

(Age <25 years)



**Aim:** To provide guidance for management of COVID-19.

## REFERENCES

#### **Corticosteroids**

- 20. The Recovery Collaborative Group. Effect of Dexamethasone in Hospitalized Patients with COVID-19. N Engl J Med. 2021 Feb 25;384(8):693-704.
- 21. Jeronimo CMP et al., for the Metcovid Team. Methylprednisolone as Adjunctive Therapy for Patients Hospitalized With COVID-19 (Metcovid): A Randomised, Double-Blind, Phase Ilb, Placebo-Controlled Trial. Clin Infect Dis. 2021 May 4:72(9):e373-e381.
- 22. Writing Committee for the REMAP-CAP Investigators. Effect of Hydrocortisone on Mortality and Organ Support in Patients With Severe COVID-19: The REMAP-CAP COVID-19 Corticosteroid Domain Randomized Clinical Trial. JAMA. 2020 Sep 2. doi: 10.1001/jama.2020.17022.
- 23. Dequin PF et al., CAPE COVID Trial Group and the CRICS-TriGGERSep Network. Effect of Hydrocortisone on 21-Day Mortality or Respiratory Support Among Critically III Patients With COVID-19: A Randomized Clinical Trial. JAMA. 2020 Sep 2. doi: 10.1001/jama.2020.16761.
- 24. WHO Rapid Evidence Appraisal for COVID-19 Therapies (REACT) Working Group. Association Between Administration of Systemic Corticosteroids and Mortality Among Critically III Patients With COVID-19: A Meta-analysis. JAMA. 2020 Sep 2. doi: 10.1001/jama.2020.17023.

#### **Tocilizumab**

- 25. FDA Fact Sheet for Healthcare Providers for Emergency Use Authorization (EUA) of tocilizumab https://www.fda.gov/media/150321/download
- 26. FDA Fact Sheet for Patients And Parent/Caregivers for Emergency Use Authorization (EUA) of tocilizumab https://www.fda.gov/media/150320/download
- 27. RECOVERY Collaborative Group. Tocilizumab in patients admitted to hospital with COVID-19 (RECOVERY): a randomised, controlled, open-label, platform trial. Lancet. 2021 May 1;397(10285):1637-1645.
- 28. REMAP-CAP Investigators. Interleukin-6 Receptor Antagonists in Critically III Patients with Covid-19. N Engl J Med. 2021;384(16):1491-1502.

#### **Baricitinib**

- 29. FDA Fact Sheet for Healthcare Providers for Emergency Use Authorization (EUA) of baricitinib https://www.fda.gov/media/143823/download
- 30. FDA Fact Sheet for Patients And Parent/Caregivers for Emergency Use Authorization (EUA) of baricitinib https://www.fda.gov/media/143824/download
- 31. COV-BARRIER Study Group. Efficacy and safety of baricitinib for the treatment of hospitalised adults with COVID-19 (COV-BARRIER): a randomised, double-blind, parallel-group, placebo-controlled phase 3 trial. Lancet Respir Med 2021; 9:1407–18.

(Age <25 years)



Aim: To provide guidance for management of COVID-19.

#### **COVID-19 Interim Clinical Guidance Workgroup**

Mary Ullman PharmD (ASP/ID) [Lead], Bill Pomputius MD (ASP/ID) [Lead], Katie Brunsberg MD (Hospitalist and Quality) [Lead], Anu Kalaskar MD (ID), Pamela Chawla MD (Primary Care), Tamara Pozos MD PhD (Immunology), Lane Miller MD (Hem/Onc), Jeffrey Nowak MD (Intensive Care), Brooke Moore MD (Pulmonology), Kelly Bergmann (ED)

Created: 04/08/20 by Christina Koutsari PharmD PhD (ASP/ID) [Lead], Bill Pomputius MD (ASP/ID) [Lead], Katie Brunsberg MD (Hospitalist) [Lead], Anu Kalaskar MD (ID), Pamela Chawla MD (Primary Care), Tamara Pozos MD PhD (Immunology), Manar Abdalgani MBBS (Immunology), Lane Miller MD (Hem/Onc), Jeffrey Nowak MD (Intensive Care), Brooke Moore MD (Pulmonology), Gabrielle Hester MD MS (Quality)

Revised: 05/11/20 1) Added criteria for use and dosing of remdesivir per Emergency Use Authorization; 2) Revised criteria for use of remdesivir via compassionate use (eIND); 3) Added required laboratory monitoring prior to initiation and daily during remdesivir therapy; 4) Replaced cytokine panel with rapid 4-plex cytokine panel; 5) Included recommendation that doxycycline is preferred over azithromycin for empiric coverage of atypical bacteria if hydroxychloroquine is considered due to QTc prolongation concerns; 6) Included recommendation for hydroxychloroquine dose reduction by 50% if GFR < 10 mL/min, hemodialysis or peritoneal dialysis per hydroxychloroquine Emergency Use Authorization; 7) Added Appendix A for guidance with QTc prolonging pharmacotherapies; 8) Updated literature

Revised: 05/25/20 1) Added convalescent plasma as investigational option for prophylaxis or treatment of COVID-19; 2) Added Appendix B with eligibility criteria for use of convalescent plasma; 3) Updated literature

Revised: 05/29/20 1) Added clarification regarding remdesivir dosing in pediatric patients ≤ 7 days of age or born prematurely; 2) Updated literature

Revised: 06/17/20 1) Added restriction of remdesivir to Infectious Disease per P&T Committee approval on 6.17.20; 2) Removed hydroxychloroquine as treatment option; 3) Removed doxycycline as alternative to azithromycin if concern for community-acquired pneumonic bacterial coinfection; 4) Removed original Appendix A that provided guidance with QTc prolonging pharmacotherapies; 5) Updated literature

Revised: 07/07/20 1) Added dexamethasone as treatment consideration in patients requiring supplemental oxygen or mechanical ventilation; 2) Added methylprednisolone and prednisolone as alternative agents if dexamethasone is unavailable; 3) Updated convalescent plasma eligibility criteria for the pediatric study to: a) include medically complex children on technological support associated with developmental delay or genetic anomalies, and b) extend the onset of symptoms up to 7 days; 4) Updated convalescent plasma eligibility criteria for the adult study to include patients with clinically-suspected SARS-CoV-2 infection; 5) Updated literature

Revised: 09/25/20 1) Removed tocilizumab as treatment consideration in patients with severe pneumonia or ARDS; 2) Removed IVIG 400 mg/kg/day × 3 days as treatment consideration if admission or follow-up labs suggest HLH physiology or cytokine storm; providers are now referred to discuss with Immunology use of biologic modulators, including IVIG, for severe pneumonia or ARDS; 3) Included dosing weight recommendations for IVIG replacement; 4) Removed Gilead's compassionate use program (https://rdvcu.gilead.com/) as a pathway for obtaining remdesivir; 5) Replaced IRB 2005-051 (Expanded Access Program via Mayo Clinic) for use of convalescent plasma in adults with the FDA Emergency Use Authorization (EUA); 6) Removed language regarding use of convalescent plasma for prophylaxis or treatment prior to or during hospitalization not interfering with eligibility for initiation or continuation of remdesivir (both remdesivir and convalescent plasma are available via EUA with no restrictions in place); 7) Updated literature

Revised: 01/20/21 1) Added rapid antigen as confirmation for COVID-19; 2) Revised daily labs to daily labs as clinically indicated; 3) Removed the rapid 4-plex cytokine panel and the immune comprehensive panel from the admission labs (except in ARDS); 4) Added prothrombin time (PT) as required lab prior to and during remdesivir treatment; 5) Added a new section on page 3 for asymptomatic patients with high-risk SARS-CoV-2 exposure; 6) Added guiding statements "May consider" vs. "Consider" vs. Recommend" for all COVID-19 therapeutic agents; 7) Added anti-SARS-CoV-2 monoclonal antibodies as a treatment option for eligible, non-hospitalized patients with mild or moderate COVID-19; 8) Included information about timing of Covid-19 vaccination after administration of monoclonal antibodies treatment for Covid-19 or convalescent plasma; 9) Revised the remdesivir section to include information on a) patient populations that are covered under FDA approval vs. FDA EUA; b) the process for using remdesivir in patients < 3.5 kg who are not covered under FDA approval or EUA; and c) recommendations for remdesivir use in renal and hepatic dysfunction; 10) Added documentation and reporting requirements for FDA EUA convalescent plasma, FDA EUA remdesivir, and remdesivir use in patients <3.5 kg; 11) Added recommendations for oseltamivir use when influenza is co-circulating with COVID-19; 12) Removed convalescent plasma from Severe Pneumonia and ARDS; 13) Updated literature

Revised: 02/10/21 Removed convalescent plasma for confirmed infection or high risk exposure in pediatric patients (IRB 2005-044) as a treatment option

Revised: 03/30/21 1) ARDS and critical pneumonia (pneumonia requiring invasive mechanical ventilation or ECMO) were categorized under the same clinical severity (page 5); 2) Included tocilizumab in combination with systemic corticosteroids as a treatment consideration for certain hospitalized patients who are exhibiting rapid respiratory decompensation due to COVID-19

Revised: 04/17/21 Removed bamlanivimab monotherapy for outpatient treatment of mild to moderate COVID-19 in response to the bamlanivimab EUA revocation by the FDA on 4/16/21

Revised: 06/03/21 Included casirivimab/imdevimab for outpatient treatment of mild to moderate COVID-19 per the expanded criteria of the 5/17/21 FDA EUA

(Age <25 years)



Aim: To provide guidance for management of COVID-19.

#### **COVID-19 Interim Clinical Guidance Workgroup**

Mary Ullman PharmD (ASP/ID) [Lead], Bill Pomputius MD (ASP/ID) [Lead], Katie Brunsberg MD (Hospitalist and Quality) [Lead], Anu Kalaskar MD (ID), Pamela Chawla MD (Primary Care), Tamara Pozos MD PhD (Immunology), Lane Miller MD (Hem/Onc), Jeffrey Nowak MD (Intensive Care), Brooke Moore MD (Pulmonology), Kelly Bergmann (ED)

#### Revisions (continued)

Revised: 09/13/21 1) Included casirivimab/imdevimab for outpatient post-exposure prophylaxis of COVID-19; 2) Added tocilizumab FDA EUA information; 3) Included baricitinib in combination with systemic corticosteroids as an FDA EUA treatment consideration for certain hospitalized patients who are exhibiting rapid respiratory decompensation due to COVID-19 and tocilizumab is not available

Revised: 10/14/21 1) Removed convalescent plasma as treatment consideration on case-by-case basis in hospitalized patients with primary or secondary immunodeficiency; 2) Included strong recommendation to discuss with Immunology before initiating biologic modulators under EUA (tocilizumab, baricitinib) in patients < 12 years of age or in patients with COVID symptoms for < 1 week; 3) Included statement to use baricitinib with caution if increased risk of GI perforation

Revised: 10/20/21 1) Removed first 2 pages of original guideline providing general overview of clinical management. Information from the removed pages was incorporated in the remaining guideline (e.g. supportive care, anticoagulation, treatment of suspected community-acquired bacterial coinfection)

Revised: 11/22/21 1) Included casirivimab/imdevimab post-exposure prophylaxis for eligible patients with asymptomatic COVID-19; 2) Reduced BMI percentile from 99th to 95th for eligibility of pediatric patients for casirivimab/imdevimab

Revised: 12/30/21 1) Removed casirivimab/imdevimab as an option for treatment and post-exposure prophylaxis of mild or moderate COVID-19 in high risk patients due to its clack of activity against the Omicron variant; 1) Added sotrovimab as treatment option for mild or moderate COVID-19 in patients at high risk for progressing to severe disease.

Revised: 1/26/22 1) Added remdesivir for treatment of mild-to-moderate COVID-19 in patients at high risk of progression to severe COVID-19; 2) Implemented restriction of sotrovimab to Infectious Disease providers.

Revised: 2/7/22 1) Added nirmatrelvir/ritonavir (Paxlovid<sup>™</sup>) for treatment of mild-to-moderate COVID-19 in patients at high risk of progression to severe COVID-19; 2) Added two summary pages with overview of disease management

Revised: 3/11/22 1) Reduced timeframe for sotrovimab administration from 10 days to 7 days of symptom onset per sotrovimab EUA update; 2) Added comparison table with outpatient COVID-19 therapeutics

Revised: 4/3/22 1) Removed sotrovimab as an option for treatment of mild to moderate COVID-19 in high risk patients due to its lack of activity against the Omicron BA.2 subvariant; 1) Added bebtelovimab as treatment option for mild to moderate COVID-19 in patients at high risk for progressing to severe COVID-19.

Revised: 4/28/22 1) Removed remdesivir EUA to align with the expansion of FDA approval to include pediatric patients who are at least 28 days of age weighing at least 3 kg.

Revised: 6/16/22 1) Removed the ID approval requirement for Paxlovid™ and included a Paxlovid™ prescribing process for guidance.

Revised: 7/11/22 1) Added reference to guidance document for use of tixagevimab/cilgavimab (Evusheld™) for COVID-19 pre-exposure prophylaxis (page 1).

Revised: 11/30/22 1) Removed bebtelovimab as an option for treatment of mild to moderate COVID-19 in high risk patients due to its lack of activity against the Omicron BQ.1 and BQ.1.1.subvariants.

Revised: 1/10/23 1) Included the FDA approval of tocilizumab for adult patients. Tocilizumab remains under EUA for pediatric patients ≥ 2 years of age to < 18 years of age; 2) Revised Note 3 [Antibiotic recommendations for suspected or proven bacterial coinfection (community-acquired)] to refer to the updated Children's Minnesota CAP guideline.

Revised: 1/26/23 1) Removed tixagevimab/cilgavimab (Evusheld™) as an option for pre-exposure prophylaxis of COVID-19 due to the removal of the Emergency Use Authorization by the FDA.

Revised: 3/29/23 1) Removed the note "Outpatient remdesivir is not routinely available at Children's Minnesota". Outpatient remdesivir was implemented on 3/29/23.

(Age <25 years)



Aim: To provide guidance for management of COVID-19.

#### **COVID-19 Interim Clinical Guidance Workgroup**

Mary Ullman PharmD (ASP/ID) [Lead], Bill Pomputius MD (ASP/ID) [Lead], Katie Brunsberg MD (Hospitalist and Quality) [Lead], Anu Kalaskar MD (ID), Pamela Chawla MD (Primary Care), Tamara Pozos MD PhD (Immunology), Lane Miller MD (Hem/Onc), Jeffrey Nowak MD (Intensive Care), Brooke Moore MD (Pulmonology), Kelly Bergmann (ED)

#### **Revisions (continued)**

Revised: 7/21/23 1) Removed ID restriction for inpatient remdesivir; 2) Included FDA-approval of Paxlovid™ in adults; 3) Updated criteria for use of immunomodulators to align with NIH recommendations; 4) Added clarification that clinical benefit of remdesivir in severe and critical illness is greatest if it is initiated within 10 days of symptom onset; 5) Removed contraindication of remdesivir in patients with eGFR < 30 mL/min to align with recent revision of the remdesivir package insert allowing use without dose adjustment in patients with eGFR<30 mL/min, including those on dialysis; 6) Transitioned from the MDH consensus high-risk criteria to the NIH high-risk criteria for treatment of mild to moderate COVID-19 in patients at high risk for severe COVID-19.

Revised: 11/8/23: 1) Removed required discussion inpatient with ID for remdesivir. 2) Modified lab recommendations. 3) Added notes to remdesivir usage for younger children admitted for bronchiolitis, croup, asthma. 4) Review of NIH Guidelines updates as of 12/5/2023

Revised: 9/13/24: Updated links for risk stratification to PIDS in place of retired NIH guidelines. Updated treatment guidelines to match PIDS.

Revised 4/1/25: Updated age and weight based remdesivir requirements based on package insert.