CLINICAL GUIDELINE

COVID-19: MEDICAL MANAGEMENT

(Age <25 years)

Children's MINNESOTA

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

Patient with COVID-19 (confirmed or presumed) → Appropriate PPE, rooming and staffing. Educate family on positive test and isolation.

Assess COVID-19 Illness Level.
Screen all patients for abnormal immunity: severe or unusual infections in the past, poor growth, a genetic inflammatory disorder, family history of immune disorder, or has secondary immunosuppression. Consult 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_2 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 COVID VTE guideline.

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.

Severe

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

- **Pediatric patients**: SpO_2< 90% or acute respiratory distress (e.g. grunting, retractions, tachypnea)
- **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 COVID VTE guideline.

COVID-19 Therapeutics: see page 5
- New/Stable low flow oxygen requirement: remdesivir*
- Increasing low flow oxygen requirement: remdesivir*, consider corticosteroids
- High flow oxygen: remdesivir* + corticosteroids
  - If not showing improvement in oxygenation within 24 hours of steroid initiation, consult ID/immunology to discuss other therapies (see page 5)

See current NIH guidelines

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 COVID VTE guideline.

COVID-19 Therapeutics:
- COVID-19 Therapeutics: see page 6 and current NIH guidelines

*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.[2] Utilize shared decision making with family. Consider viral co-infections in your decision management.

Disclaimer: This guideline is designed for general use with most patients; each clinician should use their own independent judgment to meet the needs of each individual patient. This guideline is not a substitute for professional medical advice, diagnosis or treatment.

COVID-19: MEDICAL MANAGEMENT

(Age <25 years)

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

Treatment of Mild-to-Moderate COVID-19 in Patients at High Risk for Progression to Severe COVID-19

Oral (PO) ← **1st line** → **Intravenous (IV)**

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 adult patients
- Within 5 days of symptom onset
- Ability to swallow pills
- eGFR ≥ 30 mL/min
- No severe hepatic impairment (Child-Pugh Class C)
- No contraindicated drug interactions
- Outpatient or inpatient mild-to-moderate COVID-19

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

Remdesivir

Must meet all criteria below:

- ≥ 28 days of age and weighing ≥ 3 kg to 24 years of age
- 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.

COVID-19: MEDICAL MANAGEMENT

(Age <25 years)

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

Comparison of Outpatient Therapeutics for Mild-to-Moderate COVID-19 (Omicron variant)

	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	≥ 28 days of age AND ≥ 3 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)

NNT: Number needed to treat

COVID-19: MEDICAL MANAGEMENT

(Age <25 years)

Children's MINNESOTA

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 ≥ 28 days of age and weighing ≥ 3 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 weighing 3 kg to < 40 kg:** 5 mg/kg IV × 1, followed by 2.5 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** • 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™ 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 ≥ 28 days of age and weighing ≥ 3 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 weighing 3 kg to < 40 kg:** 5 mg/kg IV × 1, followed by 2.5 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	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

COVID-19: MEDICAL MANAGEMENT

(Age <25 years)

Children's MINNESOTA

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

CLINICAL SEVERITY	THERAPEUTIC AGENTS	COMMENTS	MONITORING
Severe Illness	**Consider referencing the current NIH COVID-19 treatment guidelines when making choices regarding therapeutic agents:** https://www.covid19treatmentguidelines.nih.gov/ **Consider 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 illness severity **Consider Remdesivir (clinical benefit of remdesivir is greatest if it is initiated within 10 days of symptom onset)** • FDA approval applies to pediatric patients ≥ 28 days of age and weighing ≥ 3 kg, and to all adult patients • 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.[2] Utilize 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 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, treatment can be extended to up to a total of 10 days. Discontinue when meets discharge criteria. **Consider Biologic Modulators (tocilizumab, baricitinib):** for patients who require HFNC (or NIV) and do not have rapid (e.g., within 24 hours) improvement in oxygenation after initiation of dexamethasone, baricitinib or tocilizumab may be considered in patients ≥ 2 yo. Recommendations are extrapolated from data in adults. **Such patients should be transferred to the PICU** and have involvement of PICU/immuno/ID in that consideration. See page 6 for further information. **May Consider Empiric Antibiotics** • **If concern for concurrent community-acquired bacterial pneumonia (incidence <10%):** see Note 3 • **If recent or prolonged hospitalization, consider coverage for health-care associated pneumonia:** Cefepime IV plus vancomycin IV	**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** 1. https://www.covid19treatmentguidelines.nih.gov/ 2. COVID-19 drug interactions http://www.covid19-druginteractions.org/

COVID-19: MEDICAL MANAGEMENT

(Age <25 years)

Children's MINNESOTA

Aim: To provide guidance for management of Covid-19

CLINICAL SEVERITY	THERAPEUTIC AGENTS	COMMENTS	MONITORING

Critical Illness	**Consider referencing the current NIH COVID-19 treatment guidelines when making choices regarding therapeutic agents:** https://www.covid19treatmentguidelines.nih.gov/
	
	Recommend 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 illness severity
	
	Consider remdesivir if patient is not yet on invasive mechanical ventilation or ECMO (clinical benefit of remdesivir is greatest if it is initiated within 10 days of symptom onset)
	• FDA approval applies to pediatric patients ≥ 28 days of age and weighing ≥ 3 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
	  • **Pediatric patients ≥ 28 days of age weighing 3 kg to < 40 kg:** 5 mg/kg IV × 1, followed by 2.5 mg/kg q24h
	• **Duration**:
	  • **No mechanical ventilation or ECMO**: 5 days. Discontinue when meets discharge criteria. If no clinical improvement after a total of 5 days of treatment, treatment can be extended to up to a total of 10 days
	  • **Mechanical ventilation or ECMO**: 10 days. For patients who progress to requiring mechanical ventilation or ECMO after they initiate remdesivir, the Panel suggests continuing remdesivir until the treatment course is completed.
	
	Consider Biologic Modulators (tocilizumab, baricitinib): For patients who require HFNC or NIV and do not have rapid (e.g., within 24 hours) improvement in oxygenation after initiation of dexamethasone, baricitinib or tocilizumab may be considered in patients ≥ 2 yo. Recommendations are extrapolated from data in adults. Consult Immunology and/or Infectious Disease if considering tocilizumab in patients <12 yo or if considering baricitinib in any age. Also, may consider rheumatology phone consult for specific recommendations on dosing and contraindications for these medications.
	•**Tocilizumab [Restricted to Immunology, Hem/Onc, and PICU] in combination with systemic corticosteroids.** Specifically**:** Tocilizumab can be considered in children without rapid (e.g. within 24 hours) improvement in oxygenation after initiation of dexamethasone.
	•Tocilizumab is **FDA-approved in adults** but under an **EUA for pediatric patients** ages ≥ 2 years to < 18 years of age.
	  ▪ < 30 kg (EUA for ages ≥ 2 years): 12 mg/kg actual body weight × 1
	  ▪ ≥ 30 kg: 8 mg/kg actual body weight (max 800 mg) × 1
	  ▪ One additional dose may be given ≥ 8 hours after initial dose if patient worsening or not improving. See **Note 4** for tocilizumab counselling/reporting EUA requirements.
	
	• **If tocilizumab is not available**, **consider Baricitinib** via EUA **[Restricted to Immunology, Hem/Onc, and PICU] in combination with systemic corticosteroids. Baricitinib is BROADER cytokine blocker than tocilizumab.** See **Note 5** for EUA documentation/reporting requirements.
	  ▪ 2 to < 9 years old (EUA for ages ≥ 2 years): 2 mg PO once daily for 14 days or until hospital discharge, whichever comes first
	  • ≥ 9 years old: 4 mg PO once daily for 14 days or until hospital discharge, whichever comes first
	
	Consider Empiric Antibiotics
	• **if concern for concurrent community-acquired bacterial pneumonia (incidence <10%):** see Note 3
	• **If recent or prolonged hospitalization, consider coverage for health-care associated pneumonia:** Cefepime IV plus vancomycin IV
		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 EUA Baricitinib Fact Sheet for Providers
		• FDA EUA Baricitinib Fact Sheet for Patients
		• FDA EUA Baricitinib FAQs
		
		Baricitinib warnings/contraindications
		• Not recommended if active tuberculosis or other active non-SARS-CoV-2 infection, or chronic/recurrent infection; Renal dialysis; ESRD; AKI
		• Consider interruption until ALC is ≥200 cells/μL and ANC is ≥500 cells/μL
		• Use with caution if increased risk of GI perforation
		• VTE prophylaxis recommended for adults and adolescents. Consult Hem/Onc re: younger patients
		
		EUA: Emergency Use Authorization
			All hospitalized patients
			• **On admission:** CBC+diff, CRP, CMP, blood culture, serum to save (≥ 3 mL). Labs per COVID VTE guideline if starting prophylaxis
			
			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. https://www.covid19treatmentguidelines.nih.gov/
			2. COVID-19 drug interactions http://www.covid19-druginteractions

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 FDA EUA Paxlovid™ Fact Sheet for Healthcare Providers and provided them with the FDA EUA Paxlovid™ Fact Sheet for Healthcare Providers; 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 Tocilizumab EUA Fact Sheet for Patients and Caregivers 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 us_drug.safety@gene.com

NOTE 5: Baricitinib FDA EUA Documentation and Reporting Requirements
- 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

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

REFERENCES

Corticosteroids

18. The Recovery Collaborative Group. Effect of Dexamethasone in Hospitalized Patients with COVID-19. N Engl J Med. 2021 Feb 25;384(8):693-704.
19. Jeronimo CMP et al., for the Metcovid Team. Methylprednisolone as Adjunctive Therapy for Patients Hospitalized With COVID-19 (Metcovid): A Randomised, Double-Blind, Phase IIb, Placebo-Controlled Trial. Clin Infect Dis. 2021 May 4;72(9):e373-e381.
20. 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.
21. 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 Ill Patients With COVID-19: A Randomized Clinical Trial. JAMA. 2020 Sep 2. doi: 10.1001/jama.2020.16761.
22. WHO Rapid Evidence Appraisal for COVID-19 Therapies (REACT) Working Group. Association Between Administration of Systemic Corticosteroids and Mortality Among Critically Ill Patients With COVID-19: A Meta-analysis. JAMA. 2020 Sep 2. doi: 10.1001/jama.2020.17023.

Tocilizumab

23. FDA Fact Sheet for Healthcare Providers for Emergency Use Authorization (EUA) of tocilizumab https://www.fda.gov/media/150321/download
24. FDA Fact Sheet for Patients And Parent/Caregivers for Emergency Use Authorization (EUA) of tocilizumab https://www.fda.gov/media/150320/download
25. 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.
26. REMAP-CAP Investigators. Interleukin-6 Receptor Antagonists in Critically Ill Patients with Covid-19. *N Engl J Med*. 2021;384(16):1491-1502.

Baricitinib

27. FDA Fact Sheet for Healthcare Providers for Emergency Use Authorization (EUA) of baricitinib https://www.fda.gov/media/143823/download
28. FDA Fact Sheet for Patients And Parent/Caregivers for Emergency Use Authorization (EUA) of baricitinib https://www.fda.gov/media/143824/download
29. 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.

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

REFERENCES

Guidelines, Expert Reviews, Evidence Summaries

1. National Institutes of Health COVID-19: Clinical Management of **Adults**. https://www.covid19treatmentguidelines.nih.gov/management/clinical-management-of-adults/clinical-management-of-adults-summary/
2. National Institutes of Health COVID-19: Clinical Management of **Children**. https://www.covid19treatmentguidelines.nih.gov/management/clinical-management-of-children/clinical-management-of-children-summary/ 3.
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

Drug Interactions

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

Nirmatrelvir/Ritonavir (Paxlovid™)

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

Remdesivir

11. Remdesivir (Veklury) Prescribing Information: https://www.gilead.com/-/media/files/pdfs/medicines/covid-19/veklury/veklury_pi.pdf
12. 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.
13. Beigel JH et al. Remdesivir for the treatment of Covid-19 – Final report. N Engl J Med. 2020;383(19):1813-1826.
14. 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.
15. 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.
16. WHO Solidarity Trial Consortium. Repurposed Antiviral Drugs for Covid-19 - Interim WHO Solidarity Trial Results. N Engl J Med. 2021; 384(6):497-511.
17. 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.

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

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™) 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.

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