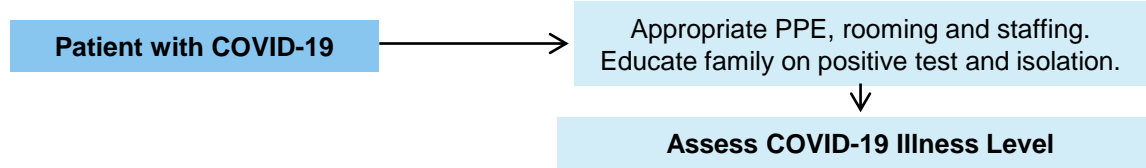


Aim: To provide guidance for management of COVID-19.

As of 1/26/23, there are no options available for COVID-19 pre-exposure prophylaxis.



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 O₂ requirement; able to self-hydrate (may be after initial fluid support). Suitable for outpatient care.

Supportive care 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
- Consults:** none
- Labs:** If meets criteria to start VTE prophylaxis, CBC+diff, BMP, PT/PTT/fibrinogen, D-dimer. Consider other labs based on clinical scenario.
- Consider CXR**
- VTE prophylaxis:** if patient ≥ 12 years of age OR has additional VTE risk factors per [COVID VTE guideline](#).
- Escalate illness level if clinical status worsens.

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:** SpO₂ < 90% or acute respiratory distress (e.g. grunting, retractions, tachypnea)
- Adolescent and adult patients:** Fever or suspected respiratory infection plus one of the following:
 - Respiratory rate > 30 breaths/min
 - SpO₂ ≤ 94% on room air
 - Severe respiratory distress (e.g. dyspnea, retractions)

- Supportive care
- Discussion with Infectious Disease**
- Labs:** CBC+diff, CRP, CMP, ferritin, D-dimer, IgA, IgG, IgM, blood culture, serum to save (≥ 3 mL). If meets criteria for VTE prophylaxis, also obtain PT/PTT/fibrinogen.
- CXR**
- VTE prophylaxis:** if patient ≥ 12 yrs age OR has additional VTE risk factors per [COVID VTE guideline](#).
- IgG replacement** as indicated: see p. 5.

COVID-19 Therapeutics

- Remdesivir
- Systemic corticosteroids

See p. 5 for more detail.

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

- Supportive care
- Consults:** Infectious Disease, Immunology, Pulmonology, and other specialists as indicated.
- Labs:** CBC+diff, CRP, CMP, ferritin, D-dimer, PT/PTT/fibrinogen, troponin, IgA, IgG, IgM, cytokine storm 4-plex panel, immune status panel (ISP), blood culture, serum to save (≥ 3 mL).
- CXR**
- VTE prophylaxis:** if patient ≥ 12 years of age OR has additional VTE risk factors per [COVID VTE guideline](#).
- IgG replacement** as indicated: see p 6.

COVID-19 Therapeutics

- Remdesivir
- Systemic corticosteroids
- Tocilizumab or baricitinib

See p. 6 for more detail.

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 (Contact Children's Physician Access at 612-343-2121 to discuss with the ID provider on call for the St. Paul campus.)

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 Not readily available option at Children's Minnesota
Side effects	Dysgeusia (6%), diarrhea (3%), hypertension (1%), myalgia (1%)	Nausea (6%), transaminase elevation (~2% of hospitalized patients with moderate COVID-19)
Supply	Donated by the Federal government.	Commercially available

NNT: Number needed to treat

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

CLINICAL SEVERITY	THERAPEUTIC AGENTS	COMMENTS	MONITORING
Mild illness	<p>SUPPORTIVE CARE (Note 1)</p> <p>Consider Nirmatrelvir/Ritonavir (Paxlovid™) or Remdesivir in patients at high-risk for progression to severe COVID-19</p> <ul style="list-style-type: none"> 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. <p>Dosing Paxlovid™:</p> <ul style="list-style-type: none"> Paxlovid is FDA-approved in adults but under an EUA for pediatric patients 12-17 years of age weighing ≥ 40 kg. Dose: <ul style="list-style-type: none"> eGFR ≥ 60 mL/min: Nirmatrelvir 300 mg (2 × 150 mg tablets) and ritonavir 100 mg (1 × 100 mg tablet) twice daily × 5 days. eGFR 30 to < 60 mL/min: Nirmatrelvir 150 mg (1 × 150 mg tablet) and 100 mg ritonavir (1 × 100 mg tablet) twice daily × 5 days. <p>Dosing Remdesivir:</p> <ul style="list-style-type: none"> FDA approval applies to pediatric patients ≥ 28 days of age and weighing ≥ 3 kg, and to all adult patients Dose: <ul style="list-style-type: none"> 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) <p>See Note 2 (Paxlovid™) on p.7 for EUA documentation/reporting requirements</p>	<p>Provider Tools for Paxlovid™</p> <ul style="list-style-type: none"> 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 <p>Provider Tools for Remdesivir</p> <ul style="list-style-type: none"> FDA remdesivir package insert <p>EUA: Emergency Use Authorization</p>	<p>Patients on Remdesivir</p> <ul style="list-style-type: none"> Labs once prior to initiation and trend as clinically indicated: AST, ALT, alkaline phosphatase, T/D bilirubin, PT (PT at least on initiation)
Moderate Illness	<p>SUPPORTIVE CARE (Note 1)</p> <p>VTE PROPHYLAXIS if hospitalized and as indicated per VTE prophylaxis in COVID-19 guideline</p> <p>Consider Nirmatrelvir/Ritonavir (Paxlovid™) or Remdesivir in patients at high-risk for progression to severe COVID-19</p> <ul style="list-style-type: none"> 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. <p>Dosing Paxlovid™:</p> <ul style="list-style-type: none"> Paxlovid is FDA-approved in adults but under an EUA for pediatric patients 12-17 years of age weighing ≥ 40 kg. Dose: <ul style="list-style-type: none"> eGFR ≥ 60 mL/min: Nirmatrelvir 300 mg (2 × 150 mg tablets) and ritonavir 100 mg (1 × 100 mg tablet) twice daily × 5 days. eGFR 30 to < 60 mL/min: Nirmatrelvir 150 mg (1 × 150 mg tablet) and 100 mg ritonavir (1 × 100 mg tablet) twice daily × 5 days. <p>Dosing Remdesivir:</p> <ul style="list-style-type: none"> FDA approval applies to pediatric patients ≥ 28 days of age and weighing ≥ 3 kg, and to all adult patients Dose: <ul style="list-style-type: none"> 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) <p>See Note 2 (Paxlovid™) on p.7 for EUA documentation/reporting requirements</p>	<p>Provider Tools for Paxlovid™</p> <ul style="list-style-type: none"> 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 <p>Provider Tools for Remdesivir</p> <ul style="list-style-type: none"> FDA remdesivir package insert <p>EUA: Emergency Use Authorization</p>	<p>Lab monitoring as clinically relevant. If symptom progression, refer to severe/critical pathway.</p> <p>Patients on Remdesivir</p> <ul style="list-style-type: none"> Labs once prior to initiation and trend as clinically indicated: AST, ALT, alkaline phosphatase, T/D bilirubin, PT (PT at least on initiation)

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

CLINICAL SEVERITY	THERAPEUTIC AGENTS	COMMENTS	MONITORING
<p>Severe Illness</p>	<p>SUPPORTIVE CARE (Note 1)</p> <p>VTE PROPHYLAXIS as indicated per VTE prophylaxis in COVID-19 guideline</p> <p>Recommend Systemic Corticosteroids</p> <ul style="list-style-type: none"> Dexamethasone 0.15 mg/kg (max 6 mg/dose) PO/NG/IV q24h for up to 10 days for patients requiring persistent supplemental oxygen Recommend against use in patients not requiring supplemental oxygen In preterm neonates, risks vs. benefits should be considered based on gestational age, postnatal age, and illness severity <p>Recommend Remdesivir (clinical benefit of remdesivir is greatest if it is initiated within 10 days of symptom onset)</p> <ul style="list-style-type: none"> FDA approval applies to pediatric patients ≥ 28 days of age and weighing ≥ 3 kg, and to all adult patients Dose: <ul style="list-style-type: none"> 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 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 <p>May Consider Empiric Antibiotics</p> <ul style="list-style-type: none"> 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 <p>Consider Replacement Dose of IVIG if low IgG for age (Discuss with Immunology if questions)</p> <p>If initial IgG is below the following age-based thresholds, consider IVIG at 400 mg/kg (based on ideal body weight) × 1 dose: 0 to 1 month: <400 mg/dL; 1 to < 7 month: <200 mg/dL; 7 month to <3 year: < 250 mg/dL; 3 to < 6 year: <350 mg/dL; 6 years to adulthood <500 mg/dL</p> <p>Consider Biologic Modulators (tocilizumab, baricitinib): Recommendations are extrapolated from data in adults. Proposed benefit is to minimize damage from developing cytokine storm in 2nd stage (typically 2nd week) of acute infection. Strongly recommend discussing with Immunology before initiating tocilizumab or baricitinib in patients < 12 years of age or in patients with COVID symptoms for < 1 week.</p> <ul style="list-style-type: none"> 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. <ul style="list-style-type: none"> < 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 <p>Tocilizumab is FDA-approved in adults but under an EUA for pediatric patients ages ≥ 2 years to < 18 years of age.</p> <p>One additional dose may be given ≥ 8 hours after initial dose if patient worsening or not improving. See Note 4 for tocilizumab EUA counselling/reporting requirements.</p> <ul style="list-style-type: none"> 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 baricitinib EUA documentation/reporting requirements. <ul style="list-style-type: none"> 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 	<p>Systemic Corticosteroids Recommend gastric ulcer prophylaxis</p> <p>Systemic Corticosteroid Alternatives (If dexamethasone is not available)</p> <ul style="list-style-type: none"> 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 <p>Provider Tools for Tocilizumab</p> <ul style="list-style-type: none"> FDA Tocilizumab package insert (approved indication) FDA EUA Tocilizumab Fact Sheet for Providers FDA EUA Tocilizumab Fact Sheet for Patients FDA EUA Tocilizumab FAQs <p>Tocilizumab should be avoided or benefit/risk assessed if any of the following:</p> <ul style="list-style-type: none"> 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) <p>Provider Tools for Baricitinib</p> <ul style="list-style-type: none"> FDA EUA Baricitinib Fact Sheet for Providers FDA EUA Baricitinib Fact Sheet for Patients FDA EUA Baricitinib FAQs <p>Baricitinib warnings/contraindications</p> <ul style="list-style-type: none"> 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 <p>EUA: Emergency Use Authorization</p>	<p>All hospitalized patients</p> <ul style="list-style-type: none"> On admission: CBC+diff, CRP, CMP, ferritin, D-dimer, IgA, IgG, IgM, blood culture, serum to save (≥ 3 mL) During hospitalization <ul style="list-style-type: none"> Daily labs as clinically indicated If symptom progression (persistent high fever, worsening respiratory distress, increasing O2 requirements, or transfer to ICU): CBC+diff, CRP, CMP, ferritin, D-dimer, PT/PTT/fibrinogen, troponin, IgA, IgG, IgM, cytokine storm 4-plex panel, immune status panel (ISP), blood culture, serum to save (≥ 3 mL) <p>Patients on Remdesivir</p> <ul style="list-style-type: none"> Labs prior to initiation and daily: BMP, CBC+diff, AST, ALT, alkaline phosphatase, T/D bilirubin, PT (PT at least on initiation) Consider discontinuation if ALT > 10 × ULN during treatment Discontinue if ALT elevation is accompanied by s/s of liver inflammation <p>Patients on Empiric Antibiotics</p> <p>Need, duration, and spectrum of antibiotics should be assessed daily based on microbiology results and clinical status</p> <p>Patients on Tocilizumab</p> <p>Monitor for hepatotoxicity, leukopenia, neutropenia, infection reactivation (e.g. HSV, VZV, TB, Strongyloides), GI perforation</p> <p>Patients on Baricitinib</p> <ul style="list-style-type: none"> Labs prior to initiation and daily: eGFR, ALT, AST, CBC+diff Requires dose adjustments for drug interactions and if abnormal renal, hematological and hepatic labs. Monitor for thromboembolism (PE, DVT), GI perforation <p>Useful websites COVID-19 drug interactions http://www.covid19-druginteractions.org/</p>

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CLINICAL SEVERITY	THERAPEUTIC AGENTS	COMMENTS	MONITORING
<p>Critical Illness</p>	<p>SUPPORTIVE CARE (Note 1)</p> <p>VTE PROPHYLAXIS as indicated per VTE prophylaxis in COVID-19 guideline</p> <p>Recommend Systemic Corticosteroids</p> <ul style="list-style-type: none"> Dexamethasone 0.15 mg/kg (max 6 mg/dose) PO/NG/IV q24h for up to 10 days In preterm neonates, risks vs. benefits should be considered based on gestational age, postnatal age, and illness severity <p>Consider Remdesivir (clinical benefit of remdesivir is greatest if it is initiated within 10 days of symptom onset)</p> <ul style="list-style-type: none"> FDA approval applies to pediatric patients ≥ 28 days of age and weighing ≥ 3 kg, and to all adult patients Dose: <ul style="list-style-type: none"> 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: <ul style="list-style-type: none"> No mechanical ventilation or ECMO: 5 days. 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 <p>Consider Empiric Antibiotics</p> <ul style="list-style-type: none"> if concern for concurrent community-acquired bacterial pneumonia (incidence <10%): see Note 4 If recent or prolonged hospitalization, consider coverage for health-care associated pneumonia: Cefepime IV plus vancomycin IV <p>Consider Replacement Dose of IVIG if low IgG for age (Discuss with Immunology if questions)</p> <p>If initial IgG is below the following age-based thresholds, consider IVIG at 400 mg/kg (based on ideal body weight) × 1 dose: 0 to 1 month: <400 mg/dL; 1 to < 7 month: <200 mg/dL; 7 month to <3 year: < 250 mg/dL; 3 to < 6 year: <350 mg/dL; 6 years to adulthood <500 mg/dL</p> <p>Consider Biologic Modulators (tocilizumab, baricitinib): Recommendations are extrapolated from data in adults. Proposed benefit is to minimize damage from developing cytokine storm in the 2nd stage (typically 2nd week) of acute infection. Strongly recommend discussing with Immunology before initiating these agents in patients < 12 years of age or in patients with COVID symptoms for < 1 week.</p> <ul style="list-style-type: none"> 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. <ul style="list-style-type: none"> < 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 <p>Tocilizumab is FDA-approved in adults but under an EUA for pediatric patients ages ≥ 2 years to < 18 years of age.</p> <p>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.</p> <ul style="list-style-type: none"> 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. <ul style="list-style-type: none"> 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 	<p>Systemic Corticosteroids Recommend gastric ulcer prophylaxis</p> <p>Systemic Corticosteroid Alternatives (If dexamethasone is unavailable)</p> <ul style="list-style-type: none"> 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 <p>Provider Tools for Tocilizumab</p> <ul style="list-style-type: none"> FDA Tocilizumab package insert (approved indication) FDA EUA Tocilizumab Fact Sheet for Providers FDA EUA Tocilizumab Fact Sheet for Patients FDA EUA Tocilizumab FAQs <p>Tocilizumab should be avoided or benefit/risk assessed if any of the following:</p> <ul style="list-style-type: none"> 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) <p>Provider Tools for Baricitinib</p> <ul style="list-style-type: none"> FDA EUA Baricitinib Fact Sheet for Providers FDA EUA Baricitinib Fact Sheet for Patients FDA EUA Baricitinib FAQs <p>Baricitinib warnings/contraindications</p> <ul style="list-style-type: none"> 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 <p>EUA: Emergency Use Authorization</p>	<p>All hospitalized patients</p> <ul style="list-style-type: none"> On admission: CBC+diff, CRP, CMP, ferritin, D-dimer, PT/PTT/fibrinogen, troponin, IgA, IgG, IgM, cytokine storm 4-plex panel, immune status panel (ISP), blood culture, serum to save (≥ 3 mL) During hospitalization <ul style="list-style-type: none"> Daily labs as clinically indicated <p>Patients on Remdesivir</p> <ul style="list-style-type: none"> Labs prior to initiation and daily: BMP, CBC+diff, AST, ALT, alkaline phosphatase, T/D bilirubin, PT (PT at least on initiation) Consider discontinuation if ALT > 10 × ULN during treatment Discontinue if ALT elevation is accompanied by s/s of liver inflammation <p>Patients on Empiric Antibiotics</p> <p>Need, duration, and spectrum of antibiotics should be assessed daily based on microbiology results and clinical status</p> <p>Patients on Tocilizumab</p> <p>Monitor for hepatotoxicity, leukopenia, neutropenia, infection reactivation (e.g. HSV, VZV, TB, Strongyloides), GI perforation</p> <p>Patients on Baricitinib</p> <ul style="list-style-type: none"> 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 <p>Useful websites</p> <p>COVID-19 drug interactions http://www.covid19-druginteractions.org/</p>

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 mild/moderate COVID-19.
- Maintain euolemia, avoid overhydration as this may increase ARDS risk.

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 [Fact Sheet for Patients and Caregives](#) and provided them with the [Fact Sheet for Patients and Caregives](#); 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)

- Age ≤ 60 days OR preterm infant (less than 37 weeks gestation) with postmenstrual age less than 41 weeks:
 - Follow [febrile infant guideline](#) for workup, use Ampicillin plus Cefazidime.
- 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

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.
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<p>Created: 04/08/20</p>
<p>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</p>
<p>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</p>
<p>Revised: 05/29/20 1) Added clarification regarding remdesivir dosing in pediatric patients ≤ 7 days of age or born prematurely; 2) Updated literature</p>
<p>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</p>
<p>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</p>
<p>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</p>
<p>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</p>
<p>Revised: 02/10/21 Removed convalescent plasma for confirmed infection or high risk exposure in pediatric patients (IRB 2005-044) as a treatment option</p>
<p>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</p>
<p>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</p>
<p>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</p>

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<p>Revisions (continued)</p>
<p>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</p>
<p>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</p>
<p>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)</p>
<p>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</p>
<p>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 lack 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.</p>
<p>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.</p>
<p>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</p>
<p>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</p>
<p>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.</p>
<p>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.</p>
<p>Revised: 6/16/22 1) Removed the ID approval requirement for Paxlovid™ and included a Paxlovid™ prescribing process for guidance.</p>
<p>Revised: 7/11/22 1) Added reference to guidance document for use of tixagevimab/cilgavimab (Evusheld™) for COVID-19 pre-exposure prophylaxis (page 1).</p>
<p>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.</p>
<p>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.</p>
<p>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.</p>
<p>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.</p>

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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.