**CLINICAL GUIDELINE**

COVID-19: MEDICAL MANAGEMENT

(Age <25 years)

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

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**Assess COVID-19 Illness Level**

- **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 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 C0 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.

- **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.

- **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, 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. 5.

- **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**

- Asymptomatic
  - Assess eligibility for Paxlovid™, sotrovimab or remdesivir if high-risk factors for progression to severe COVID-19. See p. 2-3 for more detail.

- Mild
  - Assess eligibility for Paxlovid™, sotrovimab or remdesivir if high-risk factors for progression to severe COVID-19. See p. 2-3 for more detail.

- Moderate
  - Assess eligibility for Paxlovid™, sotrovimab or remdesivir if high-risk factors for progression to severe COVID-19. See p. 2-3 for more detail.

- Severe
  - Assess eligibility for Paxlovid™, sotrovimab or remdesivir if high-risk factors for progression to severe COVID-19. See p. 2-3 for more detail.

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**Reviewer:** Workgroup | Rev 2/22 | Exp 2/25 | Page 1
**Treatment of mild-to-moderate COVID-19 in patients at high risk for progression to severe COVID-19**

**Mild-to-moderate COVID-19 symptoms and positive direct SARS-CoV-2 test (PCR or antigen)**

**Oral (PO)**

**Preferred formulation**

**Intravenous (IV)**

<table>
<thead>
<tr>
<th>Nirmatrelvir/Ritonavir (Paxlovid™)</th>
<th>Sotrovimab</th>
<th>Remdesivir</th>
</tr>
</thead>
<tbody>
<tr>
<td>(88% efficacy in preventing hospitalization or death in adults)</td>
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</tr>
<tr>
<td>Must meet all criteria below:</td>
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</tr>
<tr>
<td>• 18-24 years of age OR 12-17 years of age and weighing ≥ 40 kg</td>
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<td>• Neonate (body weight ≥ 3.5 kg) to 24 years of age</td>
</tr>
<tr>
<td>• Presence of high-risk factors for progression to severe COVID-19</td>
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</tr>
<tr>
<td>• Within 5 days of symptom onset</td>
<td>• Within 10 days of symptom onset</td>
<td>• Within 7 days of symptom onset</td>
</tr>
<tr>
<td>• eGFR ≥ 30 mL/min</td>
<td>• eGFR ≥ 30 mL/min</td>
<td>• eGFR ≥ 30 mL/min (if &gt; 28 days old) or SCR &lt; 1 mg/dL (if term neonate ≥ 7 days to ≤ 28 days old)</td>
</tr>
<tr>
<td>• No severe hepatic impairment (Child-Pugh Class C)</td>
<td>• Outpatient or hospitalized for reasons other than COVID-19 and without requiring new/increased oxygen therapy.</td>
<td>• Outpatient or inpatient mild-to-moderate COVID-19</td>
</tr>
<tr>
<td>• No contraindicated drug interactions (link)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Outpatient or inpatient mild-to-moderate COVID-19</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Nirmatrelvir/Ritonavir (Paxlovid™)**

- (88% efficacy in preventing hospitalization or death in adults)
- Must meet all criteria below:
  - 18-24 years of age OR 12-17 years of age and weighing ≥ 40 kg
  - Presence of high-risk factors for progression to severe COVID-19
  - Within 5 days of symptom onset
  - eGFR ≥ 30 mL/min
  - No severe hepatic impairment (Child-Pugh Class C)
  - No contraindicated drug interactions (link)
  - Outpatient or inpatient mild-to-moderate COVID-19

**Sotrovimab**

- (85% efficacy in preventing hospitalization or death in adults)
- Must meet all criteria below:
  - 18-24 years of age OR 12-17 years of age and weighing ≥ 40 kg
  - Presence of high-risk factors for progression to severe COVID-19
  - Within 10 days of symptom onset
  - Outpatient or hospitalized for reasons other than COVID-19 and without requiring new/increased oxygen therapy.

**Remdesivir**

- (87% efficacy in preventing hospitalization or death in adults)
- Must meet all criteria below:
  - Neonate (body weight ≥ 3.5 kg) to 24 years of age
  - Presence of high-risk factors for progression to severe COVID-19
  - Within 7 days of symptom onset
  - eGFR ≥ 30 mL/min (if > 28 days old) or SCR < 1 mg/dL (if term neonate ≥ 7 days to ≤ 28 days old)
  - Outpatient or inpatient mild-to-moderate COVID-19

**Preferred formulation**

- **Oral (PO)**
  - Nirmatrelvir/Ritonavir (Paxlovid™)
    - (88% efficacy in preventing hospitalization or death in adults)
    - Must meet all criteria below:
      - 18-24 years of age OR 12-17 years of age and weighing ≥ 40 kg
      - Presence of high-risk factors for progression to severe COVID-19
      - Within 5 days of symptom onset
      - eGFR ≥ 30 mL/min
      - No severe hepatic impairment (Child-Pugh Class C)
      - No contraindicated drug interactions (link)
      - Outpatient or inpatient mild-to-moderate COVID-19

- **Sotrovimab**
  - (85% efficacy in preventing hospitalization or death in adults)
  - Must meet all criteria below:
    - 18-24 years of age OR 12-17 years of age and weighing ≥ 40 kg
    - Presence of high-risk factors for progression to severe COVID-19
    - Within 10 days of symptom onset
    - Outpatient or hospitalized for reasons other than COVID-19 and without requiring new/increased oxygen therapy.

- **Remdesivir**
  - (87% efficacy in preventing hospitalization or death in adults)
  - Must meet all criteria below:
    - Neonate (body weight ≥ 3.5 kg) to 24 years of age
    - Presence of high-risk factors for progression to severe COVID-19
    - Within 7 days of symptom onset
    - eGFR ≥ 30 mL/min (if > 28 days old) or SCR < 1 mg/dL (if term neonate ≥ 7 days to ≤ 28 days old)
    - Outpatient or inpatient mild-to-moderate COVID-19

**Intravenous (IV)**

- **Nirmatrelvir/Ritonavir (Paxlovid™)**
  - (88% efficacy in preventing hospitalization or death in adults)
  - Must meet all criteria below:
    - 18-24 years of age OR 12-17 years of age and weighing ≥ 40 kg
    - Presence of high-risk factors for progression to severe COVID-19
    - Within 5 days of symptom onset
    - eGFR ≥ 30 mL/min
    - No severe hepatic impairment (Child-Pugh Class C)
    - No contraindicated drug interactions (link)
    - Outpatient or inpatient mild-to-moderate COVID-19

- **Sotrovimab**
  - (85% efficacy in preventing hospitalization or death in adults)
  - Must meet all criteria below:
    - 18-24 years of age OR 12-17 years of age and weighing ≥ 40 kg
    - Presence of high-risk factors for progression to severe COVID-19
    - Within 10 days of symptom onset
    - Outpatient or hospitalized for reasons other than COVID-19 and without requiring new/increased oxygen therapy.

- **Remdesivir**
  - (87% efficacy in preventing hospitalization or death in adults)
  - Must meet all criteria below:
    - Neonate (body weight ≥ 3.5 kg) to 24 years of age
    - Presence of high-risk factors for progression to severe COVID-19
    - Within 7 days of symptom onset
    - eGFR ≥ 30 mL/min (if > 28 days old) or SCR < 1 mg/dL (if term neonate ≥ 7 days to ≤ 28 days old)
    - Outpatient or inpatient mild-to-moderate COVID-19

**Dosage**

- **Nirmatrelvir/Ritonavir (Paxlovid™)**
  - For high-risk factors for progression to severe COVID-19, see specific eligible conditions for Paxlovid™, sotrovimab, and remdesivir.
  - Infectious Disease approval is required for Paxlovid™, sotrovimab, and remdesivir. Contact Children’s Physician Access at 612-343-2121 to discuss with the Infectious Disease provider on call for the Saint Paul campus.
  - Selection of agent depends on patient’s age, body weight, ability to swallow tablets (Paxlovid™ tablets cannot be crushed), timing from onset of symptoms, interacting medications, renal and hepatic function, and drug availability.
  - See page 6 for documentation and reporting requirements for Emergency Use Authorization (EUA) agents.

- **Sotrovimab**
  - 500 mg IV infusion × 1

- **Remdesivir**
  - 3.5 kg to < 40 kg: 5 mg/kg IV × 1, followed by 2.5 mg/kg q24h × 2 days
  - ≥ 40 kg: 200 mg IV × 1, followed by 100 mg IV q24h × 2 days

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# COVID-19: Medical Management (Age <25 years)

This guidance document is based on available knowledge and multidisciplinary input. It is intended as a living document that will be updated in real time as more data emerge.

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### Therapeutic Agents

<table>
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<tr>
<th>Clinical Severity</th>
<th>Supportive Care (Note 1)</th>
<th>Therapeutic Agents</th>
<th>Comments</th>
<th>Monitoring</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mild illness</strong></td>
<td>Consider Nirmatrelvir/Ritonavir (Paxlovid™), Sotrovimab, or Remdesivir in patients at high-risk for progression to severe COVID-19</td>
<td><strong>Supportive Care (Note 1)</strong></td>
<td>Provider Tools for EUA Paxlovid™</td>
<td>Patients on Remdesivir</td>
</tr>
<tr>
<td></td>
<td>• Paxlovid™, Sotrovimab, and Remdesivir require ID approval. Call Children's Physician Access at 812-343-2121 to discuss with ID provider on-call for Saint Paul campus.</td>
<td></td>
<td><strong>Emergency Use Authorization</strong></td>
<td><strong>Monitor as clinically indicated:</strong> BMP, AST, ALT, alkaline phosphatase, T/D bilirubin, PT (PT at least on initiation)</td>
</tr>
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<td></td>
<td>• See p.2 for eligibility criteria and dosing.</td>
<td></td>
<td><strong>Note 2 (Paxlovid™), Note 3 (sotrov imab), and Note 4 (Remdesivir) on p.6 for EUA documentation/reporting requirements</strong></td>
<td><strong>Provider Tools for EUA Sotrovimab</strong></td>
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<td><strong>Provider Tools for EUA Remdesivir</strong></td>
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<td><strong>VTE prophylaxis</strong>: Initiated and as indicated per VTE prophylaxis in COVID-19 guideline</td>
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<td>• Sotrovimab provider talking points/FAQ</td>
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**CLINICAL GUIDELINE**
### Covid-19: Medical Management

#### (Age < 25 years)

**Clinical Guideline**

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<td><strong>VTE prophylaxis</strong> as indicated per VTE prophylaxis in COVID-19 guideline</td>
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**Systemic Corticosteroids**

- Dexamethasone: 0.15 mg/kg (max 6 mg/dose) P0/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.

**Recommend Responsiveness in Reports**

- FDA Approval applies to pediatric patients 12-17 years of age weighing ≥ 40 kg, and to all adult patients.
- FDEA approval applies to patients ≥ 18 years of age who weigh ≥ 35 kg to ≤ 40 kg and to patients < 12 years of age who weigh at least 3.5 kg. See Note 4 for FDA EUA documentation/reporting requirements.

**May Consider Use in Neonates < 3.5 kg** (not covered under FDA EUA or FDA Approval).

**Recommend Remdesivir (Requires ID approval)**

- Remdesivir is not available.

**Resume Reversal (Qualifies for coverage under the FDA EUA)**

- 3.5 kg to 20 kg: 2 mg/kg IV 1x, followed by:
  - 2.5 mg/kg q24h for 4 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
- ≥ 20 kg: 200 mg IV 1x, followed by:
  - 100 mg IV q24h for 4 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

**May Consider Empiric Antibiotics**

- If concern for concurrent community-acquired bacterial pneumonia (incidence <10%); see Note 6.
- If recent or prolonged hospitalization, consider coverage for healthcare-associated pneumonia: Ceftazidime IV (plus varonicumycin IV).

**Consider Replacement Dose of IVIG if low IgG for age (Discuss with Immunology if questions)**

- 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 months: <200 mg/dL, 7 months to 3 years: <250 mg/dL, 3 to 6 years: <350 mg/dL, 6 years to adulthood <500 mg/dL.

**Consider Biologic Modulators via EUA (tocilizumab, baricitinib)**

- Tocilizumab via EUA [Restricted to Immunology, Hem/Onc, and PICU] in combination with systemic corticosteroids in patients with early rapidly progressive disease. Specifically: Patients hospitalized within last 5 days and admitted to ICU within prior 24 hours requiring invasive mechanical ventilation, noninvasive mechanical ventilation or high-flow nasal cannula oxygen (o2 > 30 L/min and >40 FiO2).
- < 30 kg (EUA for ages ≥ 2 years): 12 mg/kg actual body weight x 1
- ≥ 30 kg: 8 mg/kg actual body weight (max 800 mg) x 1

- One additional dose may be given within 2 weeks after initial dose if patient worsening or not improving. See Note 7 for tocilizumab EUA counselling/reporting requirements.

- 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 8 for baricitinib EUA documentation/reporting requirements.

- 2 to 9 years old: 4 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

**Systemic Corticosteroids**

- Consider gastric ulcer prophylaxis.

**Systemic Corticosteroid Alternatives**

- If dexamethasone is not available:
  - Prednisolone 1 mg/kg (max 40 mg/dose) PO q4h for up to 10 days
  - Methylprednisolone 0.8 mg/kg (max 32 mg/dose) IV q4h for up to 10 days.

**Remdesivir not recommended for**:

- Adult and pediatric patients (> 28 days of age) with eGFR < 30 mL/min. OR full-term neonates (≥ 7 days to ≤ 28 days of age) with SCR > 1 mg/dL.

**EUA Emergency Use Authorization**

- **Provider Tools for Tocilizumab**
  - EUA Tocilizumab Fact Sheet for Providers
  - FDA EUA Tocilizumab Fact Sheet for Patients
  - EUA Tocilizumab FAQs

**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; Severe or persistent gastrointestinal upset.
- Consider interruption until aLCC ≥ 2000 cells/µL and ANC ≥ 5000 cells/µL.
- If ANC <500 cells/µL, also with caution if increased risk of GI perforation.
- Use prophylaxis recommended for adults and adolescents. Consult Hem/Onc re: younger patients.

**All hospitalized patients**

- On admission: CBC, CRP, CMP, ferritin, D-dimer, IgA, IgG, IgM, blood culture, serum lsoase (≥ 3 mL).
- During hospitalization: Daily labs as clinically indicated - if symptom progression (persistent high fever, worsening respiratory distress, increasing O2 requirements, or transfer to ICU): CBC, CMP, ferritin, D-dimer, PT/PTT/INR, troponin, IgA, IgG, IgM, cytokine storm 4-plex panel, immune status panel (ISP), blood culture, serum lsoase (≥ 3 mL).

**Patients on Remdesivir**

- Labs prior to initiation and daily: BMP, CBC, CRP, 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 ≥ 3 of liver inflammation.

**Patients with 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**

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

**Useful websites**

- COVID-19 drug interactions
  - http://www.covid19-druginteractions.org/

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**CLINICAL GUIDELINE**

**COVID-19: MEDICAL MANAGEMENT**

**(Age <25 years)**

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**CLINICAL SEVERITY**

- Critical Illness
  - SUPPORTIVE CARE (Note 1)
    - VTE PROPHYLAXIS as indicated per VTE prophylaxis in COVID-19 guideline

**THERAPEUTIC AGENTS**

**RECOMMEND SYSTEMIC CYTOKINE BLOCKERS**

- **Tocilizumab**
  - Dexamethasone 0.15 mg/kg (max 6 mg) PO/NV/IV q24h for up to 10 days
  - In preterm neonates, risk vs. benefits should be considered based on gestational age, postnatal age, and illness severity

**CONSIDER REMDESIVIR (Requires ID approval)**

- FDA approval: pediatric patients 2-12 years of age and ≥ 40 kg, and all adult patients
- FDA EUA: pediatric patients < 18 years of age who weigh 3.5 kg to < 40 kg and to patients < 12 years of age who weigh at least 3.5 kg. See Note 4 for remdesivir EUA documentation and reporting requirements

**CONSIDER MONOCLONAL ANTI-IL-6 RECEPTOR**

- FDA EUA for ages ≥ 2 years: 1 dose: 200 mg IV q24h for up to 10 days, OR
  - 5 mg/kg IV × 3 days, followed by:
    - 2.5 mg/kg IV q4h × 4 days if no mechanical ventilation or ECMO. If no clinical improvement after a total of 5 days of treatment, treatment can be extended up to a total of 10 days, OR
    - 2.5 mg/kg IV q4h × 9 days if mechanical ventilation or ECMO

**CONSIDER SYSTEMIC CYTOKINE BLOCKERS**

- **Baricitinib**
  - Methyprednisolone 0.8 mg/kg (max 32 mg/dose) IV
  - Requires interruption until ALC is ≥200 cells/μL

**COMMENTS**

- Systemic Corticosteroids
  - Recommend gastric ulcer prophylaxis

- Systemic Corticosteroid Alternatives
  - Prednisolone 1 mg/kg (max 40 mg/dose) PO/NG
  - On admission:
    - Consider replacement dose of IVIG if low IgG for age (discuss with Immunology if questions)
  - Followed by:
    - Methylprednisolone 0.8 mg/kg (max 32 mg/dose) IV q24h for up to 10 days
    - Methyprednisolone 0.8 mg/kg (max 32 mg/dose) IV q24h for up to 10 days

**MONITORING**

- All hospitalized patients
  - On admission: CBC-diff, CRP, CMP, ferritin, D-dimer, PT/PTT, fibrinogen, troponin, IgA, IgG, IgM, cytokine storm 4-plex panel, immune status panel (SSP), blood culture, serum to A3 (2 mL)
  - During hospitalization:
    - Daily labs as clinically indicated

**CONSIDER INTERRUPTION/REDUCTION OF SYSTEMIC CYTOKINE BLOCKERS**

- **Remdesivir**
  - Not recommended for:
    - Adult and pediatric patients (≥ 28 days old) with eGFR < 30 mL/min, OR full-term neonates (≤ 2 days to ≤ 28 days old) with SCR ≥ 1 mg/dL
  - May consider interruption until ALC is ≥ 200 cells/μL and to all adult patients ≥ 40 kg, and to all adult patients

**USEFUL WEBSITES**


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NOTE 1: Supportive Care
- Systemic corticosteroids may be used for asthma/croup indications in patient with mild/moderate COVID-19.
- Maintain euvelaemia, avoid overhydration as this may increase ARDS risk.

NOTE 2: Niratrevir/Ritonavir (Paxlovid™) FDA EUA Documentation and Reporting Requirements
- Providers must document in EMR that they:
  1) Communicated to the patient/caregiver information consistent with the Fact Sheet for Patients and Caregivers and provided them with the Fact Sheet for Patients and Caregivers 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: Sotrovimab FDA EUA Documentation and Reporting Requirements
- Providers must document in EMR that patient/caregiver was:
  1) Given the Fact Sheet for Patients and Caregivers;
  2) Informed of alternatives to sotrovimab;
  3) Informed that sotrovimab is an unapproved drug that is authorized for use under this Emergency Use Authorization.
- Providers must report all medication errors and serious adverse events potentially related to sotrovimab within 7 calendar days from the event by:
  1) Submitting a MedWatch Report, and
  2) Emailing completed MedWatch form to GlaxoSmithKline at WW.GSKAEReportingUS@gsk.com.

NOTE 4: Remdesivir FDA EUA Documentation and Reporting Requirements (applies to patients < 18 years of age who weigh 3.5 kg to < 40 kg and to patients <12 years of age who weigh at least 3.5 kg)
- Providers must document in EMR that patient/caregiver was:
  1) Given the Fact Sheet for Patients and Caregivers;
  2) Informed of alternatives to remdesivir, and
  3) Informed that remdesivir is an approved drug that is authorized for this unapproved use.
- Providers must report all medication errors and serious adverse events potentially related to remdesivir within 7 calendar days from the event by:
  1) Submitting a MedWatch Report, and
  2) Emailing a copy of the submitted MedWatch Report to Gilead Safety_fc@gilead.com

NOTE 5: Documentation and Reporting Requirements for Remdesivir Use in Neonates < 3.5 kg who are not enrolled in GS-US-460-1823
- Providers should document the following in EMR:
  1) Remdesivir is not FDA approved or authorized for use in these patients;
  2) Reasons that patient is considered for remdesivir;
  3) All other options have been evaluated;
  4) Risk/benefit discussed with parent/caregiver;
  5) How was dosing derived; and
  6) Consent has been signed and a copy has been given to parent/caregiver
- Providers must report all medication errors and serious adverse events potentially related to remdesivir within 7 calendar days from the event by:
  1) Submitting a MedWatch Report, and
  2) Emailing a copy of the submitted MedWatch Report to Gilead Safety_fc@gilead.com

NOTE 6: Antibiotic recommendations for suspected or proven bacterial coinfection (community-acquired)
- Age ≤ 28 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; Cefdinir for ongoing oral CAP treatment.
- For any of the following infants, use Ceftriaxone/Cefdinir:
  1) > 28 days old – 3 months old
  2) Preterm infant (≤ 37 weeks’ gestation) with PMA ≥ 41 weeks – 3 months old
  3) > 3 mo and has not received appropriate Hib and Pneumococcal vaccine doses for age.
- If PCN exposure in the last 30 days or allergy to ceftriaxone/Cefdinir
  - Consider adding Azithromycin for patients ≥ 5 yr.

NOTE 7: Tocilizumab FDA EUA Counseling and Reporting Requirements
- 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.drugsafety@gene.com

NOTE 8: 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 maildata_osmtindy@illy.com

Discharge Criteria:
- Routine medical criteria
- Encourage virtual or in-clinic follow-up with PCP
REFERENCES

Guidelines, Expert Reviews, Evidence Summaries

Minnesota Department of Health (MDH) Ethical Frameworks and Clinical Guidance
10. MDH. Interim Guidance on Use of Sotrovimab and Nirmatrelvir/Remdesivir (Veklory) for Pediatric Patients. https://www.health.state.mn.us/diseases/coronavirus/hcp/sotrapxpdfs.pdf

Drug Interactions

Remdesivir
21. FDA Fact Sheet for Healthcare Providers for Emergency Use Authorization of Remdesivir for COVID-19 for Hospitalized Pediatric Patients Weighing 3.5 kg to less than 40 kg OR Pediatric Patients less than 12 Years of Age Weighing at least 3.5 kg https://www.fda.gov/media/137566/download
22. FDA Fact Sheet for Patients And Parent/Caregivers for Emergency Use Authorization of Remdesivir for COVID-19 for Hospitalized Pediatric Patients Weighing 3.5 kg to less than 40 kg OR Pediatric Patients less than 12 Years of Age Weighing at least 3.5 kg https://www.fda.gov/media/137565/download

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Corticosteroids


Anti-SARS-CoV-2 Monoclonal Antibodies

32. FDA Fact Sheet for Patients And Parent/Caregivers for Emergency Use Authorization (EUA) of Sotrovimab. https://www.fda.gov/media/149533/dow nload

Nirmatrelvir/Ritonavir (Paxlovid ™)

34. FDA Fact Sheet for Healthcare Providers for Emergency Use Authorization (EUA) of Nirmatrelvir/Ritonavir. https://www.fda.gov/media/155050/dow nload
35. FDA Fact Sheet for Patients And Parent/Caregivers for Emergency Use Authorization (EUA) of Nirmatrelvir/Ritonavir. https://www.fda.gov/media/155051/dow nload

IVIG


Tocilizumab

40. FDA Fact Sheet for Patients And Parent/Caregivers for Emergency Use Authorization (EUA) of tocilizumab. https://www.fda.gov/media/150320/dow nload

Baricitinib

43. FDA Fact Sheet for Healthcare Providers for Emergency Use Authorization (EUA) of baricitinib. https://www.fda.gov/media/143823/dow nload
44. FDA Fact Sheet for Patients And Parent/Caregivers for Emergency Use Authorization (EUA) of baricitinib. https://www.fda.gov/media/143824/dow nload

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COVID-19 Interim Clinical Guidance Workgroup
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Created: 04/08/20

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 (eND); 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: 05/30/20
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 an investigational consideration for 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 technical 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 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) Removed 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 to 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 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; 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 oral remdesivir use when influenza is co-circulating with COVID-19; 12) Added convalescent plasma from Severe Pneumonia and ARDS; 13) Updated literature

Revised: 02/10/21
1) Removed remdesivir therapy for outpatient treatment of mild to moderate COVID-19 in response to the bamlanivimab EUA revocation by the FDA on 4/16/21

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 compensation due to COVID-19

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

Revised: 06/33/21
1) Included casirivimab/Imdevimab for outpatient treatment of mild to moderate COVID-19 per the expanded criteria of the 5/17/21 FDA EUA

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 compensation due to COVID-19 and tocilizumab is not available

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CLINICAL GUIDELINE
COVID-19: MEDICAL MANAGEMENT
(Age <25 years)

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Revisions (continued)
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 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.

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