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

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

Assess COVID-19 Illness Level (note 1)
- Signs/symptoms, vital signs, hydration respiratory status. Consider also alternate etiologies for illness.

Asymptomatic
- Tested for reasons other than symptoms (e.g., pre-op, behavioral health admission).
- No additional tests/treatments needed
  - Manage primary condition
  - See “behavioral health” order set for updated guidance on retesting in behavioral health patients

Mild
- Symptomatic, but not generally requiring hospitalization for COVID-19.¹
- Guide tests/treatments on symptoms
  - Supportive cares in clinic/ED and recommendations for home (note 2).
  - Evaluate and treat suspected coinfections based on symptoms (note 3).
  - Hospitalized patients with mild symptoms may be managed as above. Escalate testing/therapies if clinical status worsens.

Mild
- Signs or symptoms of COVID-19 requiring med-surg care but not generally meeting criteria for critical care.
- Guide tests/treatments on symptoms
  - Supportive cares in clinic/ED and recommendations for home (note 2).
  - Evaluate and treat suspected coinfections based on symptoms (note 3).
  - Antibiotics per suspected sepsis order set if sepsis is present
  - Consult immunology, pulmonology, ID and other specialists as indicated.
  - See separate MIS-C guideline if primary diagnosis of acute COVID-19 uncertain and concern for MIS-C
  - Consider additional therapies specific to COVID-19 (see subsequent pages for detail)

Severe/Critical
- Critically ill, requiring ICU level of care.
- Guide tests/treatments on symptoms
  - Supportive cares in clinic/ED and recommendations for home (note 2).
  - Evaluate and treat suspected coinfections based on symptoms (note 3).
  - Antibiotics per suspected sepsis order set if sepsis is present
  - Consult immunology, pulmonology, ID and other specialists as indicated.
  - See separate MIS-C guideline if primary diagnosis of acute COVID-19 uncertain and concern for MIS-C
  - Additional therapies specific to COVID-19 (see subsequent pages for detail)

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

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Reviewer: Workgroup | Rev 4/21 | Exp 4/24 | Page 1
NOTE 1: SEVERITY OF ILLNESS CATEGORIES

- **Mild**: No respiratory distress or oxygen requirement; able to self-hydrate (may be after initial fluid support)
- **Moderate**: Requiring ongoing IVF support OR requiring respiratory support including low flow nasal cannula for hypoxia or high flow nasal cannula for increased work of breathing. If hypoxia and/or respiratory distress are not improved with trial of low or high flow nasal cannula, escalate to severe category. If suspected MIS-C but no cardiac dysfunction (e.g. abnormal echo, EKG or troponin, etc.) and patient without shock or hemodynamic stability may consider admitted to med-surg unit.
- **Severe/Critical**: Hypoxia or work of breathing requiring non-invasive or invasive ventilation or concern that patient status is worsening on high flow nasal cannula OR SIRS/Sepsis/Shock OR rapidly worsening status. If suspected MIS-C and any cardiac dysfunction (e.g. abnormal echo, EKG or troponin, etc.), and/or shock/hypotension or concern for rapid progression patient should be admitted to ICU.

Consider also risk factors for more severe COVID-19 in considering to step-up to next level of severity for disposition decisions (shared decision making with family and other providers) in your patient: immunocompromise, age < 12 months, complex chronic conditions, obesity, chronic kidney disease, chronic hepatitis, endocrine disorders. Consider also ability of family/guardian to provide supportive cares as well as follow-up options.

NOTE 2

- If bronchodilator indicated, use MDI instead of nebulizer, follow treatment with inhaled corticosteroid.
- Systemic corticosteroids may be used for asthma/croup indications. Discuss with multidisciplinary team in patients requiring persistent/escalating supplemental oxygen or mechanical ventilation.
- Acetaminophen preferred 1st line. Ibuprofen can be used as 2nd line analgesic/antipyretic agent.
- Maintain euvolemia, avoid overhydration as this may increase ARDS risk.

NOTE 3

Bacterial co-infection at time of presentation with COVID-19 is uncommon (<2% in adult patients). Only use antibiotics with strong suspicion for bacterial pneumonia based on clinical exam and imaging findings.

*Treatment Recommendations for Pneumonia (CAP):
- **Age ≤ 28 days OR preterm infant (less than 37 weeks gestation) with PMA less than 41 weeks**
  - Follow febrile infant guideline for workup, use Ampicillin plus Ceftazidime; Cefdinir for ongoing oral CAP treatment
- **> 28 days OR preterm infant (less than 37 weeks gestation) with PMA ≥ 41 weeks 4 months**
  - Ceftriaxone/Cefdinir
- **> 4 mo and fully immunized for age**
  - Ampicillin/Amoxicillin (PCN exposure or allergy not anaphylaxis - Cefuroxime/Cefprozil)
- **> 4 mo and has not received 2 Hib and Pneumococcal vaccine doses**
  - Ceftriaxone/Cefdinir
- **Consider adding Azithromycin for patients ≥ 5 yr.**
- Oseltamivir if influenza positive.
- Antibiotics per suspected sepsis orderset if sepsis is present.
- Consult ID for empiric antibiotic recommendations if hospital-acquired infection suspected.

Discharge criteria:

- Routine medical criteria
- Encourage virtual or in-clinic follow-up with PCP
- Speak with MDH/infection prevention on-call for guidance for home isolation.

* Note that information on COVID-19 incidence and management is rapidly evolving. Please refer to www.CDC.gov, www.who.int, https://www.health.state.mn.us/ or Children’s Minnesota infection prevention team for updates. Due to the dynamic nature of this guideline, it is not run through the Guideline Governance Council but is updated regularly by clinical leadership.

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<table>
<thead>
<tr>
<th>CLINICAL SEVERITY</th>
<th>CLINICAL PRESENTATION</th>
<th>THERAPEUTIC AGENTS</th>
<th>COMMENTS</th>
<th>MONITORING</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild Illness</td>
<td>Uncomplicated URT viral infection, with non-specific symptoms: e.g. fever, fatigue, cough, anorexia, malaise, muscle pain, sore throat, dyspnea, nasal congestion, or headache</td>
<td>SUPPORTIVE CARE</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-Severe Pneumonia</td>
<td>Pediatric Patients: Cough or dyspnea plus tachypnea Tachypnea (breaths/min): - &lt; 2 months: ≥ 60 - 2–11 months: ≥ 50 - 1–5 years: ≥ 40 - 6–12 years: ≥ 35 - 13–18 years: ≥ 30 and no signs of severe pneumonia</td>
<td>May Consider Convalescent Plasma under FDA EUA (hospitalized pediatric and adult patients) • Consider on case-by-case basis for patients with primary or secondary immunodeficiency including children with trisomy 21 (i.e. patients with impaired antibody production) • Pediatric dose: 5 mL/kg (max 2 units) • No lower age limit • See Note 4 for documentation and reporting requirements</td>
<td>Consider Oseltamivir when influenza is co-circulating with COVID-19 (hospitalized patients) • Oseltamivir until upper respiratory tract (NP swab) influenza PCR test is negative</td>
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<tr>
<td></td>
<td>Adult Patients: No signs of severe pneumonia and no need for supplemental oxygen</td>
<td>Treat suspected pneumonic coinfections per recommendations included in Note 3, page 2.</td>
<td>Consider IVIG Replacement If initial IgG is below the following age-based thresholds, consider IVIG at 400 mg/kg (based on ideal body weight)×1 dose: 0 - 1 month: &lt;400 mg/dL 1 - &lt; 7 months: &lt;200 mg/dL 7 months: &lt;3 year: &gt; 250 mg/dL 3 - &lt; 6 year: &gt;350 mg/dL 6 years - adults: &lt;500 mg/dL</td>
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Provider Tools for FDA EUA Convalescent Plasma • FDA EUA Convalescent Plasma Fact Sheet for Healthcare Providers • FDA EUA Convalescent Plasma Fact Sheet for Patients and Caregivers • Convalescent plasma might interfere with the vaccine-induced immune response. Deferral of immunization for 90 days is recommended. EUA Emergency Use Authorization

All hospitalized patients • On admission: Baseline CBC+diff, CRP, CMP, IgG, serum to save (≥ 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+diff, CRP, procalcitonin, CMP, IgG, PT/PTT/fibrinogen, D-dimer, cytokine storm 4-plex panel, LDH, ferritin, triglycerides, CPK, troponin, blood culture, CXR

Last updated March 30, 2021
**CLINICAL GUIDELINE**

**MEDICAL MANAGEMENT FOR PATIENTS WITH CONFIRMED COVID-19**

**(Age <25 years)**

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### Severe Pneumonia

<table>
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<tr>
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<th>COMMENTS</th>
<th>MONITORING</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pediatric Patients</td>
<td>Cough or dyspnea, plus at least one of the following:</td>
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<td></td>
<td>• Central cyanosis or SpO₂ &lt; 90%</td>
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<td></td>
<td>• Severe respiratory distress (e.g. grunting, very severe chest inadrawing)</td>
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<td></td>
<td>• Signs of pneumonia with a general clinical instability to breastfeed or drink, lethargy or unconsciousness, or confusion</td>
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<tr>
<td>Adolescent and Adult Patients</td>
<td>Fever or suspected respiratory infection, plus one of the following:</td>
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<td></td>
<td>• Respiratory rate &gt; 30 breaths/min</td>
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<tr>
<td></td>
<td>• Severe respiratory distress</td>
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<tr>
<td></td>
<td>• SpO₂ ≤ 93% on room air</td>
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</table>

Recommended Systemic Corticosteroids:

- Dexamethasone 0.15 mg/kg (max 6 mg/dose) PO/NG/IV q24h for up to 10 days for patients requiring persistent supplemental oxygen or mechanical ventilation
- Consider use in patients not requiring supplemental oxygen or mechanical ventilation
- In preterm neonates, risks of benefit should be considered based on gestational age, postnatal age, and illness severity

Recommend Remdesivir [Restricted to ID]

- FDA approval applies to pediatric patients ≥ 12 years of age and ≥ 40 kg and to all adult patients
- FDA EUA applies to pediatric patients < 12 years of age who weigh 3.5 kg to 40 kg and to pediatric patients < 12 years of age who weigh at least 3.5 kg.

See Note 5 for documentation and reporting requirements

May Consider Use in Neonates < 3.5 kg who are not covered under either FDA EUA or FDA approval

Recommend Systemic Corticosteroid Alternatives

- If symptom progression (persistent high fever, worsening respiratory distress, increasing O₂ requirements, or transfer to ICU): CBC-cdf, CRP, procalcitonin, CMP, IgG, RTP/TT/ribonogen, D-dimer, cytokine storm 4-plex panel, immune status panel (ISD), LDH, ferritin, triglycerides, CPK, troponin, blood culture, consider repeat CXR

Remdesivir Dosing

- 3.5 kg to < 40 kg: 5 mg/kg IV × 1, followed by:
  - 2.5 mg/kg q24h × 4 days (if no mechanical ventilation or ECMO). If no clinical improvement after a total of 5 days of treatment, treatment can be extended to up to a total of 10 days, OR
  - 2.5 mg/kg q24h × 9 days (if mechanical ventilation or ECMO)
- ≥ 40 kg: 200 mg IV × 1, followed by:
  - 100 mg IV q24h × 4 days (if no mechanical ventilation or ECMO). If no clinical improvement after a total of 5 days of treatment, treatment can be extended to up to a total of 10 days, OR
  - 100 mg IV q24h × 9 days (if mechanical ventilation or ECMO)

Recommend Oseltamivir when influenza is co-circulating with COVID-19

- Non-intubated patients: Oseltamivir is until upper respiratory tract (NP swab) influenza PCR test is negative

Recommend Empiric Antibiotics if concern for pneumonic bacterial coinfecction

- Coming from the community, and no concern for MRDR: Refer to recommendations included in Note 3, page 2
- Concern for health-care associated infection or MRDR: Cefepime IV plus vancomycin IV

Consider IVIG and Biologic Modulators

- Consider replacement dose of IVIG if low IgG for age (see recommended doses under “Non-Severe Pneumonia”) and
- Consider Tocilizumab [Restricted to Immunology, Hematology/Oncology, and PICU providers] in combination with systemic corticosteroids in patients with early rapidly progressive disease. Specifically:

- Patients hospitalized within last 3 days and admitted to ICU within prior 24 hours requiring invasive mechanical ventilation, noninvasive mechanical ventilation, or high-flow nasal cannula oxygen (e.g. > 30 L/min and >0.4 FiO₂)

  - 15 kg (FDA approved for other indications for ages ≥ 2 years): 12.5 mg/kg actual body weight × 1
  - ≥ 30 kg: 8 mg/kg actual body weight (max 800 mg) × 1

- Systemic Corticosteroids

  Recommend systemic glucocorticoid prophylaxis

- Systemic Corticosteroid Alternatives

  (If dexamethasone is unavailable)

    - Prednisolone 1 mg/kg (max 40 mg/dose) PO/NG/IV q24h for up to 10 days
    - Methylprednisolone 0.8 mg/kg (max 32 mg/dose) IV q24h for up to 10 days

- Remdesivir not recommended for:

  • Adult and pediatric patients (> 28 days old) with eGFR < 30 mL/min, OR
  • Full-term neonates (≥ 7 days to ≤ 28 days old) with Scr ≥ 1 mg/dL.

Useful websites:


EUA Emergency Use Authorization

Tocilizumab should be avoided if any of the following:

- Significant immunosuppression, especially if recent use of other biologic immunomodulators
- ALT > 10 × ULN
- High risk for GI perforation
- Uncontrolled, serious bacterial, fungal, or non-SARS-CoV-2 viral infection
- ANC <500 cells/µL
- Platelet count <50,000 cells/µL

Consider prophylactic lactic acidemia for patients receiving tocilizumab who are from areas where Strongyloides is endemic (e.g. SE Asia, sub-Saharan Africa)

All hospitalized patients

- On admission: Baseline CBC-cdf, CRP, CMP, ferritin, LDH, CPK, D-dimer, IgG, IgQ, IgM blood culture, serum to save (≥ 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-cdf, CRP, procalcitonin, CMP, IgG, RTP/TT/ribonogen, D-dimer, cytokine storm 4-plex panel, immune status panel (ISD), LDH, ferritin, triglycerides, CPK, troponin, blood culture, consider repeat CXR

Patients on Remdesivir

- Labs prior to initiation and daily: BMP, CBC-cdf, AST, ALK, alkaline phosphatase, T/Bil bun, 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

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 hypotension, leukopenia, neutropenia, infection reactivation (e.g. HSV, VZV, TB, Strongyloides)

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**Recommend Systemic Corticosteroids**

- **Dexamethasone 0.15 mg/kg (max 60 mg/dose)** PO/NG/IV q24h for up to 10 days if for patients requiring persistent supplemental oxygen or mechanical ventilation.
- In preterm neonates, risks vs. benefits should be considered based on gestational age, postnatal age, and illness severity.

**Consider Remdesivir (Restricted to IC)**

- FDA approval applies to pediatric patients ≥ 12 years of age and ≥ 40 kg and to all adult patients.
- FDA EUA applies to pediatric patients < 18 years of age who weigh 3.5 kg to < 40 kg and to pediatric patients 3 years of age who weigh at least 3.5 kg.
- See Note 5 for documentation and reporting requirements.

**Consider Oseltamivir when influenza is co-circulating with COVID-19**

- Non-intubated patient: Oseltamivir is given up to 4 days after onset of symptoms.
- Intubated patient: Oseltamivir is given up to 4 days after onset of symptoms.

**Recommend Empiric Antibiotics if concern for pneumonia**

- Coming from the community, and no co-infections for ages ≥ 2 years old: 12 mg/kg actual body weight × 1 day
- Concern for health-care-associated infection or MR3O: Cefepime IV plus vancomycin IV

**Consider IVIG and Biologic Modulators**

- Consider replacement dose of IVIG if low IgG for age (see recommended doses under “Non-Severe Pneumonia”)

**Systemic Corticosteroids**

- **Recommend systemic glucocorticoids** for patients requiring persistent supplemental oxygen or mechanical ventilation.

**Systemic Corticosteroid Alternatives**

- **(If dexamethasone is unavailable)**
  - Prednisolone 1 mg/kg (max 40 mg/dose) PO/NG q24h for up to 10 days
  - Methyprednisolone 0.8 mg/kg (max 32 mg/dose) IV q24h for up to 10 days

**Remdesivir not recommended for:**

- Adult and pediatric patients (≥ 2 days old) with eGFR < 30 mL/min, OR
- Full-term neonates (≥ 7 days to ≤ 28 days old) with Scr ≥ 1 mg/dL.

**Useful websites**

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

**EUA: Emergency Use Authorization**

- **Tocilizumab should be avoided if any of the following:**
  - Significant immunosuppression, especially if recent use of other biologic immunomodulators.
  - ALT > 5 ULN.
  - High risk for GI perforation.
  - Uncontrolled, serious bacterial, fungal, or non-SARS-CoV-2 viral infection.
  - ANC <500 cells/µL.
  - Platelet count <50,000 cells/µL.

**Patients on Tocilizumab**

- Labs prior to initiation and daily: BMP, CBC+diff, ALT, AST, alkaline phosphatase, T/D bilirubin, PT (PT ULN), labs prior to hospitalization.
- **Discontinue if ALT elevation is accompanied by s/o of liver inflammation.**

**Patients on Remdesivir**

- Labs prior to hospitalization and daily: BMP, CBC+diff, ALT, AST, alkaline phosphatase, T/D bilirubin, PT (PT ULN), labs prior to hospitalization.
- **Discontinue if ALT elevation is accompanied by s/o of liver inflammation.**

**Patients on Empiric Antibiotics**

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

**Patients on Tocilizumab**

- Monitor for hepatotoxicity, leukopenia, neutropenia, infection reaction (e.g. HSV, VZV, TB, Streptococci).

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NOTE 4: Convalescent Plasma 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 convalescent plasma;
  3) Informed of risks and benefits of convalescent plasma, and
  4) Informed that convalescent plasma is not an FDA approved biological product

- Providers must report any infusion reactions to the Blood Bank which will initiate appropriate investigations if necessary

NOTE 5: Remdesivir 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 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 an MedWatch Report, and
  2) Emailing a copy of the submitted MedWatch Report to Gilead Safety_fc@gilead.com

NOTE 6: Documentation and Reporting Requirements for Remdesivir Use in Neonates < 3.5 kg who are not enrolled in GS-US-540-5823

- Providers should document the following in EMR:
  1) Remdesivir is not FDA approved or authorized for use in these patients;
  2) Why patient is considered for remdesivir;
  3) All other options have been evaluated;
  4) Risk/benefits discussed with parents/caregivers;
  5) How was dosing derived; and
  6) Consent has been signed and a copy has been given to parent/caregiver

- Providers should report all medication errors and serious adverse events potentially related to remdesivir within 7 calendar days from the event by:
  1) Submitting an MedWatch Report, and
  2) Emailing a copy of the submitted MedWatch Report to Gilead Safety_fc@gilead.com
REFERENCES

Guidelines, Expert Reviews, Evidence Summaries


10. Alhazzani W et al. Surviving Sepsis Campaign: Guidelines on the management of critically ill adults with Coronavirus disease 2019 (COVID-19). Published online 3.20.20


Drug Interactions


Remdesivir


Corticosteroids


Convalescent Plasma


IVIG


Tocilizumab

CLINICAL GUIDELINE

MEDICAL MANAGEMENT FOR PATIENTS WITH CONFIRMED COVID-19

(Age <25 years)

COVID-19 Interim Clinical Guidance Workgroup
Christina Koutsari PharmD PhD (ASHPD) [Lead], Bill Pomputius MD (ASHPD) [Lead], Anu Kalaskar MD (ID), Tamara Pozos MD RhD, (Immunology), Manar Abdalgani MBBS (Immunology), Lane Miller MD (Hem/Onc), Jeffrey Nowalk MD (Intensive Care), Brooke Moore MD (Pulmonology), Gabrielle Hester MD MS (Quality)

Created: 04/08/20

Revised: 05/11/20 1) Added criteria for use and dosage of remdesivir per Emergency Use Authorization; 2) Revised criteria for use of remdesivir via compassionate use (eNID); 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 infection; 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: 01/20/20 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. 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: 02/10/20 1) Removed tocilizumab as treatment consideration in patients with severe pneumonia or ARDS; 2) Removed hydroxychloroquine as an investigational option for treatment of COVID-19; 3) Updated criteria for use of convalescent plasma; 4) 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: 03/30/20 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 COVID-19 in patients who are exhibiting rapid respiratory decompensation due to COVID-19

Revised: 04/17/21

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