

#### Common clinical characteristics

- Temperature instability
- Lethargy
- Poor feeding
- Mild respiratory symptoms such as increased work of breathing and cough
- Pneumonia with history of possible COVID 19 exposure
- Increased oxygen requirement
- Apnea

Criteria for diagnosis (must meet all criteria)<sup>2</sup>

- At least one clinical symptom (unstable body temperature, lethargic/poor feeding, SOB)
- CXR with unilateral or bilateral milled glass opacities or CT with unilateral or bilateral milled glass opacities
- COVID 19 diagnosis in patient's family or caregiver
- Close contact with people who may have or have confirmed COVID19; patients with unexplained PNA

#### Mild-Moderate Criteria

No respiratory support or Non-invasive mode of support < 40% FiO2 (CPAP, NIPPV)

### Severe/Critical Criteria

Non-invasive mode of support requiring > 40% FiO2

Invasive ventilatory support (conventional or high-frequency ventilation)

Inotropic support

Clinical Assessment	Treatment for Hospitalized Patients	Duration of treatment*		
Mild to Moderate	<ul> <li>Supportive care only – If clinically stable, consider discharge for quarantine.</li> <li>Discharged patients should be offered supportive care (anti-pyretics, MDIs, etc)</li> </ul>	N/A		
Severe to Critical	<ul> <li>If eligible: remdesivir (FDA-approved, ID consult preferred)</li> <li>If ineligible for remdesivir: supportive care and ID consult</li> </ul>	Not requiring invasive mechanical ventilation and/or ECMO: 5 days*  Requires invasive mechanical ventilation and/or ECMO: 10 days		

<sup>\*</sup>May consider an additional 5 days of treatment (10 days total), if no clinical improvement.

Drug	Dosing	Formulations	Monitoring	Adverse Effects	Notes
Remdesivir  FDA approved (weight ≥3 kg AND PNA ≥ 28 days)  Off-label use in patients <3 kg or PNA < 28 days	Should be requested by ID  Weight <sup>3</sup> 3 kg AND PNA <sup>3</sup> 28 days**  Loading dose: 5 mg/kg/dose  Maintenance dose: 2.5 mg/kg/dose IV daily  Weight 2-2.999 kg or PNA < 28 days**  Loading dose: 2.5 mg/kg/dose  Maintenance dose: 1.25 mg/kg/dose IV Daily  **Consider decreasing dose by 50% if on CVVH or hemodialysis	IV infusion	CMP Daily CBC with differential PT/INR Daily If possible CoV PCR Physical and vital signs at least daily	Transient elevations in ALT and AST Dose-dependent, reversible kidney injury and dysfunction Prolonged QT interval	See inclusion/exclusion criteria below. Contact pharmacy to initiate request.  Do not use if baseline eGFR is <30 mL/min (PNA >28 days) or serum creatinine is >1 mg/dL (PNA 7-28 days).
<b>Dexamethasone</b> For PMA <sup>3</sup> 36 weeks	0.15 mg/kg/dose (Max 0.5 mg/kg/dose) daily x up to 10 days*  *May consider wean if duration > 3 days	IV/NG	BMP Blood pressure CBC w/ differential	· Hypertension · Hyperglycemia	May consider if escalating oxygen needs
<b>Hydrocortisone</b> For PMA < 36 weeks	0.5 mg/kg q12h x 7 days, then 0.5 mg/kg daily x 3 days	IV/NG	BMP Blood pressure CBC w/ differential	· Hypertension · Hyperglycemia	

### All patients should receive supportive care (IV fluids, anti-pyretics, etc.).

### • Nebulized respiratory medications for patients:

- o Nebulized respiratory medications should be avoided in non-intubated patients unless otherwise indicated in patients with bronchospasms to further prevent the spread of the COVID-19 if indicated, inhalers (MDIs) with spacers are preferred for non-intubated patients
- o If indicated, nebulized medications with a closed circuit may be used in intubated patients
- o For COVID-19 negative non-intubated patients, nebulized respiratory medications are preferred over MDIs

PNA = Post-natal age; PMA = Post-menstrual age

### Recommendations for baseline laboratory testing before starting remdesivir

## Baseline laboratory testing needed

- Neo-19
  - Liver function test
  - Serum creatinine
- PTT/INR

## Discontinue remdesivir if:

- Signs/symptoms of infusion-related/anaphylactic reactions
  - o CV: Hypotension, hypertension, tachycardia, bradycardia
  - o Resp: Hypoxia, dyspnea, wheezing
  - o Other: Fever, angioedema, rash, nausea, diaphoresis, shivering
- ALT > 10x upper limit of normal
- ALT elevation + signs/symptoms of liver inflammation

#### References:

- 1. Karimi A, Rafiei Tabatabaei S, Rajabnejad M, Pourmoghaddas Z, Rahimi H, et al. An Algorithmic Approach to Diagnosis and Treatment of Coronavirus Disease 2019 (COVID-19) in Children: Iranian Expert's Consensus Statement, *Arch Pediatr Infect Dis.* 2020; 8(2):e102400. doi: 10.5812/pedinfect.102400
- 2. Hong H, Wang Y, Chung HT, and Chen CJ. Clinical characteristics of novel coronavirus disease 2019 (COVID 19) in newborns, infants and children. *Pediatr Neonatol.* 2020
- 3. Sun D, Li H, Lu XX, et al. Clinical features of severe pediatric patients with coronavirus disease 2019 in Wuhan: a single center's observational study. *World J Pediatr.* 2020.
- 4. Lu X, Zhang L, Du H, et al. SARS-CoV-2 Infection in Children. N Engl J Med. 2020.
- 5. Cui Y and Tian M. A 55 day old female infected with COVID 19: presenting pneumonia, liver injury, and heart damage manuscript. *IDSA*. 2020.
- 6. Inpatient guidance for treatment of COVID-19 in adults and children. University of Michigan. Available from: http://www.med.umich.edu/asp/pdf/adult\_guidelines/COVID-19-treatment.pdf
- 7. Wang L, Shi Y, Xiao T, et al. Chinese expert consensus on the perinatal and neonatal management for the prevention and control of the 2019 novel coronavirus infection (First edition). *Ann Transl Med.* 2020;8(3):47.
- 8. Zeng L, Xia S, Yuan W, et al. Neonatal early-onset infection with SARS-CoV-2 in 33 neonates born to mothers with COVID-19 in Wuhan, China (Research Letter). *JAMA Pediatr.* 2020
- 9. Fact sheet for healthcare providers emergency use authorization (EUA) of Veklury® (remdesivir) for hospitalized pediatric patients weighing 3.5 kg to less than 40 kg or hospitalized pediatric patients less than 12 years of age weighing at least 3.5 kg. Available from: https://www.fda.gov/media/137566/download (Accessed on 3 June 2021).
- 10. Saikia B, Tang J, Robinson S, et al. Neonates With SARS-CoV-2 infection and Pulmonary Disease Safely Treated With Remdesivir. Pediatr Infect Dis J 2021; 40:e194-196.
- 11. Saikia B & Bandi S. RE: Remdesivir use in premature neonates with SARS-CoV-2 Infection. Available from: https://pediatrics.aappublications.org/content/re-redesivir-use-premature-neonates-sars-cov-2-infection (Accessed on 3 June 2021).
- 12. Parsons S and Tran VL. The Triology of SARS-CoV-2 in Pediatrics (Part 1): Acute COVID-19 in Special Populations. J Pediatr Pharmacol Ther. 2021; 26(3): 220-239
- 13. Children's Hospital of the King's Daugthers Treatment Guideline for COVID-10 in Children (Accessed 3 June 2021)
- 14. COVID-19 Treatment Guidelines Panel. Coronavirus Disease 2019 (COVID-19) Treatment Guidelines:Therapeutic Management of Hospitalized Children With COVID-19. Available at: <a href="https://www.covid19treatmentguidelines.nih.gov/management/clinical-management-of-children/hospitalized-children-therapeutic-management/">https://www.covid19treatmentguidelines.nih.gov/management/clinical-management-of-children/hospitalized-children-therapeutic-management/</a> (Accessed 15 November 2022)
- 15. RECOVERY Collaborative Group: Randomized Evaluation of COVID-19 Therapy (RECOVERY. Available at: <a href="https://www.recoverytrial.net/files/recovery-protocol-v23-1-2022-03-15.pdf">https://www.recoverytrial.net/files/recovery-protocol-v23-1-2022-03-15.pdf</a>) (Accessed 15 November 2022).
- 16. Sarhan MA, Casalino M, Paopongsawan P, et al. SARS-CoV-2 Associated Respiratory Failure in a Preterm Infant and the Outcome after Remdesivir Treatment. Pediatr Infect Dis J 2022;41: e233-234
- 17. Potential Cardiotoxic Effects of Remdesivir on Cardiovascular System: A Literature Review. Cardiovasc Toxicol. 2022; 22(3): 268-272

18. Verheijen AC, Janssen EER, van der Putten ME, et al. Management of severe neonatal respiratory disress due to vertical transmission of severe acute respiratory syndrome coronavirus 2:a case report. J Med Case Rep. 2022; 16: 140

### Summary of Revisions

- 6/10/2021
  - o Changed ID consult required to recommended when ordering remdesivir
  - o Common clinical characteristics added apnea
  - o Changed remdesivir from compassionate use to EUA
  - o Added Duration of treatment pending on mechanical ventilation/ECMO status
  - Remdesivir
    - Changed remdesivir dosing based on weight and post-natal age
    - Modified age range cut-off for pediatric use
    - Included dosing recommendation for CVVH or hemodialysis
    - Omitted urinalysis from remdesivir monitoring
    - Updated inclusion/exclusion criteria
    - Included baseline laboratory testing required
    - Added criteria to consider discontinuation of remdesivir
    - Removed procuring/turnaround time for initiating remdesivir treatment.
  - o Corticosteroids added dexamethasone/hydrocortisone with comments on place in therapy
  - Hydroxychloroquine removed as recommended therapy
- 11/16/22
  - Remdesivir
    - FDA approved for weight ≥3 kg AND PNA ≥ 28 days
    - Decreased weight cut-off
    - Increased PNA cut-off
    - Added Prolonged QT interval
  - o Changed corticosteroid selection by PMA cut-off
  - o Removed EUA information
  - o Revised wording for Gilead baseline laboratory testing