Treatment Recommendations for Hospitalized Patients with COVID-19

Latest Revision

- The latest revision of this guideline includes updates based on the National Institute of Health (NIH, Table 1), the Southwest Texas Regional Advisory Council (STRAC), and FDA Emergency Use Authorization (EUA) recommendations for the pharmacologic treatment of COVID-19:
    - **Additions of remdesivir, baricitinib, bamlanivimab and casirivimab/imdevimab**
    - **Updates on corticosteroids**

Background

- Contact COVID-ID team upon diagnosis of COVID-19 for hospitalized adult patients at UH
    - Pager: 210-203-4139
- All patients with COVID-19 should be evaluated for enrollment in an active clinical trial if applicable prior to initiation of non-study therapies
- Pediatric considerations
    - Pediatric patients may receive EUA (emergency use authorization) remdesivir, baricitinib or bamlanivimab at physician discretion
    - Recommend consultation with pediatric infectious disease prior to initiation
    - Remdesivir EUA: > 3.5 - 40 kg
        - Dosing: 5 mg/kg IV x 1 loading dose, followed by 2.5 mg/kg IV once daily
    - Baricitinib EUA: > 2 years old
        - 2 - 9 years of age dosing: 2 mg daily
        - > 9 years of age dosing: 4 mg daily
    - Bamlanivimab EUA: > 12 years old and > 40 kg
        - 700 mg IV X 1 dose
    - Casirivimab/imdevimab EUA: > 12 years old and > 40 kg
        - 1200 mg/1200 mg IV x 1 dose

Remdesivir

- Remdesivir (Veklury®) was approved by the FDA in October 2020 for treatment of hospitalized patients (≥ 12 years of age weighing ≥ 40 kg) with COVID-19
- STRAC criteria for all patients
    - Symptom onset within 14 days
    - COVID-19 infection confirmed by molecular amplification or antigen laboratory test
    - eGFR ≥ 30 (ID consultation recommended for exceptions)
    - AST/ALT < 5x upper limit of normal
    - Age ≥ 12 years and weight ≥ 40 kg

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- STRAC recommendations for patients who should NOT receive remdesivir
    - Patients who are already on hospice/comfort care or unlikely to survive for 24 hours
    - Patients who are improving and likely will be discharged from the hospital within 72 hours.
    - Patients who have been intubated for COVID symptoms > 36 hours
- In the event of limited supply, Infectious Diseases may tier eligible patients, giving preference to those most likely to benefit.

Baricitinib

- Baricitinib (Olumiant®) received emergency use authorization (EUA) from the FDA in November of 2020 in combination with remdesivir for the treatment of hospitalized COVID-19 patients needing oxygen.
- Patient selection:
    - Evaluate baseline eGFR, liver enzymes, and complete blood count to determine treatment suitability and dose. Monitor closely patients with abnormal baseline and post-baseline laboratory values. Dosage adjustments necessary for patients with laboratory abnormalities. (See Appendix A)
    - Baricitinib is not recommended for patients:
        - On dialysis
        - With end-stage renal disease (ESRD, EGFR < 15 mL/min/1.73 m^2)
        - With acute kidney injury

Bamlanivimab and casirivimab/imdevimab

- These products received emergency use authorization (EUA) from the FDA in November 2020 for the treatment of mild to moderate COVID-19 in adults and pediatrics with positive tests who are ≥ 12 years old and > 40 kg and who are at high risk for progressing to severe disease and hospitalization (see appendix B).
- Benefit of treatment with bamlanivimab has not been observed in patients hospitalized due to COVID-19. Monoclonal antibodies, such as bamlanivimab, may be associated with worse clinical outcomes when administered to hospitalized patients with COVID-19 requiring high flow oxygen or mechanical ventilation.

Table 1: UH Treatment Recommendations for Adults with COVID-19	
Disease Severity	**Recommended Therapy**
Patients in ED not meeting criteria for hospitalization, not requiring supplemental O_2, with symptoms < 10 days, weigh at least > 40 kg, and are at high risk for progressing to severe COVID-19 and/or hospitalization (see Appendix B)	May consider **bamlanivimab** 700 mg IV X 1 dose, if available* OR **casirivimab/imdevimab** 1200 mg/1200 mg X 1 dose, if available* Higher consideration warranted in severely immunosuppressed patients and those with multiple risk factors
Not hospitalized or hospitalized but does not require supplemental oxygen	No specific therapy recommended May consider **remdesivir** for patients with particularly high risk of clinical deterioration
Hospitalized and requires supplemental oxygen (but does not require high-flow, non-invasive or invasive mechanical ventilation, or ECMO)	**Remdesivir** 200 mg IV x 1 day, followed by remdesivir 100 mg x 4 days or until hospital discharge May consider addition of **dexamethasone** 6 mg IV or PO daily for up to 10 days or until discharge and/or **baricitinib** 4 mg daily X 14 days or until discharge
Hospitalized and requires oxygen delivery through a high-flow device or non-invasive ventilation	**Remdesivir** 200 mg IV x 1 day, followed by remdesivir 100 mg x 4 days or until hospital discharge + **Dexamethasone** 6 mg IV or PO daily for up to 10 days or until discharge and/or **baricitinib** 4 mg daily X 14 days or until discharge
Hospitalized and requires invasive mechanical ventilation or ECMO	**Dexamethasone** 6 mg IV or PO daily for up to 10 days or until discharge + *(For patients who have been intubated < 36 hours)* **Remdesivir** 200 mg IV x 1 day, followed by remdesivir 100 mg x 4 days or until hospital discharge

*There is limited supply of bamlanivimab or casirivimab/imdevimab available for ED use. If it is unavailable at UH consider referring patient to the STRAC Regional Infusion Center (RIC) at 210/934-0733 or email refer@strac.org. A patient MUST have a referral and appointment for the RIC.

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Appendix A
Dosage Adjustment for Baricitinib in Patients with Abnormal Laboratory Values

Laboratory Analyte	Laboratory Analyte Value	Recommendation*
eGFR	≥ 60 mL/min/1.73 m^2	• Adults and pediatric patients 9 years of age and older: No dosage adjustment • Pediatric patients 2 years to less than 9 years of age: 2 mg once daily
	30 – 60 mL/min/1.73 m^2	• Adults and pediatric patients 9 years of age and older: 2 mg once daily • Pediatric patients 2 years to less than 9 years of age: 1 mg once daily
	15 - < 30 mL/min/1.73 m^2	• Adults and pediatric patients 9 years of age and older: 1 mg once daily • Pediatric patients 2 years to less than 9 years of age: Not recommended
	< 15 mL/min/1.73 m^2	Not recommended
Absolute Lymphocyte Count (ALC)	≥ 200 cells/µL	Maintain dose
	< 200 cells/µL	Consider interruption until ALC is ≥ 200 cells/µL
Absolute Neutrophil Count (ANC)	≥ 500 cells/µL	Maintain dose
	< 500 cells/µL	Consider interruption until ANC is ≥ 500 cells/µL
Aminotransferases	If increase in ALT or AST are observed and drug-induced liver injury (DILI) is suspected	Interrupt baricitinib until the diagnosis of DILI is excluded

ALC = absolute lymphocyte count, ALT = alanine transaminase, ANC = absolute neutrophil count, AST = aspartate transaminase, DILI = drug induced liver injury, eGFR = estimated glomerular filtration rate, hrs = hours.
*If a laboratory abnormality is likely due to the underlying disease state, consider the risks and benefits of continuing baricitinib at the same or a reduced dose.

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Appendix B
Patient Factors with High Risk for Progressing to Severe COVID-19 and/or Hospitalization

- Body mass index (BMI) ≥ 35
- Chronic kidney disease
- Diabetes
- Immunosuppressive disease
- Currently receiving immunosuppressive treatment
- ≥ 65 years of age
- ≥ 55 years of age AND
    - Cardiovascular disease, OR
    - Hypertension, OR
    - Chronic obstructive pulmonary disease/other chronic respiratory disease.
- 12 – 17 years of age AND
    - BMI ≥ 85th percentile for their age and gender based on CDC growth charts, https://www.cdc.gov/growthcharts/clinical_charts.htm , OR
    - Sickle cell disease, OR
    - Congenital or acquired heart disease, OR
    - Neurodevelopmental disorders, for example, cerebral palsy, OR
    - A medical-related technological dependence, for example, tracheostomy, gastrostomy, or positive pressure ventilation (not related to COVID-19), OR
    - Asthma, reactive airway or other chronic respiratory disease that requires daily medication for control

References:

1. Therapeutic Management of Patients with COVID-19. Last updated 10/9/2020. https://www.covid19treatmentguidelines.nih.gov/therapeutic-management/
2. Beigel JH et al. Remdesivir for the treatment of COVID-19- final report. N Engl J Med 2020; 383:1813-26.
3. RECOVERY collaborative group. Dexamethasone in hospitalized patients with COVID-19-preliminary report. N Engl J Med 2020.
4. Baricitinab. Emergency use authorization fact sheet for health care providers. Eli Lilly and Company. 2020.

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