COVID-19 Treatment Recommendations for Hospitalized Patients

Latest Revisions

- The latest revision of this guideline includes updates based on the National Institute of Health (NIH, Table 1) guidelines and FDA Emergency Use Authorization (EUA) recommendations for the pharmacologic treatment of COVID-19:
  - **Addition of referral to "COVID-19 Treatment Recommendations for Outpatients"**
  - **Incorporating expansion of remdesivir to allow for administration in hospitalized patients not requiring supplemental oxygen who are at high risk for progression to severe COVID with a three day duration.**

Background

- Contact COVID-ID team upon diagnosis of COVID-19 for hospitalized adult patients at UH for questions about treatment recommendations
  - Phone: 210-990-4630
  - 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
- All recommendations are subject to change based on updates to FDA EUA updates and most recent EUA recommendations should be followed

Table 1: UH Treatment Recommendations for Adults with COVID-19

Disease Severity	Recommended Therapy
Not hospitalized/Outpatient	Steroids are NOT recommended Refer to COVID-19 Treatment Recommendations for Outpatients
Patients in ED not meeting criteria for hospitalization, in the observation unit or hospitalized for indication other than COVID • Do not require supplemental O_2 • Symptoms < 10 days • Weigh at least > 40 kg and ≥ 12 years • Considered high risk for progressing to severe COVID-19 and/or hospitalization (see Appendix B)	May consider administration of **monoclonal antibodies** or remdesivir or may provide outpatient prescription for **oral antivirals** as specified in COVID-19 Treatment Recommendations for Outpatients Higher consideration for treatment warranted in severely immunosuppressed patients and those with multiple risk factors (see Appendix B)

Approved by Antimicrobial P&T Subcommittee: 12/01/2020; 12/07/2020, 12/28/2020, 04/26/2021, 07/26/21, 09/21/21, 12/21/21, 01/20/22,
Approved by Pulmonary P&T Subcommittee: 07/26/21
Approved by Pharmacy &Therapeutics Committee: 12/3/2020 (expedited); 12/11/2020, 01/08/2021, 05/14/2021, 07/30/2021 (expedited), 10/01/21, 01/06/22 (expedited), 1/27/2022 (expedited)

Table 1: UH Treatment Recommendations for Adults with COVID-19	
Disease Severity	**Recommended Therapy**
Hospitalized but does not require supplemental oxygen • Symptoms < 7 days • Positive COVID test within last 4 days • Anticipate to remain hospitalized for at least 3 days • Considered high risk for progression to severe COVID-19 (see Appendix B)	May consider **monoclonal antibodies** or **remdesivir** 200 mg IV x 1 dose on day 1, 100 mg IV x 1 on days 2 and 3
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 IV x 4 days or until hospital discharge + **Dexamethasone** 6 mg IV or PO daily for up to 10 days + ***EITHER*** baricitinib 4 mg daily x 14 days **OR** tocilizumab 8 mg/kg IV (up to 800 mg) ***Do not use baricitinib and tocilizumab in combination** **In patients not currently receiving baricitinib**, may consider tocilizumab as one-time dose of 8 mg/kg IV (up to 800 mg) in patients requiring high-flow nasal cannula (40% FiO2, 30 L/min) with a C-reactive protein (CRP) ≥75 mg/L who were admitted within the previous 3 days
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 + May consider addition of tocilizumab as one-time dose of 8 mg/kg IV (up to 800 mg) in patients within 24 hours of ICU admission

*There is a limited supply of monoclonal antibodies available for hospital ED use. If it is unavailable at UH or patient is outpatient, please call 1-800-742-5990 or e-mail infusionreferral@bcsf.net for more information on outpatient administration of monoclonal antibodies.

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Approved by Pharmacy &Therapeutics Committee: 12/3/2020 (expedited); 12/11/2020, 01/08/2021, 05/14/2021, 07/30/2021 (expedited), 10/01/21, 01/06/22 (expedited), 1/27/2022 (expedited)

Remdesivir

- Remdesivir (Veklury®) was approved by the FDA in October 2020 for treatment of hospitalized patients with COVID-19. Criteria was expanded in January 2022 to include patients with mild-to-moderate COVID-19 who are at high risk for progression to severe COVID-19
- **Duration: will depend on severity of COVID symptoms (see Table 1)**
    - **Inpatients REQUIRING supplemental oxygen = 5 days**
        - **Symptom onset within 10 days**
        - **Positive COVID test**
        - **AST/ALT < 10 x upper limit of normal**
        - **CrCl > 30 ml/min**
    - **Inpatients NOT REQUIRING supplement oxygen = 3 days**
        - **Symptoms < 7 days**
        - **Positive COVID test within last 4 days**
        - **Anticipate to remain hospitalized for at least 3 days**
        - **Considered high risk for progression to severe COVID-19 (see Appendix B)**
- In the event of limited supply, Infectious Diseases may tier eligible patients, giving preference to those most likely to benefit

Baricitinib

- Baricitinib (Olumiant®) received EUA from the FDA in November of 2020 in combination with remdesivir for the treatment of hospitalized COVID-19 patients needing oxygen.
- Patient selection:
    - Patients receiving supplemental oxygen with a contraindication to corticosteroids
    - Baricitinib should not be used in combination with tocilizumab
    - 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
    - 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)
- In the event of limited supply, Infectious Diseases may tier eligible patients, giving preference to those most likely to benefit.

Monoclonal Antibodies

- Received emergency use authorization (EUA) from the FDA 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).
    - Bamlanivimab/etesevimab 700 mg/1400 mg IV x 1 dose
    - Casirivimab/imdevimab 600 mg/600 mg IV x 1 dose
    - Sotrovimab 500 mg IV x 1 dose

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- Product availability is determined by: allocation from the government and efficacy against predominant variant(s)

Tocilizumab

- Tocilizumab (Actemra®) is an IL-6 inhibitor that received EUA from the FDA in June of 2021
    - May be effective for treatment of COVID-19 in hospitalized adults and pediatric patients (2 years of age and older) who are receiving systemic corticosteroids and require supplemental oxygen, non-invasive or invasive mechanical ventilation, or ECMO
- Patient selection:
    - Tocilizumab should be given as a one-time dose of 8 mg/kg up to 800 mg in combination with corticosteroids in hospitalized adult patients with COVID-19 who meet the following criteria
        - NOT currently receiving baricitinib
        - Critically ill patients within 24 hours of admit to the intensive care unit
        - Non-critically ill patients:
            - Timing: within first 3 days of hospitalization
            - Oxygenation: patients requiring high-flow nasal cannula oxygen (40% FIO2, 30 L/min), noninvasive ventilation or mechanical ventilation
        - Inflammatory markers: CRP ≥ 75 mg/L
- In the event of limited supply, Infectious Diseases may tier eligible patients, giving preference to those most likely to benefit.

Pediatric Considerations

- Pediatric patients may receive EUA (emergency use authorization) remdesivir or baricitinib 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
- Casirivimab/imdevimab EUA: ≥ 12 years old and ≥ 40 kg
    - 600 mg/600 mg IV x 1 dose
- Bamlanivimab/etesevimab EUA: ≥ 12 years old and ≥ 40 kg
    - 700 mg/1400 mg IV x 1 dose
- Sotrovimab EAU: ≥12 years old and ≥40 kg
    - 500 mg IV x 1 dose
- Tocilizumab EUA: > 2 years old
    - Patients weighing <30 kg: 12 mg/kg IV x 1 (up to 800 mg)
    - Patients weighing ≥30 kg: 8 mg/kg IV x 1 (up to 800 mg)

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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

***Not listed in order of degree of risk conferred**

- Body mass index (BMI) ≥ 25 (age 12-17 you BMI ≥85th percentile)
- Pregnancy
- Chronic kidney disease
- Diabetes
- Immunosuppressive disease
- Currently receiving immunosuppressive treatment
- ≥ 65 years of age
- Cardiovascular disease (including congenital heart disease)
- Hypertension
- Chronic obstructive pulmonary disease/other chronic respiratory disease (including asthma, interstitial lung disease, cystic fibrosis and pulmonary hypertension)
- Sickle cell disease
- Neurodevelopmental disorders, for example, cerebral palsy or Down's Syndrome, OR
- A medical-related technological dependence, for example, tracheostomy, gastrostomy, or positive pressure ventilation (not related to COVID-19)
- Other risk factors for severe COVID as identified by CDC
- Or most recent criteria in FDAs most recent EUA update

Reference

1. Therapeutic Management of Patients with COVID-19. Last updated 01/05/2022. https://www.covid19treatmentguidelines.nih.gov/therapeutic-management/

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