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RISK MANAGEMENT SERVICES

CDC Update - Therapeutic Management of Adults with COVID-19

Executive Summary

Two main processes are thought to drive the pathogenesis of COVID-19. Early in the clinical course, the disease is primarily driven by replication of SARS-CoV-2. Later in the clinical course, the disease appears to be driven by a dysregulated immune/inflammatory response to SARS-CoV-2 that leads to tissue damage. Based on this understanding, it is anticipated that antiviral therapies would have the greatest effect early in the course of the disease, while immunosuppressive/anti-inflammatory therapies are likely to be more beneficial in the later states of COVID-19.

No therapy has been proven to be beneficial in outpatients with mild to moderate COVID-19 who are not at high risk for disease progression. The COVID-19 Treatment Guidelines Panel (the Panel) recommends providing supportive care and symptomatic management to outpatients with COVID-19; steps should also be taken to reduce the risk of SARS-CoV-2 transmission to others. Patients should be advised about when to seek in-person evaluation. See Outpatient Management of Acute COVID-19 for more information https://www.covid19treatmentguidelines.nih.gov/outpatient-management/.

In outpatients with mild to moderate COVID-19 who are at high risk for disease progression, anti-SARS-CoV-2 antibody-based therapies may have the greatest potential for clinical benefit during the earliest stages of infection. For these patients, the Panel recommends administering **bamlanivimab plus etesevimab (Alla) or casirivimab plus imdevimab (Alla),** both of which are available through Emergency Use Authorizations (EUAs) from the Food and Drug Administration (FDA). See Anti-SARS-CoV-2 Monoclonal Antibodies for more information about using these combinations and other monoclonal antibodies. https://www.covid19treatmentguidelines.nih.gov/anti-sars-cov-2-antibody-products/anti-sars-cov-2-monoclonal-antibodies/

Remdesivir, an antiviral agent, is currently the only drug that is approved by the FDA for the treatment of COVID-19. It is recommended for use in hospitalized patients who require supplemental oxygen. However, it is not routinely recommended for patients who require mechanical ventilation due to the lack of data showing benefit at this advanced stage of the disease.

Dexamethasone, a corticosteroid, has been found to improve survival in hospitalized patients who require supplemental oxygen, with the greatest benefit observed in patients who require mechanical ventilation. Therefore, the use of dexamethasone is strongly recommended in this setting.

Adding tocilizumab, a recombinant humanized anti-interleukin-6 receptor monoclonal antibody, to dexamethasone therapy was found to improve survival among patients who were exhibiting rapid respiratory decompensation due to COVID-19.

The Panel continues to review the most recent clinical data to provide up-to-date treatment recommendations for clinicians who are caring for patients with COVID-19. The chart below summarizes the Panel's recommendations for managing patients with varying severities of the disease.

https://www.covid19treatmentguidelines.nih.gov/therapeutic-management/
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Figure 1. Pharmacologic Management of Patients with COVID-19 Based on Disease Severity

Doses and durations are listed in the footnotes.

DISEASE SEVERITY	PANEL'S RECOMMENDATIONS
Not Hospitalized, Mild to Moderate COVID-19	For patients who are not at high risk for disease progression, provide supportive care and symptomatic management **(AIII)**. For patients who are at high risk of disease progression (as defined by the FDA EUA criteria for treatment with anti-SARS-CoV-2 monoclonal antibodies), use one of the following combinations: • **Bamlanivimab plus etesevimab (AIIa)** • **Casirivimab plus imdevimab (AIIa)**
Hospitalized but Does Not Require Supplemental Oxygen	There are insufficient data to recommend either for or against the routine use of remdesivir. For patients at high risk of disease progression, the use of remdesivir may be appropriate.
Hospitalized and Requires Supplemental Oxygen	Use one of the following options: • **Remdesivir**[a,b] (e.g., for patients who require minimal supplemental oxygen) **(BIIa)** • **Dexamethasone**[c] **plus remdesivir**[a,b] (e.g., for patients who require increasing amounts of supplemental oxygen) **(BIII)**[d,e] • **Dexamethasone**[c] (e.g., when combination therapy with remdesivir cannot be used or is not available) **(BI)**
Hospitalized and Requires Oxygen Delivery Through a High-Flow Device or Noninvasive Ventilation	Use one of the following options: • **Dexamethasone**[c] **(AI)**[e] • **Dexamethasone**[c] **plus remdesivir**[a,b] **(BIII)**[d,e] For patients who were recently hospitalized[f] with rapidly increasing oxygen needs and systemic inflammation: • Add **tocilizumab**[g] to one of the two options above **(BIIa)**
Hospitalized and Requires Invasive Mechanical Ventilation or ECMO	• **Dexamethasone**[c] **(AI)**[h] For patients who are within 24 hours of admission to the ICU: • **Dexamethasone**[c] **plus tocilizumab**[g] **(BIIa)**

Rating of Recommendations: A = Strong; B = Moderate; C = Optional
Rating of Evidence: I = One or more randomized trials without major limitations; IIa = Other randomized trials or subgroup analyses of randomized trials; IIb = Nonrandomized trials or observational cohort studies; III = Expert opinion

[a] The remdesivir dose is 200 mg IV for one dose, followed by remdesivir 100 mg IV once daily for 4 days or until hospital discharge (unless the patient is in a health care setting that can provide acute care that is similar to inpatient hospital care). Treatment duration may be extended to up to 10 days if there is no substantial clinical improvement by Day 5.

[b] For patients who are receiving remdesivir but progress to requiring oxygen through a high-flow device, noninvasive ventilation, invasive mechanical ventilation, or ECMO, remdesivir should be continued until the treatment course is completed.

[c] The dexamethasone dose is 6 mg IV or PO once daily for 10 days or until hospital discharge. If dexamethasone is not available, equivalent doses of other corticosteroids (e.g., prednisone, methylprednisolone, hydrocortisone) may be used. See the Corticosteroids section for more information.

[d] The combination of dexamethasone and remdesivir has not been studied in clinical trials.

[e] In the rare circumstances where corticosteroids cannot be used, **baricitinib plus remdesivir** can be used **(BIIa)**. The FDA has issued an EUA for baricitinib use in combination with remdesivir. The dose for baricitinib is 4 mg PO once daily for 14 days or until hospital discharge.

[f] For example, within 3 days of hospital admission. See the Interleukin-6 Inhibitors section for more information.

[g] The tocilizumab dose is 8 mg/kg of actual body weight (up to 800 mg) administered as a single IV dose. Tocilizumab should not be combined with baricitinib and should be avoided in certain groups of patients who are at increased risk for complications. See the Interleukin-6 Inhibitors section for more information.

[h] The combination of **dexamethasone plus remdesivir** may be considered for patients who have recently been intubated **(CIII)**. The Panel **recommends against** the use of remdesivir monotherapy in these patients.

Key: ECMO = extracorporeal membrane oxygenation; EUA = Emergency Use Authorization; FDA = Food and Drug Administration; ICU = intensive care unit; IV = intravenous; the Panel = the COVID-19 Treatment Guidelines Panel; PO = orally