

# Therapeutic Management of Patients with COVID-19

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## Executive Summary

Two main processes are thought to drive the pathogenesis of COVID-19. Early in the course of the infection, the disease is primarily driven by replication of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Later in the course of infection, the disease is driven by an exaggerated immune/inflammatory response to the virus 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 disease, while immunosuppressive/anti-inflammatory therapies are likely to be more beneficial in the later stages of COVID-19.

In the earliest stages of infection, before the host has mounted an effective immune response, anti-SARS-CoV-2 antibody-based therapies may have their greatest likelihood of having an effect. In this regard, although there are insufficient data from clinical trials to recommend either for or against the use of any specific therapy in this setting, preliminary data suggests that outpatients may benefit from receiving anti-SARS-CoV-2 monoclonal antibodies early in the course of infection. The anti-SARS-CoV-2 monoclonal antibodies [bamlanivimab](#) and [casirivimab plus imdevimab](#) are available through Emergency Use Authorizations for outpatients who are at high risk for disease progression.

Remdesivir, an antiviral agent, is currently the only drug that is approved by the Food and Drug Administration 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.<sup>1-4</sup>

Dexamethasone, a corticosteroid, has been found to improve survival in hospitalized patients who require supplemental oxygen, with the greatest effect observed in patients who require mechanical ventilation. Therefore, the use of dexamethasone is strongly recommended in this setting.<sup>5-8</sup>

The COVID-19 Treatment Guidelines Panel (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. Figure 1 summarizes the Panel's recommendations for managing patients with varying severities of disease. A comprehensive summary of the clinical data for the drugs that are being investigated for the treatment of COVID-19 can be found in the [Antiviral Therapy](#), [Immune-Based Therapy](#), and [Adjunctive Therapy](#) sections of these Guidelines.

# Figure 1. Pharmacologic Management of Patients with COVID-19 Based on Disease Severity

Doses and durations are listed in the footnote.

DISEASE SEVERITY	PANEL'S RECOMMENDATIONS
<p><b>Not Hospitalized, Mild to Moderate COVID-19</b></p>	<p>There are insufficient data to recommend either for or against any specific antiviral or antibody therapy. SARS-CoV-2 neutralizing antibodies (<b>bamlanivimab</b> or <b>casirivimab plus imdevimab</b>) are available through EUAs for outpatients who are at high risk of disease progression.<sup>a</sup> These EUAs do not authorize use in hospitalized patients.</p> <p><b>Dexamethasone</b> should not be used (<b>AIII</b>).</p>
<p><b>Hospitalized<sup>a</sup> But Does Not Require Supplemental Oxygen</b></p>	<p><b>Dexamethasone</b> should not be used (<b>AIIa</b>).</p> <p>There are insufficient data to recommend either for or against the routine use of <b>remdesivir</b>. For patients at high risk of disease progression, the use of remdesivir may be appropriate.</p>
<p><b>Hospitalized<sup>a</sup> and Requires Supplemental Oxygen</b> (But Does Not Require Oxygen Delivery Through a High-Flow Device, Noninvasive Ventilation, Invasive Mechanical Ventilation, or ECMO)</p>	<p>Use one of the following options:</p> <ul style="list-style-type: none"> <li>• <b>Remdesivir<sup>b,c</sup></b> (e.g., for patients who require minimal supplemental oxygen) (<b>BIIa</b>)</li> <li>• <b>Dexamethasone<sup>d</sup> plus remdesivir<sup>b,c</sup></b> (e.g., for patients who require increasing amounts of supplemental oxygen) (<b>BIII</b>)<sup>e,f</sup></li> <li>• <b>Dexamethasone<sup>d</sup></b> (e.g., when combination therapy with remdesivir cannot be used or is not available) (<b>BI</b>)</li> </ul>
<p><b>Hospitalized<sup>a</sup> and Requires Oxygen Delivery Through a High-Flow Device or Noninvasive Ventilation</b></p>	<p>Use one of the following options:</p> <ul style="list-style-type: none"> <li>• <b>Dexamethasone<sup>d,f</sup></b> (<b>AI</b>)</li> <li>• <b>Dexamethasone<sup>d</sup> plus remdesivir<sup>b,c</sup></b> (<b>BIII</b>)<sup>e,f</sup></li> </ul>
<p><b>Hospitalized<sup>a</sup> and Requires Invasive Mechanical Ventilation or ECMO</b></p>	<p><b>Dexamethasone<sup>d</sup></b> (<b>AI</b>)<sup>g</sup></p>
<p><b>Rating of Recommendations:</b> A = Strong; B = Moderate; C = Optional  <b>Rating of Evidence:</b> 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</p>	

<sup>a</sup> See the Panel's statements on the FDA EUAs for bamlanivimab and casirivimab plus imdevimab. These EUAs do not authorize use in hospitalized patients.

<sup>b</sup> The remdesivir dose is 200 mg IV for one dose, followed by 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.

<sup>c</sup> 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.

<sup>d</sup> 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, such as prednisone, methylprednisolone, or hydrocortisone, may be used. See the Corticosteroids section for more information.

<sup>e</sup> The combination of dexamethasone and remdesivir has not been studied in clinical trials.

<sup>f</sup> 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.

<sup>g</sup> The combination of dexamethasone and remdesivir may be considered for patients who have recently been intubated (**CIII**). Remdesivir alone is **not recommended**.

**Key:** ECMO = extracorporeal membrane oxygenation; EUA = Emergency Use Authorization; FDA = Food and Drug Administration; IV = intravenous; the Panel = the COVID-19 Treatment Guidelines Panel; PO = orally; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2

## References

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