What’s New in the Guidelines

Last Updated: March 5, 2021

The Coronavirus Disease 2019 (COVID-19) Treatment Guidelines is published in an electronic format that can be updated in step with the rapid pace and growing volume of information regarding the treatment of COVID-19.

The COVID-19 Treatment Guidelines Panel (the Panel) is committed to updating this document to ensure that health care providers, patients, and policy experts have the most recent information regarding the optimal management of COVID-19 (see the Panel Roster for a list of Panel members).

New Guidelines sections and recommendations and updates to existing Guidelines sections are developed by working groups of Panel members. All recommendations included in the Guidelines are endorsed by a majority of Panel members (see the Introduction for additional details on the Guidelines development process).

Major revisions to the Guidelines within the last month are as follows:

March 5, 2021

The COVID-19 Treatment Guidelines Panel’s Statement on the Use of Tocilizumab for the Treatment of COVID-19

On February 3, 2021, the Panel issued a statement on the use of tocilizumab for the treatment of COVID-19. The statement included recommendations based on a preliminary report of results from Randomized, Embedded, Multifactorial Adaptive Platform Trial for Community-Acquired Pneumonia (REMAP-CAP). Since the statement was issued, the Panel has reviewed the published results of REMAP-CAP and the preliminary results of the open-label, pragmatic Randomized Evaluation of COVID-19 Therapy (RECOVERY) trial, released on February 11, 2021. Based on this review, the Panel has updated its recommendations on the use of tocilizumab in selected populations of patients with COVID-19, as outlined below.

- The Panel recommends the use of tocilizumab (single intravenous dose of 8 mg/kg of actual body weight, up to 800 mg) in combination with dexamethasone (6 mg daily for up to 10 days) in certain hospitalized patients who are exhibiting rapid respiratory decompensation due to COVID-19. These patients are:
  - Recently hospitalized patients who have been admitted to an intensive care unit (ICU) within the prior 24 hours and who require invasive mechanical ventilation, noninvasive mechanical ventilation (NIV) or high-flow nasal canula (HFNC) oxygen (>0.4 FiO\textsubscript{2}/30 L/min of oxygen flow) (BII\textsubscript{a}); or
  - Recently hospitalized patients (not in an ICU) with rapidly increasing oxygen needs who require NIV or HFNC and have significantly increased markers of inflammation (BII\textsubscript{a}). (Note: The RECOVERY trial inclusion criterion for inflammation was C-reactive protein [CRP] ≥75 mg/L).

- In hospitalized patients with hypoxemia who require conventional oxygen therapy, the Panel recommends using one of the following options: remdesivir (BII\textsubscript{a}), dexamethasone plus remdesivir (BIII), or dexamethasone alone (BII) (see Therapeutic Management of Adults With COVID-19).

- There is insufficient evidence to specify which of these patients would benefit from the addition of tocilizumab. Some Panel members would also give tocilizumab to patients who are exhibiting rapidly increasing oxygen needs while on dexamethasone and have a CRP ≥75.
mg/L, but who do not yet require NIV or HFNC, as described above.

The Panel’s statement includes a detailed discussion of the rationale for these recommendations.

February 23, 2021


On February 9, 2021, the Food and Drug Administration (FDA) issued an Emergency Use Authorization (EUA) to make the anti-severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) monoclonal antibodies bamlanivimab 700 mg and etesevimab 1,400 mg available for the treatment of outpatients with mild to moderate COVID-19 who are at high risk for progressing to severe disease and/or hospitalization. After reviewing the available evidence, the Panel has determined the following:

- The Panel recommends the use of bamlanivimab 700 mg plus etesevimab 1,400 mg for the treatment of outpatients with mild to moderate COVID-19 who are at high risk of clinical progression as defined by the EUA criteria (BIIa). Treatment should be started as soon as possible after the patient has received a positive result on a SARS-CoV-2 antigen or nucleic acid amplification test and within 10 days of symptom onset.

- It is important to note that the authorized dose of bamlanivimab 700 mg plus etesevimab 1,400 mg is lower than the dose given to participants in the Phase 3 study that provides clinical data in support of this therapy. The authorized dose was extrapolated from data demonstrating its antiviral activity, as well as from in vitro studies and pharmacokinetic/pharmacodynamic modeling.

- The Panel recommends against the use of bamlanivimab 700 mg plus etesevimab 1,400 mg for patients who are hospitalized because of COVID-19, except in a clinical trial. However, the combination should be considered for persons with mild to moderate COVID-19 who are hospitalized for a reason other than COVID-19 but who otherwise meet the EUA criteria.

- Given the possibility of a limited supply of bamlanivimab plus etesevimab, as well as challenges of distributing and administering the drugs, priority should be given to patients who are at highest risk for COVID-19 progression based on the EUA criteria.

- Efforts should be made to ensure that communities most affected by COVID-19 have equitable access to bamlanivimab plus etesevimab.

- Bamlanivimab plus etesevimab should not be withheld from a pregnant individual who has a condition that poses a high risk of progression to severe COVID-19 if the clinician thinks that the potential benefit of the combination outweighs the potential risk.

- There are insufficient pediatric data to recommend either for or against the use of bamlanivimab plus etesevimab or other monoclonal antibody products for children with COVID-19 who are not hospitalized but who have risk factors for severe disease. Based on adult studies, bamlanivimab plus etesevimab may be considered on a case-by-case basis for children who meet EUA criteria, especially those who meet more than one criterion or who are aged ≥16 years. In such cases, consultation with a pediatric infectious disease specialist is recommended.

February 11, 2021

Key Updates to the Guidelines

Introduction

Each recommendation in the Guidelines is assigned a rating for the strength of the recommendation.
statement and the quality of the evidence that supports the recommendation. The rating scheme for the quality of evidence has been revised to better define the type of scientific evidence used to support the Panel’s recommendations. The new ratings are as follows:

<table>
<thead>
<tr>
<th>Strength of Recommendation</th>
<th>Quality of Evidence for Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>A: Strong recommendation for the statement</td>
<td>I: One or more randomized trials without major limitations</td>
</tr>
<tr>
<td>B: Moderate recommendation for the statement</td>
<td>IIa: Other randomized trials or subgroup analyses of randomized trials</td>
</tr>
<tr>
<td>C: Optional recommendation for the statement</td>
<td>IIb: Nonrandomized trials or observational cohort studies</td>
</tr>
<tr>
<td></td>
<td>III: Expert opinion</td>
</tr>
</tbody>
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Prevention and Prophylaxis of SARS-CoV-2 Infection

A brief discussion of the SARS-CoV-2 mRNA vaccines that are currently available through EUAs from the FDA has been added to this section. This section also includes updated clinical trial data on the use of hydroxychloroquine for post-exposure prophylaxis (PEP).

Therapeutic Management of Patients With COVID-19

This section has been updated to add rationale to support the recommendations presented in Figure 1. Minor clarifying updates have also been made to the text in Figure 1.

Ivermectin

This section now incorporates the new information and recommendations from the Panel’s statement on ivermectin that was released on January 14, 2021. A new table summarizes the results from several randomized clinical trials and retrospective cohort studies of ivermectin use in patients with COVID-19 that have been published in peer-reviewed journals or have been made available as manuscripts ahead of peer review.

Anti-SARS-CoV-2 Monoclonal Antibodies

Bamlanivimab and the combination of casirivimab and imdevimab are available through FDA EUAs for the treatment of outpatients with mild to moderate COVID-19 who are at high risk for progressing to severe disease and/or hospitalization. This new section of the Guidelines expands on the bamlanivimab statement that was released on November 18, 2020, and the casirivimab plus imdevimab statement that was released on December 2, 2020. This section also includes considerations for using these anti-SARS-CoV-2 monoclonal antibodies in pregnant people and children. A separate table has been created to summarize the clinical trial data that led to the issuance of the EUAs.

On February 9, 2021, the FDA issued an **EUA for bamlanivimab plus etesevimab** for the treatment of mild to moderate COVID-19 in outpatients who have received positive results on a nucleic acid amplification test or an antigen test for SARS-CoV-2 and who are at high risk for clinical progression. The Panel will issue recommendations on the use of bamlanivimab plus etesevimab shortly.

Kinase Inhibitors: Baricitinib and Other Janus Kinase Inhibitors, and Bruton's Tyrosine Kinase Inhibitors

The information and recommendations from the Panel’s December 14, 2020, statement on the use of baricitinib have been added to this section. The section also includes a more detailed description of the clinical data from the Adaptive COVID-19 Treatment Trial 2 (ACTT-2) study that led to the FDA issuing an EUA for the use of baricitinib and remdesivir for the treatment of certain hospitalized patients with COVID-19.
Other Updates to the Guidelines

The following sections received minor updates during this revision:

- General Considerations
- Testing for SARS-CoV-2 Infection
- Antithrombotic Therapy in Patients With COVID-19
- Zinc Supplementation and COVID-19