What’s New in the Guidelines

Last Updated: October 27, 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:

October 27, 2021

Influenza and COVID-19

The Panel has updated the information on administering influenza vaccines to people with COVID-19. For symptomatic COVID-19 patients, clinicians should consider deferring influenza vaccination until the patients have completed their COVID-19 isolation period and are no longer moderately or severely ill. People with SARS-CoV-2 infection who are not moderately or severely ill (including those who are asymptomatic) should seek influenza vaccination when they no longer require isolation. They can be vaccinated sooner if they are in a health care setting for other reasons.

This section also notes that an influenza vaccine and a COVID-19 vaccine may be administered concurrently at different injection sites.

October 19, 2021

Key Updates to the Guidelines

Prevention of SARS-CoV-2 Infection

In this section, the Panel stresses that COVID-19 vaccination remains the most effective way to prevent SARS-CoV-2 infection. The key updates include:

Vaccine-Related Updates:

• The Centers for Disease Control and Prevention (CDC) recommends giving an additional dose of an mRNA COVID-19 vaccine to people who are at high risk of having suboptimal immune responses to a two-dose series. This dose should be given at least 28 days after the person receives the second dose of the two-dose series.

• Because the effectiveness of the BNT162b2 (Pfizer-BioNTech) vaccine may wane over time in some individuals, CDC recommends administering a booster dose of the vaccine to these individuals at least 6 months after they complete the primary series. People who received the primary series of the BNT162b2 vaccine but who have an increased risk of SARS-CoV-2 exposure or transmission may also receive a booster dose.
• The Panel has updated the information on vaccine-associated adverse effects, including myocarditis, pericarditis, and Guillain-Barré syndrome.

**Anti-SARS-CoV-2 Monoclonal Antibodies for Post-Exposure Prophylaxis:**

• A new subsection provides the Panel’s recommendations for the use of either bamlanivimab plus etesevimab or casirivimab plus imdevimab as post-exposure prophylaxis (PEP) for those who have a history of exposure to individuals with SARS-CoV-2 infection and who are at high risk of progression to serious disease if they acquire the infection.

• The clinical trial data that support these recommendations are summarized in this section.

**Clinical Spectrum of SARS-CoV-2 Infection**

A new subsection entitled Infectious Complications in Patients With COVID-19 has been added to this section to discuss coinfections, reactivation of latent infection, nosocomial infections, and opportunistic fungal infections that may occur in patients with COVID-19.

**Therapeutic Management of Nonhospitalized Adults With COVID-19**

The text and figure have been updated to add bamlanivimab plus etesevimab as an anti-SARS-CoV-2 monoclonal antibody (mAb) combination option for the treatment of nonhospitalized patients with mild to moderate COVID-19 who are at high risk of progression to severe disease.

**Oxygenation and Ventilation**

The recommendations and rationale for performing awake prone positioning in nonmechanically ventilated adults have been updated. This section has also been reorganized and edited to improve readability.

**Anti-SARS-CoV-2 Monoclonal Antibodies**

In June 2021, the distribution of bamlanivimab plus etesevimab was paused in the United States because of the increase in the combined frequencies of two circulating SARS-CoV-2 variants: Gamma (P.1) and Beta (B.1.351). Since then, the Delta (B.1617.2, non-AY.1/AY.2) variant has become the predominant variant circulating in all states. Because the combination of bamlanivimab plus etesevimab retains activity against the Delta variant, the distribution of these anti-SARS-CoV-2 mAbs has resumed. The Panel now includes bamlanivimab plus etesevimab as a treatment option for nonhospitalized patients with mild to moderate COVID-19 who are at high risk for clinical progression. The information on the in vitro susceptibility of circulating variants to these mAbs and the potential activities of these mAbs against variants has been updated.

**Interleukin-1 Inhibitors**

The Panel has added recommendations to this section regarding canakinumab, a mAb that blocks interleukin-1 signaling. The Panel recommends against the use of canakinumab for the treatment of COVID-19, except in a clinical trial (BIIa). This section also now includes a detailed discussion of the data on the use of anakinra from the SAVE-MORE, REMAP-CAP, and CORIMUNO-ANA-1 trials. There is no change to the Panel’s recommendation for anakinra.

**Interleukin-6 Inhibitors**

This section has been updated to incorporate results from the sarilumab arm of the REMAP-CAP trial, an open-label, adaptive-platform randomized trial in patients with COVID-19 who were receiving invasive or noninvasive mechanical ventilation or cardiovascular support. This clinical trial data has been added to Table 4d as well.
Kinase Inhibitors: Janus Kinase Inhibitors and Bruton’s Tyrosine Kinase Inhibitors

This section now includes a detailed discussion of the COV-BARRIER trial of baricitinib and the STOP-COVID trial of tofacitinib. See Therapeutic Management of Hospitalized Adults With COVID-19 for the Panel’s recommendations on the use of baricitinib and tofacitinib in hospitalized patients who require high-flow oxygen or noninvasive ventilation.

Other Updates to the Guidelines

The following sections have been updated to include new recommendations from CDC on administering an additional dose of the mRNA vaccines to certain people:

- Special Considerations in Adults and Children With Cancer
- Special Considerations in People With HIV
- Special Considerations in Solid Organ Transplant, Hematopoietic Stem Cell Transplant, and Cellular Immunotherapy Candidates, Donors, and Recipients

Minor changes have been made to the Overview of COVID-19 and Corticosteroids sections of the Guidelines.

October 7, 2021

Updated COVID-19 Treatment Guidelines Panel’s Statement on the Prioritization of Anti-SARS-CoV-2 Monoclonal Antibodies for the Treatment or Prevention of SARS-CoV-2 Infection When There Are Logistical or Supply Constraints

The Panel has recommended using anti-SARS-CoV-2 mAbs for the treatment of mild to moderate COVID-19 and for PEP of SARS-CoV-2 infection in individuals who are at high risk for progression to severe COVID-19, as outlined in the Food and Drug Administration Emergency Use Authorizations issued for the anti-SARS-CoV-2 mAbs.

In a previous statement, the Panel suggested prioritization strategies to adopt when logistical constraints can make it difficult to administer anti-SARS-CoV-2 mAb therapy to all eligible patients.

The Panel has updated its previous statement on the prioritization of anti-SARS-CoV-2 mAbs to emphasize the following:

- To indicate that supply constraints, as well as logistical constraints, can make it impossible to administer anti-SARS-CoV-2 mAbs to all eligible patients; and
- To recommend that, in addition to the prioritization strategies suggested in the previous statement, clinicians consider prioritizing the use of anti-SARS-CoV-2 mAb therapy for patients at highest risk of clinical progression. The updated statement includes a discussion of the risk factors for progression to severe COVID-19.

The Panel suggests prioritizing the use of anti-SARS-CoV-2 mAbs only when triage becomes necessary due to logistical or supply constraints.