What’s New in the Guidelines

Last Updated: March 2, 2022

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 past month are as follows:

March 2, 2022

The COVID-19 Treatment Guidelines Panel’s Statement on the Role of Bebtelovimab for the Treatment of High-Risk, Nonhospitalized Patients With Mild to Moderate COVID-19

On February 11, 2022, the Food and Drug Administration issued an Emergency Use Authorization (EUA) for the anti-SARS-CoV-2 monoclonal antibody (mAb) bebtelovimab for the treatment of nonhospitalized patients with mild to moderate COVID-19 who are at high risk of progressing to severe disease. The issuance of this EUA was primarily based on in vitro antiviral data showing that bebtelovimab is expected to have activity against a broad range of SARS-CoV-2 variants, including the B.1.1.529 (Omicron) variant of concern and its BA.1 and BA.2 subvariants.

Clinical trial data for bebtelovimab are limited to a Phase 2, randomized, placebo-controlled trial in patients who were at low risk for progression to severe disease. The trial showed no unexpected safety events, and patients who received bebtelovimab had more rapid viral decay than those who received the placebo. Although there are insufficient data on hospitalization and mortality outcomes for patients at high risk of disease progression who have received bebtelovimab, the agent has a mechanism of action similar to other anti-SARS-CoV-2 mAbs that have been shown in Phase 3 trials to reduce hospitalization or death among high-risk patients.

The purpose of this statement is to provide clinicians with guidance on the role of bebtelovimab as an additional treatment option for nonhospitalized patients with mild to moderate COVID-19 who are at high risk of progressing to severe disease. Basing its recommendations on collective in vitro data, clinical trial results, and other factors (e.g., drug interaction potential, feasibility), the Panel has classified the 5 available treatment options as preferred or alternative therapies for use in this population. Phase 3 trials have demonstrated high efficacy for the preferred therapies. The Panel recommends 1 of the following:

Preferred therapies (listed in order of preference):

- Nirmatrelvir 300 mg with ritonavir 100 mg (Paxlovid) (AIIa); or
- Sotrovimab 500 mg (AIIa); or
- Remdesivir 200 mg (BIIa)
Alternative therapies (for use if none of the preferred therapies are available, feasible to deliver, or clinically appropriate, listed in alphabetical order):

- **Bebtelovimab 175 mg (CIII); or**
- **Molnupiravir 800 mg (CIIa)**

The statement has detailed information regarding dose, route of administration, duration of therapy, and other specific indications.

**February 24, 2022**

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

The figure and text in this section have been updated to incorporate the information and recommendations from the Panel’s statement on using therapeutic or prophylactic anticoagulation in hospitalized adults with COVID-19.

**Therapeutic Management of Hospitalized Pediatric Patients With Multisystem Inflammatory Syndrome in Children (MIS-C) (With Discussion on Multisystem Inflammatory Syndrome in Adults [MIS-A])**

In this new section, the Panel provides recommendations for the treatment of children with multisystem inflammatory syndrome in children (MIS-C). The Panel notes that there are no randomized controlled trials that compare treatment approaches for MIS-C. However, data from large descriptive and observational comparative effectiveness studies are available to guide treatment for MIS-C. Based on the available data, the Panel recommends that initial therapy for MIS-C include a combination of immunomodulatory therapy (i.e., intravenous immunoglobulin plus a low to moderate dose of a glucocorticoid) and antithrombotic therapy.

**Antiviral Drugs That Are Approved, Authorized, or Under Evaluation for the Treatment of COVID-19**

This page has been updated to include recommendations for using ritonavir-boosted nirmatrelvir (Paxlovid), remdesivir, and molnupiravir in nonhospitalized patients with mild to moderate COVID-19 who are at high risk of disease progression. The Panel has also clarified that the page specifically addresses recommendations for small-molecule antiviral drugs.

**Ritonavir-Boosted Nirmatrelvir (Paxlovid)**

This new section consolidates information from the Panel’s statements on therapies for high-risk, nonhospitalized patients and potential drug-drug interactions between ritonavir-boosted nirmatrelvir and concomitant medications, which were released in December 2021. The drug-drug interaction table has been expanded to include medications that require dose adjustments when coadministered with ritonavir-boosted nirmatrelvir.

**Remdesivir**

This section now includes the Panel’s recommendation for using remdesivir in nonhospitalized patients with mild to moderate COVID-19 and a high risk of disease progression. The PINETREE trial for outpatient therapy has also been added to the clinical data table.

**Molnupiravir**

This new section incorporates information from the Panel’s statement on therapies for high-risk,
nonhospitalized patients, which was released in December 2021.

Table 2f. Characteristics of Antiviral Agents
Ritonavir-boosted nirmatrelvir and molnupiravir have been added to this table. The remdesivir entry has also been updated to incorporate recent Food and Drug Administration labeling changes, and the Panel has clarified that this table specifically discusses small-molecule antiviral drugs.

Antithrombotic Therapy in Patients With COVID-19
This section has been updated to incorporate the information and recommendations from the Panel’s statement on using therapeutic or prophylactic anticoagulation in hospitalized adults with COVID-19. A new clinical data table has been created to describe the study designs and results from the randomized controlled trials that had the greatest impact on the Panel’s recommendations.