What’s New in the Guidelines

Last Updated: December 6, 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 Guidelines Development for additional details on the development process).

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

December 6, 2022

The COVID-19 Treatment Guidelines Panel’s Update on Bebtelovimab

The prevalence of SARS-CoV-2 Omicron subvariants that are anticipated to be resistant to bebtelovimab has been rapidly increasing in the United States. On November 30, 2022, the Food and Drug Administration announced that bebtelovimab is not currently authorized for the treatment of COVID-19 in any U.S. region. The Panel now recommends against the use of bebtelovimab for the treatment of nonhospitalized patients with COVID-19 who are at high risk of progressing to severe COVID-19 (AIII). As the antiviral drugs ritonavir-boosted nirmatrelvir (Paxlovid), remdesivir, and molnupiravir are expected to be active against the currently circulating Omicron subvariants, the Panel continues to recommend these drugs for the treatment of these patients.

December 1, 2022

Metformin

The Panel added a new section on the antidiabetic agent metformin to the Guidelines. Two randomized controlled trials have evaluated the use of metformin in nonhospitalized adults with COVID-19. Neither trial demonstrated a benefit of metformin in reducing the risk of hospitalization or death in patients with COVID-19. Based on these results, the Panel recommends against the use of metformin for the treatment of COVID-19 in nonhospitalized patients (BIIa) and hospitalized patients (BIII), except in a clinical trial. Patients with COVID-19 who are receiving metformin for an underlying condition should continue this therapy as directed by their health care provider (AIII).

Guidelines Development

The Panel’s recommendations are based on a combination of scientific evidence and expert opinion. Each recommendation receives a rating for the quality of the evidence that supports that recommendation (I, IIa, IIb, or III). These ratings are driven by the likelihood of bias in the treatment effect estimate and the precision of the estimate.

In this update, the following revisions have been made to the evidence rating scheme:
• **I: High quality of evidence:** 1 or more randomized trials without major limitations, well-powered subgroup analyses of such trials, or meta-analyses without major limitations

• **IIa: Moderate quality of evidence:** Randomized trials and subgroup analyses of randomized trials that do not meet the criteria for a I rating

• **IIb: Moderate quality of evidence:** Observational studies without major limitations

• **III: Expert opinion**

**Overview of COVID-19**

Recent data have highlighted that some racial and ethnic minority groups experience higher rates of COVID-19, subsequent hospitalization, and death in relation to their share of the total U.S. population. Disparities in access to care and receipt of treatment for COVID-19 have also been reported. The Panel recommends that health care providers, health care systems, and payers ensure equitable access to high-quality care and treatment for all patients, regardless of race, ethnic identity, or other minoritized identity or social status (AIII).

**Prevention of SARS-CoV-2 Infection**

This section was updated to include information on the new bivalent COVID-19 vaccines. In addition, the discussion on pre-exposure prophylaxis (PrEP) notes that the prevalence of Omicron subvariants that are resistant to tixagevimab plus cilgavimab (Evusheld) is rapidly increasing. However, tixagevimab plus cilgavimab is the only agent authorized by the Food and Drug Administration for use as SARS-CoV-2 PrEP in people who are not expected to mount an adequate immune response to COVID-19 vaccination or those with contraindications for COVID-19 vaccines. Therefore, the Panel continues to recommend the use of tixagevimab plus cilgavimab as PrEP for eligible individuals (BIIb). This recommendation may change if the prevalence of resistant subvariants increases.

**Prioritization of Anti-SARS-CoV-2 Therapies for the Treatment of COVID-19 in Nonhospitalized Patients When There Are Logistical Constraints**

The rapid increase in the prevalence of Omicron subvariants that have reduced susceptibility to bebtelovimab has markedly decreased bebtelovimab’s utility as a treatment option for nonhospitalized patients with COVID-19 who are at risk of progressing to severe disease. Ritonavir-boosted nirmatrelvir is the preferred treatment option for these patients.

For patients who cannot take ritonavir-boosted nirmatrelvir because of significant drug-drug interactions, the Panel recommends remdesivir as the preferred option. However, some treatment facilities may not have the ability to provide a 3-day course of remdesivir intravenous infusions to all eligible patients. In these situations, prioritizing patients who will benefit the most from the therapy becomes necessary. The Panel updated this section to provide guidance on how best to prioritize patients when logistical constraints prevent remdesivir from being administered to all eligible patients.

**COVID-19 Convalescent Plasma**

The Panel has reviewed the available literature on using COVID-19 convalescent plasma (CCP) to treat COVID-19, particularly in patients who have underlying immunosuppressive conditions or who are receiving immunosuppressive treatments. Based on the available data, the Panel revised the recommendation language for the use of CCP in patients who are immunocompromised. There is currently insufficient evidence for the Panel to recommend either for or against the use of high-titer CCP for the treatment of COVID-19 in hospitalized or nonhospitalized patients who are immunocompromised.
Some Panel members would use CCP to treat an immunocompromised patient with significant symptoms attributable to COVID-19 and with signs of active SARS-CoV-2 replication and who is having an inadequate response to available therapies. In these cases, clinicians should attempt to obtain high-titer CCP from a vaccinated donor who recently recovered from COVID-19 likely caused by a SARS-CoV-2 variant similar to the variant causing the patient’s illness.

**Minor Updates to the Guidelines**

Minor updates were made to the following Guidelines sections:

- Remdesivir
- Ritonavir-Boosted Nirmatrelvir (Paxlovid)
- Antithrombotic Therapy in Patients With COVID-19
- Special Considerations in People Who Are Immunocompromised
- Special Considerations in Adults and Children With Cancer
- Special Considerations in Solid Organ Transplant, Hematopoietic Cell Transplant, and Cellular Immunotherapy Candidates, Donors, and Recipients
- Intravenous Immunoglobulin