What’s New in the Guidelines

Last Updated: April 29, 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](https://www.covid19treatmentguidelines.nih.gov/) 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](https://www.covid19treatmentguidelines.nih.gov/) for additional details on the Guidelines development process).

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

**April 29, 2022**

**Guidelines Development**

The title of this section has been changed to better describe the contents of the section.

Previously, the Panel used the designations A (strong), B (moderate), or C (optional) to rate the strength of each recommendation in the Guidelines. Based on feedback from clinicians and Panel members, the definition for the C rating has been changed from “optional” to “weak” to better reflect the strength of the Panel’s recommendations.

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

In *vitro* data have shown that the BA.1 and BA.1.1 subvariants of the Omicron (B.1.1.529) variant have decreased susceptibility to tixagevimab plus cilgavimab (Evusheld). The Food and Drug Administration (FDA) Emergency Use Authorization (EUA) previously stated that people who received an initial dose of tixagevimab 150 mg plus cilgavimab 150 mg for pre-exposure prophylaxis (PrEP) should be given a second dose as soon as possible. The FDA recently modified the EUA to provide guidance for the specific dose of tixagevimab plus cilgavimab that a person should receive based on the amount of time that has passed since the first dose was administered. This new dosing guidance has been added to Prevention of SARS-CoV-2 Infection.

**Ivermectin**

Results from 2 recently published, large randomized controlled trials showed that the use of ivermectin did not provide a clinical benefit for patients with mild to moderate COVID-19. Based on these results, the Panel now *recommends against* the use of ivermectin for the treatment of COVID-19, except in clinical trials (AIIa). Table 2d was updated to include the results from key clinical trials that have been published since the last revision.

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

This section was updated with information on the role of bebtelovimab in the treatment of nonhospitalized patients with mild to moderate COVID-19 who are at high risk of disease progression. In addition, sotrovimab is no longer recommended as a treatment option for patients with COVID-19.
because it has substantially reduced in vitro activity against the Omicron BA.2 subvariant. Table A has been updated with information on the in vitro susceptibility of circulating variants of concern and the anticipated clinical activity of the different anti-SARS-COV-2 monoclonal antibodies (mAbs) against variants and subvariants. The Panel also added recent clinical trial results to Table 3a.

**COVID-19 Convalescent Plasma**

This section was updated to reflect changes to the COVID-19 convalescent plasma (CCP) EUA, which was revised in December 2021 to authorize the use of high-titer CCP for the treatment of COVID-19 only for outpatients or inpatients who have immunosuppressive disease or who are receiving immunosuppressive treatment. The text also addresses the use of CCP collected prior to the emergence of the Omicron variant and summarizes the clinical data on CCP use in immunocompetent and immunocompromised patients. In addition, 2 trials that investigated the use of CCP in nonhospitalized, immunocompetent populations were added to Table 3b.

Based on the available data, the Panel’s revised recommendations for the use of CCP are as follows:

- The Panel **recommends against** the use of CCP that was collected prior to the emergence of the Omicron variant for the treatment of COVID-19 (AIII).
- The Panel **recommends against** the use of CCP for the treatment of COVID-19 in hospitalized, immunocompetent patients (AI).
- There is insufficient evidence for the Panel to recommend either for or against the use of high-titer CCP that was collected after the emergence of Omicron for the treatment of immunocompromised patients and nonhospitalized, immunocompetent patients with COVID-19.

**April 8, 2022**

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

The Panel previously recommended the anti-SARS-CoV-2 mAb sotrovimab as a treatment option for certain nonhospitalized patients with COVID-19. Although sotrovimab is active against the Omicron BA.1 and BA.1.1 subvariants, it has substantially decreased in vitro activity against the Omicron BA.2 subvariant that has recently become the dominant subvariant in the United States.

Because the Omicron BA.2 subvariant is now the dominant circulating subvariant in all regions of the United States, the distribution of sotrovimab has been paused, and the Panel no longer recommends using sotrovimab to treat COVID-19. The recommendations and rationale for using sotrovimab have been removed from this section.

**Table 3c. Characteristics of SARS-CoV-2 Antibody-Based Products**

This section includes information about the pause in the distribution of sotrovimab and updated dosing information for tixagevimab plus cilgavimab.

**April 1, 2022**

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

The Omicron BA.2 subvariant is rapidly becoming the dominant subvariant in many regions of the United States. Previously, the Panel recommended sotrovimab, an anti-SARS-CoV-2 mAb, as 1 of the preferred therapies for the treatment of nonhospitalized patients with mild to moderate COVID-19 who are at high risk of progressing to severe disease. Even though sotrovimab is active against the Omicron BA.1 and BA.1.1 subvariants, it has substantially decreased in vitro activity against the BA.2 subvariant.
The FDA recently updated the EUA for sotrovimab to note that it is not authorized for use in geographic regions where infection is likely to have been caused by nonsusceptible SARS-CoV-2 variants, and distribution of sotrovimab has been paused in these regions.

As a result of these recent changes and the increasing prevalence of the BA.2 subvariant across all regions, the Panel no longer recommends sotrovimab as a preferred therapy for nonhospitalized patients with mild to moderate COVID-19 who are at high risk of progressing to severe disease.

The Panel’s revised recommendations are outlined below.

Preferred Therapies

*Listed in order of preference:*

- Ritonavir-boosted nirmatrelvir (Paxlovid) (AIIa)
- Remdesivir (BIIa)

Alternative Therapies

*For use ONLY when neither of the preferred therapies are available, feasible to use, or clinically appropriate. Listed in alphabetical order:*

- Bebtelovimab (CIII)
- Molnupiravir (CIIa)

For use ONLY in regions where the Omicron BA.2 subvariant is not the dominant subvariant and in situations where none of the preferred or alternative options are available, feasible to use, or clinically appropriate:

- Sotrovimab (CIII)

The text and Figure 1 in Therapeutic Management of Nonhospitalized Adults With COVID-19 have been updated to include the rationale that supports these new recommendations. This section also now incorporates information from the Panel’s previously published statement on the role of bebtelovimab in the treatment of these patients.

*Table 3c. Characteristics of SARS-CoV-2 Antibody-Based Products*

This section includes new information on bebtelovimab, distribution information for sotrovimab, and updated dosing information for tixagevimab plus cilgavimab.