What’s New in the Guidelines

Last Updated: May 13, 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:

May 13, 2022

Ritonavir-Boosted Nirmatrelvir (Paxlovid)

The guidance on identifying and managing drug-drug interactions has moved to a new section of the Guidelines, entitled Drug-Drug Interactions Between Ritonavir-Boosted Nirmatrelvir (Paxlovid) and Concomitant Medications. The Ritonavir-Boosted Nirmatrelvir (Paxlovid) section retains the general description of ritonavir-boosted nirmatrelvir, the Panel’s recommendations for using this regimen, and a discussion of the clinical data that support those recommendations.

This section has been updated to acknowledge reports of SARS-CoV-2 viral rebound and the recurrence of COVID-19 symptoms in patients who completed a 5-day course of ritonavir-boosted nirmatrelvir. The frequency and clinical implications of these events are not yet known.

Drug-Drug Interactions Between Ritonavir-Boosted Nirmatrelvir (Paxlovid) and Concomitant Medications

Many commonly used medications can be safely coadministered with ritonavir-boosted nirmatrelvir despite its drug-drug interaction potential. In some cases, however, drug-drug interactions with ritonavir-boosted nirmatrelvir may lead to serious or life-threatening drug toxicities. This new section highlights the importance of evaluating a patient’s medication regimen for potential drug-drug interactions before prescribing ritonavir-boosted nirmatrelvir. However, because ritonavir-boosted nirmatrelvir is the only highly effective oral antiviral for the treatment of COVID-19, drug-drug interactions that can be safely managed should not preclude the use of this regimen.

The section provides guidance on management strategies and a variety of resources that clinicians can use to identify potential interactions between ritonavir-boosted nirmatrelvir and concomitant medications.

This section also includes 2 quick reference lists:

- Box 1 lists examples of commonly prescribed medications that can be safely coadministered with ritonavir-boosted nirmatrelvir.
- Box 2 lists medications with clinically significant interactions with ritonavir-boosted nirmatrelvir.
The list is divided into categories of medications that:

• Should not be coadministered with ritonavir-boosted nirmatrelvir;
• Can be withheld temporarily, if clinically appropriate;
• May be continued with dose adjustments, if clinically appropriate; or
• May be continued while the patient is monitored for adverse effects.

**Prioritization of Anti-SARS-CoV-2 Therapies for the Treatment and Prevention of COVID-19 When There Are Logistical or Supply Constraints**

The Panel updated this section to highlight that this prioritization guidance should be used **ONLY** when logistical or supply constraints limit the availability of therapies. The Panel emphasizes that when there are no supply or logistical constraints, therapies for the prevention or treatment of SARS-CoV-2 infection can be prescribed for any eligible individual as recommended in these Guidelines.

**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 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.