What’s New in the Guidelines

Last Updated: July 8, 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:

July 8, 2021

New Sections of the Guidelines
General Management and Therapeutic Management of Nonhospitalized Patients
Outpatient Management of Acute COVID-19 has been divided into two sections:
- General Management of Nonhospitalized Patients With Acute COVID-19
- Therapeutic Management of Nonhospitalized Adults With COVID-19

A new figure has been created for Therapeutic Management of Nonhospitalized Adults With COVID-19 to provide guidance on the use of therapeutic agents (e.g., anti-SARS-CoV-2 monoclonal antibodies) based on the patient’s disposition.

Nitazoxanide
This section has been added to discuss the evidence and considerations for using nitazoxanide as an antiviral drug for the treatment of COVID-19. The Panel recommends against the use of nitazoxanide for the treatment of COVID-19, except in a clinical trial (BIIa).

Granulocyte Colony-Stimulating Factor Inhibitors
This section has been added to address the use of granulocyte-macrophage colony-stimulating factor (GM-CSF) inhibitors as immunomodulators for the treatment of COVID-19. Based on the preliminary results from two, randomized, placebo-controlled trials investigating otilimab and lenzilumab, and a small, randomized, placebo-controlled trial of mavrilimumab, the Panel has determined that there is insufficient evidence to recommend either for or against the use of GM-CSF inhibitors for the treatment of hospitalized patients with COVID-19.

Key Updates to the Guidelines
Therapeutic Management of Hospitalized Adults with COVID-19
This section has been updated to incorporate new recommendations and rationale for when to use baricitinib in combination with dexamethasone in certain hospitalized patients with COVID-19. The update is based on results from the COV-BARRIER trial. The Panel recommends against the use of baricitinib in combination with tocilizumab (AIII).
**Chloroquine or Hydroxychloroquine and/or Azithromycin**

This section has been updated with new clinical data from multiple clinical trials. The recommendation for the use of these agents in nonhospitalized patients has been revised, and a recommendation regarding azithromycin monotherapy has been added.

**Colchicine**

A large, unpublished, randomized, placebo-controlled trial (RECOVERY) evaluated the role of colchicine in hospitalized patients with COVID-19. The study showed no difference in 28-day all-cause mortality between patients who received colchicine and those who received usual care. Based on these results, the Panel has updated its recommendation, and recommends against the use of colchicine for the treatment of hospitalized patients with COVID-19 (A1).

**Special Considerations in Pregnancy**

This section has been updated to include more recent epidemiologic data indicating that some pregnant people may be at increased risk of COVID-19. In general, the therapeutic management of COVID-19 should be the same for pregnant patients as for nonpregnant patients. Developing a treatment plan should involve shared decision-making between the patient and the clinical team, with considerations based on the severity of maternal disease and the safety of the medication for the pregnant individual and the fetus. Breastfeeding in the setting of COVID-19 is not contraindicated, and decision-making surrounding feeding breast milk while the patient is receiving therapeutic agents for COVID-19 is addressed. Updates to this section also include safety data on the use of COVID-19 vaccines during pregnancy.

**Other Updates**

The following sections have been updated with more current information:

- **Overview of COVID-19** (updated information on SARS-CoV-2 variants of concern and variants of interest)
- **Prevention and Prophylaxis of SARS-CoV-2 Infection** (added information on vaccine-related adverse effects)
- **Hemodynamics** (update on rationale for using norepinephrine as vasopressor of choice)
- **Ivermectin: Selected Clinical Data** (additional clinical trial data)

**Sections Under Revision**

The following sections are currently under revision:

- **Anti-SARS-CoV-2 Monoclonal Antibodies**
- **Corticosteroids**
- **Interleukin-1 Inhibitors**
- **Interleukin-6 Inhibitors**
- **Kinase Inhibitors: Baricitinib and Other Janus Kinase Inhibitors, and Bruton’s Tyrosine Kinase Inhibitors**
- **Antithrombotic Therapy in Patients With COVID-19**

On June 3, 2021, the Food and Drug Administration (FDA) updated the Emergency Use Authorization (EUA) of the anti-SARS-CoV-2 monoclonal antibody combination casirivimab plus imdevimab for the treatment of nonhospitalized individuals with COVID-19. The authorized dosage has been reduced from a single intravenous (IV) infusion of casirivimab 1,200 mg plus imdevimab 1,200 mg to casirivimab 600 mg plus imdevimab 600 mg. In addition, the same doses of casirivimab and imdevimab may now be administered by subcutaneous (SQ) injection when IV infusion is not feasible or may delay treatment.

The Panel currently recommends that nonhospitalized patients with COVID-19 who are at high risk for disease progression receive one of three authorized anti-SARS-CoV-2 monoclonal antibody regimens (see the Panel’s Statement on the Emergency Use Authorizations of Anti-SARS-CoV-2 Monoclonal Antibodies for the Treatment of COVID-19). The Panel has reviewed the data that were provided in the updated EUA for casirivimab plus imdevimab and reported publicly. For the casirivimab plus imdevimab combination regimen (if selected from the three authorized regimens), the Panel recommends:

- Using the dose of casirivimab 600 mg plus imdevimab 600 mg (AIIa).
- Using IV infusion of casirivimab plus imdevimab (AIIa).
- When IV infusion is not feasible or would lead to delay in treatment, SQ injection of casirivimab plus imdevimab can be used as an alternative route of administration (BIII).

The Panel’s statement includes a detailed discussion of the clinical data supporting these recommendations.


On May 26, 2021, the FDA issued an EUA for the anti-SARS-CoV-2 monoclonal antibody sotrovimab (previously VIR-7831) for the treatment of nonhospitalized patients with mild to moderate COVID-19 who are at high risk of progression to severe COVID-19.

Recommendation

The Panel’s statement is an update to include sotrovimab in recommendations for the use of the authorized anti-SARS-CoV-2 monoclonal antibodies:

- The Panel recommends using one of the following anti-SARS-CoV-2 monoclonal antibodies, listed in alphabetical order, to treat nonhospitalized patients with mild to moderate COVID-19 who are at high risk of clinical progression, as defined by the EUA criteria:
  - Bamlanivimab plus etesevimab; or
  - Casirivimab plus imdevimab; or
  - Sotrovimab.

Please see the full statement for considerations regarding the use of these agents. For example, some of the considerations relate to SARS-CoV-2 variants of concern or interest.
EUA Criteria Expanded to Include Additional Medical Conditions and Factors

On May 14, 2021, the FDA updated the EUA criteria for all authorized anti-SARS-CoV-2 monoclonal antibodies for this indication by broadening the list of medical conditions and other factors that may put patients at increased risk of progression to severe COVID-19.

The quality of the data that supports the Panel’s recommendations for the use of these anti-SARS-CoV-2 monoclonal antibodies differs based on the criteria for high risk of severe COVID-19 used. Consequently, the Panel weighed the strength of the recommendations based on the evidence for the risk of progression. Treatment is recommended based on the FDA EUA criteria for:

- Patients with high-risk conditions that were represented in clinical trials (AIIa), and
- Patients with other medical conditions and factors that had limited representation in clinical trials (BIII); however, in cases where the patient has an immunocompromising condition or is receiving immunosuppressive therapy, the rating is AIII.

The Panel’s statement includes a detailed discussion of the rationale for these recommendations, information on the expanded EUA criteria, and a list of the criteria with the Panel’s ratings.