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

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Summary Recommendations

Remdesivir is the only drug that is approved by the Food and Drug Administration (FDA) for the treatment of COVID-19. Ritonavir-boosted nirmatrelvir (Paxlovid), molnupiravir, and certain anti-SARS-CoV-2 monoclonal antibodies (mAbs) have received Emergency Use Authorizations from the FDA for the treatment of COVID-19.

This section focuses on the COVID-19 Treatment Guidelines Panel's (the Panel) recommendations for using small-molecule antiviral drugs to treat COVID-19. These recommendations are based on the available data; for more information, see Table 2f. For recommendations and information regarding the use of anti-SARS-CoV-2 mAbs, see Anti-SARS-CoV-2 Monoclonal Antibodies and Table 3c.

Recommendations for Treating Nonhospitalized Patients

- The Panel recommends the use of the following anti-SARS-CoV-2 therapies as preferred treatments for COVID-19. These drugs are listed in order of preference:
  - **Ritonavir-boosted nirmatrelvir (Paxlovid) (AIIa)**
  - **Remdesivir (BIIa)**
- The Panel recommends the use of the following anti-SARS-CoV-2 therapies as alternative treatments for COVID-19 **ONLY** when neither of the preferred therapies are available, feasible to use, or clinically appropriate. These drugs are listed in alphabetical order:
  - **Bebtelovimab (CIII)**
  - **Molnupiravir (CIIa)**
- See Therapeutic Management of Nonhospitalized Adults With COVID-19 for detailed recommendations.

Recommendations for Treating Hospitalized Patients

- See Therapeutic Management of Hospitalized Adults With COVID-19 for the Panel's recommendations on using remdesivir with or without immunomodulators in certain hospitalized patients.

Antiviral Drugs That the Panel Recommends Against

- The Panel **recommends against** the use of the following drugs for the treatment of COVID-19, except in a clinical trial:
  - **Interferons** for nonhospitalized patients **(AIIa)**
  - **Interferon alfa** or **lambda** for hospitalized patients **(AIIa)**
  - **Ivermectin (AIIa)**
  - **Nitazoxanide (BIIa)**
- The Panel **recommends against** the use of the following drugs for the treatment of COVID-19:
  - **Chloroquine** or **hydroxychloroquine** and/or **azithromycin** for hospitalized **(AI)** and nonhospitalized patients **(AIIa)**
  - **Lopinavir/ritonavir** and **other HIV protease inhibitors** for hospitalized **(AI)** and nonhospitalized patients **(AIII)**
  - **Systemic interferon beta** for hospitalized patients **(AI)**

Rating of Recommendations: A = Strong; B = Moderate; C = Weak

Rating of Evidence: I = One or more randomized trials without major limitations; IIa = Other randomized trials or subgroup analyses of randomized trials; IIb = Nonrandomized trials or observational cohort studies; III = Expert opinion

Antiviral Therapy

Because SARS-CoV-2 replication leads to many of the clinical manifestations of COVID-19, antiviral therapies are being investigated for the treatment of COVID-19. These drugs prevent viral replication

through various mechanisms, including blocking SARS-CoV-2 entry, inhibiting the activity of SARS-CoV-2 3-chymotrypsin-like protease (3CLpro) and RNA-dependent RNA polymerase (RdRp), and causing lethal viral mutagenesis.[1-3] Because viral replication may be particularly active early in the course of COVID-19, antiviral therapy may have the greatest impact before the illness progresses to the hyperinflammatory state that can characterize the later stages of disease, including critical illness.[4] For this reason, it is necessary to understand the role of antiviral medications in treating mild, moderate, severe, and critical illness in order to optimize treatment for people with COVID-19.

The following sections describe the underlying rationale for using different antiviral medications, provide the COVID-19 Treatment Guidelines Panel's recommendations for using these medications to treat COVID-19, and summarize the existing clinical trial data. Additional antiviral therapies will be added to this section of the Guidelines as new evidence emerges.

References

1. Food and Drug Administration. Fact sheet for healthcare providers: emergency use authorization for molnupiravir. 2022. Available at: https://www.fda.gov/media/155054/download.
2. Food and Drug Administration. Fact sheet for healthcare providers: emergency use authorization for Paxlovid. 2022. Available at: https://www.fda.gov/media/155050/download.
3. Remdesivir (Veklury) [package insert]. Food and Drug Administration. 2020. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/214787Orig1s000lbl.pdf.
4. Siddiqi HK, Mehra MR. COVID-19 illness in native and immunosuppressed states: a clinical-therapeutic staging proposal. *J Heart Lung Transplant*. 2020;39(5):405-407. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32362390.