



## COVID-19 Treatment and Management: Two Years After the Outbreak

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Two years after the beginning of the global coronavirus disease 2019 (COVID-19) pandemic, there are still no certain and effectual treatment or cure for this infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). On the other hand, vaccination using various types of vaccines with different action mechanisms for conferring immunity has been helpful for lowering the mortality rate in comparison with pre-vaccination COVID-19 era. However, this does not indicate that efficient COVID-19 treatment methods are no longer required because many individuals are still susceptible to COVID-19 complications after vaccination. Furthermore, the emergence of new mutations and variants of SARS-CoV-2 may raise serious concerns regarding the applicability and effectiveness of the administered vaccine doses. Common COVID-19 treatment methods include drugs or various respiratory support approaches, particularly for the patients with severe disease symptoms such as respiratory system inflammation.

COVID-19 medications include drugs that target the virus or regulate the immune system's reactions to the virus in different ways. These drugs include anti-inflammatory medications that hamper our immune system's overreaction to the invasion of the virus, which results in lethal consequences related to uncontrolled cytokine and chemokine production and release, antiviral drugs that mediate the development of a condition unfavorable for the coronavirus replication inside the body, and antibody therapies that mimic our immune system responses to specifically confront the virus.

Anti-inflammation drugs for the treatment of COVID-19 patients mainly include paracetamol or non-steroidal

anti-inflammatory drugs (NSAIDs) that are used to relieve disease symptoms, including fever, fatigue, and cough. Patients with severe COVID-19 and suffering from low oxygen levels are usually administered with glucocorticoid dexamethasone as it has been shown to reduce the risk of intensive care unit (ICU) visits and death (1).

In the case of antiviral drugs, there are not many drugs approved by the United States (US) Food and Drug Administration (FDA). The FDA approved antiviral drugs for COVID-19, including ritonavir-boosted nirmatrelvir (also known as paxlovid), remdesivir, and molnupiravir (2, 3). Paxlovid is a co-packaged medication, which includes nirmatrelvir (a 3C-like protease inhibitor) and ritonavir (a protease inhibitor used for the treatment of HIV/AIDS). In December 2021, this oral antiviral drug was granted emergency use authorization (EUA) by the US FDA for the treatment of COVID-19. Remdesivir (sold under the brand name veklury) is an antiviral drug originally developed to treat hepatitis C (4). In January 2022, FDA approved this antiviral medication for the treatment of adult and adolescent non-hospitalized COVID-19 patients who experience mild-to-moderate disease symptoms but are at high risk for disease progression, hospitalization, or death. Remdesivir is a prodrug capable of diffusing into cells and is converted to GS-441524 monophosphate, which is an adenosine nucleotide analog inhibiting RNA synthesis in coronaviruses (4). Molnupiravir is another antiviral drug approved by the US FDA in December 2021 for certain COVID-19 patients where other treatments are not available. Molnupiravir inhibits viral replication through the promotion of extensive mutations in the replication of viral RNA by RNA-directed RNA polymerase. This antiviral drug is metabolized into a ribonu-

cleoside analog that is similar to cytidine (called NHC-TP). During the process of replication, the virus's enzyme incorporates NHC-TP into newly made RNA instead of using the actual cytidine (2).

Bamlanivimab/etesevimab, casirivimab/imdevimab, sotrovimab, and tixagevimab/cilgavimab are anti-SARS-CoV-2 monoclonal antibodies that have been granted EUA by the US FDA (5-8). Bamlanivimab/etesevimab (FDA-approved in February 2022) is a combination of two monoclonal antibodies, which are both specific for the surface spike protein of SARS-CoV-2 (two different but overlapping epitopes) and are delivered together through intravenous (IV) administration. Casirivimab/imdevimab (also known as REGEN-COV) is another monoclonal antibody-based treatment that consists of two monoclonal antibodies (specific non-overlapping epitopes of the spike protein of SARS-CoV-2) administered as a single infusion or subcutaneous injection. Sotrovimab (also known as Xevudy) is a human neutralizing monoclonal antibody specific for the spike protein of SARS-CoV-2. Sotrovimab was originally identified and isolated in 2003 from a patient who had survived from SARS-CoV infection. This monoclonal antibody has specificity and affinity for an epitope in the RBD of the spike protein conserved between SARS-CoV and SARS-CoV-2. Tixagevimab/cilgavimab (also known as evusheld) is a combination of two human monoclonal antibodies (both specific for the surface spike protein of SARS-CoV-2) that was granted EUA by the US FDA in December 2021 for medical use to prevent COVID-19 (before exposure) in people with compromised immune system functionality or individuals that cannot be fully vaccinated.

Various respiratory support approaches are used for individuals who experience severe disease symptoms whose respiratory systems are affected by COVID-19 inflammation. Such approaches include non-invasive ventilation which is applied as breathing support through a face mask, nasal mask, or a helmet, mechanical ventilation, which includes using a machine called a ventilator to completely or partially supply artificial ventilation and adequate oxygenation, and carbon dioxide removal for patients experiencing acute respiratory distress syndrome (ARDS) and extracorporeal membrane oxygenation (ECMO) (9, 10). ECMO is an artificial lung technology utilized for more than 30 years with the aim of treating respiratory failure and ARDS following conventional mechanical ventilation failure (10). This is an intricate procedure in which blood is withdrawn from a patient's body using a large cannula, moved through a membrane oxygenator that mimics the lung roles for oxygen delivery and carbon dioxide removal, and then reinfused to the patient (10).

As briefly discussed here, the post-COVID-19 pandemic era has a long way from the normal life we used to know before SARS-CoV-2. Even though many countries have lifted

the COVID-19-related restrictions and the majority of the people in western countries have been vaccinated, we are still away from recognizing COVID-19 as an unimportant disease circulating in the community. However, with the fast-progressing process of discovery and development of new drugs and treatments for this infectious disease, recommendations and guidelines published by major international health-related agencies should be carefully followed for taking care of people with COVID-19 to have the lowest mortality rate possible.

## Footnotes

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