Approved and Non-FDA Approved COVID-19 Treatments

A comparison

Since the onset of the COVID-19 pandemic two years ago, hundreds of studies have examined the efficacy of dozens of drugs and other compounds in treating the disease. While the research is still ongoing, a sizable number of treatments have shown promise. A growing number of them have been authorized by the U.S. government, though virtually all of those approved sport hefty price tags.

Meanwhile, doctors and public health authorities around the world have also found a number of much cheaper treatment methods to be effective. The FDA hasn't greenlit any of those, even the safest and least controversial ones.

The FDA says that in the approval process, its Center for Drug Evaluation and Research "particularly focuses on the results of randomized, controlled clinical trials, which we consider to be the gold standard." Conducting such trials is a long and expensive process, and receiving a full approval usually takes years.

An emergency use authorization (EUA), on the other hand, has different rules. As the FDA explains, first the Health and Human Services secretary needs to declare an emergency that involves "chemical, biological, radiological, and nuclear (CBRN) agents, including emerging infectious disease threats" that are "causing a serious or life-threatening disease or condition." The FDA then can issue EUAs for products that "may be effective" to treat, prevent, or diagnose whatever is causing the threat. The FDA weighs whether "the known and potential benefits of the product … outweigh the known and potential risks" and whether there's "no adequate, approved, and available alternative." The FDA thus has the latitude to authorize even drugs that aren't backed by robust or conclusive research. The totality of the evidence simply needs to weigh toward the benefits, rather than the risks.

Doctors can actually prescribe any treatment already approved by the FDA, even if it's not authorized specifically for COVID-19—so-called off-label prescription. But the authorized status makes a difference. Hospitals, for example, can get additional Medicare reimbursement for COVID-positive patients when they provide an authorized treatment.

In addition, the U.S. administration has issued documents during the COVID-19 pandemic discouraging nonauthorized treatments. As a result, many doctors have been pressured to avoid off-label prescriptions for COVID-19, even if they believe a particular patient would benefit from the treatment.

AUTHORIZED

REMDESIVIR

Cost: ~$3,300 | **EUA Date: April 16, 2020**

Pharmaceutical company Gilead Sciences was informed by the FDA on April 16, 2020, that its antiviral drug remdesivir would receive an EUA for treating COVID-19 in hospitalized patients. The drug was in the process of several clinical trials at the time. On Oct. 22, 2020, remdesivir became the only drug to receive full FDA approval for COVID-19 treatment.

For the approval, the FDA mainly relied on one trial, sponsored by the National Institute of Allergy and Infectious Diseases (NIAID), which is headed by the de facto leader of the federal COVID response, Dr. Anthony Fauci. The trial enrolled about 1,000 hospitalized COVID-positive patients, half of whom received the drug and the other half a placebo. The treatment group had a median time to recovery of 10 days, while the placebo group had a time of 15 days. At 29 days, when the monitoring for the study concluded, the treatment group still had a somewhat higher recovery rate, but the difference was no longer statistically significant—the drug didn't look particularly helpful in keeping the patients alive.

DIRK WAEM/BELGA/AFP VIA GETTY IMAGES

CONVALESCENT PLASMA

Cost: ~$5,000–$10,000 | **EUA Date: Aug. 23, 2020**

The FDA granted an EUA for convalescent plasma, an unapproved treatment using antibodies from people who've recovered from COVID-19, on Aug. 23, 2020. Current studies indicate the treatment may have some positive effect on reducing hospitalizations, but the initial EUA only applied to already hospitalized patients, where studies report underwhelming results. The treatment is in limited supply and costs thousands of dollars.

On Feb. 4, 2021, the FDA limited the treatment to hospitalized COVID-19 patients "early in the course of disease and those hospitalized with impaired humoral immunity." On Dec. 28, 2021, the FDA revised the EUA again, allowing the treatment only for patients with immunosuppressive disease or receiving immunosuppressive treatment. The authorization is no longer limited to hospitalized patients.

ALEX EDELMAN/AFP VIA GETTY IMAGES

BARICITINIB

Cost: ~$4,800 | **EUA Date: Nov. 19, 2020**

On Nov. 19, 2020, the FDA gave an EUA to baricitinib, an FDA-approved arthritis drug, to treat some COVID-19 patients, such as those on ventilators or requiring supplemental oxygen. The initial clinical trials indicated improved results, including lower mortality, in those receiving the treatment, though the results were barely within the range of statistical significance.

Baricitinib, sold under the brand name Olumiant, has a cash price of about $87 per 1 milligram tablet, according to Drugs.com. The FDA recommends 4 milligrams a day for 14 days with lower doses for some patients. The regular treatment course thus adds up to more than $4,800.

LILLY USA

MONOCLONAL ANTIBODY THERAPY

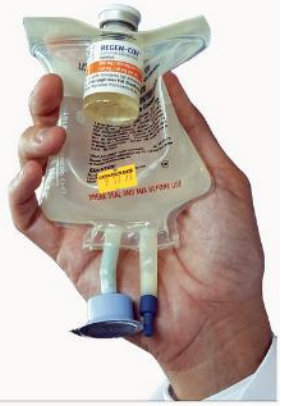
Cost: ~$1,000–$2,000 | **EUA Date: Nov. 21, 2020**

On Nov. 21, 2020, the FDA authorized the first monoclonal antibody therapy, a combination of casirivimab and imdevimab, for people with "mild to moderate" COVID-19 "who are at high risk for progression to severe COVID-19." The treatment costs more than $2,000, and the supply is limited.

Research indicates the treatment is effective at reducing mortality, but a December study found it may no longer work on the Omicron variant (pdf). The FDA noted the EUA doesn't apply to any area where Omicron is the likely variant, which is currently the entire United States.

On Feb. 9, 2021, the FDA gave a similar EUA to another monoclonal antibody treatment, a combination of bamlanivimab and etesevimab. It has also shown good results in studies, but its use is also currently prevented by the spread of Omicron. It costs over $1,000.

On May 26, 2021, the FDA gave an EUA to sotrovimab, another monoclonal antibody treatment, also for mild-to-moderate COVID-19 cases at risk of progression to severe disease. It has so far only been examined in a handful of studies, though the early treatment results were positive. One clinical trial showed the hospitalization rate cut by somewhere between 45 and 93 percent. The treatment appears to still work against Omicron, but it costs over $2,000, according to Drugs.com.



TOCILIZUMAB

Cost: ~$3,200 | **EUA Date: June 24, 2021**

The FDA authorized tocilizumab, another FDA-approved anti-arthritis drug, to treat some COVID-19 patients, such as those on ventilators or requiring supplemental oxygen, on June 24, 2021. The authorization was based on four clinical trials. Three smaller ones showed no statistically significant improvement in recovery time or mortality compared to placebo. One larger one in the UK showed 31 percent mortality in the treatment group versus 35 percent in the "usual care" group, a difference near the edge of statistical significance.

Tocilizumab, sold under brand name Actemra, has a cash price of about $120 per milliliter containing 20 milligrams of the drug, according to Drugs.com. The FDA-recommended adult dosing of one infusion of 8 milligrams per kilogram of patient weight adds up to about $3,200 for a 150-pound patient.

ROCHE

EVUSHELD

Cost: ~$10 | **EUA Date: Dec. 8, 2021**

The FDA gave an EUA for Evusheld, a nonapproved monoclonal antibody treatment consisting of tixagevimab co-packaged with cilgavimab, on Dec. 8, 2021. It costs about $10 per infusion, according to Drugs.com, but the FDA only allows its use as a prophylactic for immunocompromised patients or those allergic to the COVID-19 vaccines. Research indicates it still has some effect on Omicron.

ASTRAZENECA

PAXLOVID

Cost: ~$530 | **EUA Date: Dec. 22, 2021**

The FDA gave on Dec. 22, 2021, an EUA to Paxlovid, a combination of nonapproved nirmatrelvir and ritonavir marketed by Pfizer, for treatment of "mild-to-moderate" COVID-19 in people with "high risk for progressing to severe COVID-19."

There have only been a few studies on Paxlovid, but so far it appears to significantly lower hospitalization and mortality risk. The drug isn't yet available. The U.S. government has agreed to buy 10 million treatment courses at a price of about $530 per course.

SHUTTERSTOCK

MOLNUPIRAVIR

Cost: ~$700 | **EUA Date: Dec. 23, 2021**

The FDA gave on Dec. 23, 2021, an EUA to Molnupiravir, a nonapproved antiviral marketed by Merck, for the same use as Paxlovid, except it could also be used in people "for whom alternative COVID-19 treatment options authorized by FDA are not accessible or clinically appropriate."

The drug went through a handful of clinical trials. The largest one, with about 1,400 participants, showed mortality risk cut by somewhere between 14 and 99 percent. Relative risk of hospitalization or death was cut by somewhere between 1 and 51 percent. The results indicated reduced effectiveness against the Delta variant.

Molnupiravir works by inducing mutations in a virus, making it mutate so much the virus can't function anymore. Some researchers have raised the concern, though, that this may also lead to new, potentially dangerous virus variants.

Molnupiravir isn't yet available, but the U.S. government has already agreed to buy 1.7 million rounds of treatment at a cost of about $700 per course. The drugmaker said the contract doesn't represent what the drug's list price will be.

NOT AUTHORIZED

There have been over two dozen other drugs and compounds studied for potential efficacy against COVID-19 that haven't been authorized by the FDA for treating COVID-19. Almost all of them cost $60 or less per treatment course.

IVERMECTIN

Cost: ~$100–$1,000

Ivermectin is one of the most extensively studied drugs as a potential COVID-19 therapeutic. There have been more than 70 studies in 26 countries involving over 85,000 participants. Most of the studies show positive effects, especially in early treatment.

Only a minority of the studies were randomized, controlled clinical trials (RCT). Most of the RCTs were small, only involving up to a few hundred patients. One exception is an RCT in Singapore with over 3,000 low-risk patients showing a nearly 50 percent reduced risk of symptomatic infection when a combination of drugs, including ivermectin, hydroxychloroquine, povidone-iodine, zinc, and vitamin C, was used as a prophylactic. When 19 of the RCTs were combined into a meta-analysis last year, the data indicated risk of death reduction of somewhere between 38 to 85 percent.

Ivermectin costs about $100 to $1,000 per treatment course, depending on the dosage and length of treatment. It has been used for decades as an antiparasitic and for other ailments.

THE EPOCH TIMES

HYDROXYCHLOROQUINE

Cost: ~$7 | **EUA Date: March 28, 2020 (revoked on June 15, 2020)**

Hydroxychloroquine was the first to receive an EUA for treating COVID-19, on March 28, 2020. The authorization, however, only applied to hospitalized patients. While the drug has antiviral properties, that appears to be of little use to hospitalized patients since the disease at that point tends to proceed to its inflammatory phase and it's then too late to block the virus. The FDA revoked the EUA on June 15, 2020.

By now, hydroxychloroquine has been studied even more extensively than ivermectin. Its bane has been flawed research. The drug's theoretical mechanism of action is slowing viral replication. As such, its effect would be expected early on in the disease. The existing research, over 300 studies involving more than 400,000 patients, shows mixed results. Only a few dozen studies examined early treatment, showing statistically significant positive effects on mortality. So far, there has been only one early treatment RCT with over 1,000 participants. It looked at 1,360 U.S. health care workers and showed a 25 percent lower risk of symptomatic COVID-19 in the half that received the drug as a prophylactic. The results lacked statistical significance. When all the prophylactic RCTs were combined in a meta-analysis published last month, it showed that risk of a positive case was cut by 28 percent.

Hydroxychloroquine costs about $7 per treatment course and has been used for decades to prevent malaria and treat other diseases.

GEORGE FREY/AFP VIA GETTY IMAGES

FLUVOXAMINE

Cost: ~$45

Fluvoxamine, an antidepressant that costs about $45 per treatment course, hasn't been studied as extensively as hydroxychloroquine or ivermectin, but the available research indicates an impact on hospitalization and mortality. One RCT with about 1,500 participants showed a statistically significant reduction in hospitalization or extended emergency room observation by about 30 percent.

GEORGE FREY/AFP VIA GETTY IMAGES

BASIC COMPOUNDS

Cost: ~$3.50

Some basic compounds such as zinc and vitamins A and D have shown positive results, but suffer a dearth of robust RCTs. For vitamin D and zinc, if the available RCTs are pooled together in a meta-analysis, they add up to a statistically significant impact on mortality or other indicators. There's also the question, though, of whether taking the compounds helps in general, or whether people deficient in the compounds have a harder time fighting off the infection and the positive results come at least partly from mitigating the deficiency.

SHUTTERSTOCK

OTHERS

Cost: ~$10–$230

A number of other, less researched treatments have shown some positive results, including povidone-iodine ($10), lactoferrin ($60), budesonide ($50), colchicine ($115–$230), favipiravir ($20), and metformin ($13).