Coronavirus Disease 2019 (COVID-19) - The Search for a Treatment
Issues Document

Updated: August 28, 2020

Summary

SARS-CoV-2, the virus that can cause coronavirus disease 2019 (COVID-19), has officially been labeled a pandemic by the World Health Organization (WHO). While treatment of the disease currently centers on managing symptoms and supportive care for patients, there is a need for effective vaccines and medications to prevent and treat COVID-19. While pharmaceutical companies, universities and government agencies around the world are working to develop these therapies, there are currently no vaccines or medications approved by the U.S. Food and Drug Administration (FDA) specifically for COVID-19. This document is intended to provide information regarding therapies in development for COVID-19; it will be updated as new data become available.

Highlights

- Coronavirus disease 2019 (COVID-19) is an infection from a new strain of coronavirus that has been associated with respiratory symptoms, including progression to severe respiratory illness and death in some patients.
- Currently, there are no FDA-approved therapies specifically indicated for the treatment or prevention of COVID-19.
- Pharmaceutical companies, universities and government agencies around the world are working to develop vaccines and treatments for COVID-19.
- Vaccines are in early clinical development with options reaching clinical trials within months. However, commercial availability of a vaccine is still likely at least several months away.
- There are a vast array of compounds in early trials being evaluated for the treatment of COVID-19. The promising options will move rapidly through the FDA approval process.
- Another approach is to evaluate currently available therapeutic options to assess their effectiveness in treating and preventing the disease. Some data surrounding SARS and MERS coronaviruses have led investigators to a handful of products, hoping the similarity between these viruses and SARS-CoV-2 will lead to treatment options.
- As development of therapies is rapidly evolving, we intend to update this document frequently to provide the latest information on potential therapies for treating and preventing COVID-19.

Current Treatment Recommendations

To date, there are no vaccines or drugs approved by the U.S. Food and Drug Administration (FDA) to treat or prevent SARS-CoV-2, the virus that can cause the disease known as COVID-19. Although there are investigational COVID-19 vaccines and treatments under development, these investigational products are in the early stages of product development and have not yet been fully tested for safety or effectiveness. According to the CDC, clinical management includes prompt implementation of recommended infection prevention and control measures and supportive management of complications, including advanced organ support if indicated.

FDA and Government Actions

To help expedite the availability of therapies for COVID-19, the FDA can loosen the process for medications and vaccines to enter the market. An Emergency Use Application (EUA) can be issued to permit the use, based on scientific data, of medical products that may be effective for the diagnosis, treatment, or prevention of a disease or condition when the U.S. Department of Health and Human Services makes the determination that there is a public health emergency that has a significant potential to affect national security or the health and security of U.S. citizens. Recently, the agency issued an EUA to expedite the availability of additional diagnostic tests for the SARS-CoV-2 virus.

The Search for Coronavirus Treatments

While there are currently no therapies approved by the FDA for the treatment or prevention of COVID-19, pharmaceutical manufacturers, universities and government agencies are casting a wide net looking for effective therapies to treat and/or prevent the disease. SARS-CoV-2 is a coronavirus similar to viruses that cause Middle Eastern Respiratory Syndrome Coronavirus (MERS-CoV) and Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV), previously have been associated with the development of severe illness. Therefore, many investigated compounds for treating MERS and SARS are now being evaluated for COVID-19.

Vaccines in Development

Several vaccines are in early-phase development to protect against COVID-19. Once they reach clinical trials, data will be collected over at least six months, if not more, to determine if the vaccines are both safe and effective for preventing infection with SARS-CoV-2. FDA will expedite the more promising vaccines through the FDA approval process; however, the first vaccine is not expected to be approved for several months. Table 1 includes examples of vaccines in development for COVID-19.

Table 1

Vaccine	Manufacturer	Route	Status
BNT-162	Pfizer/BioNTech	Unspecified	Phase 2/3
ChAdOx1 nCoV-19	Oxford/AstraZeneca	Intramuscular	Phase 3
mRNA-1273	Moderna	Intramuscular (two doses)	Phase 3
NVX-CoV2373	Novavax	Unspecified	Phase 3
Coronavirus Vaccine	Janssen	Unspecified	Phase 1/2
COVID-19 S-Trimer	GlaxoSmithKline/Clover	Unspecified	Phase 1
INO-4800	Inovio	Intradermal	Phase 1
Coronavirus Vaccine	CureVac	Intramuscular (1-3 doses)	Phase 1
Coronavirus Vaccine	Altimmune	Intranasal (one dose)	Preclinical

Novel Drugs in Development

There are multiple therapies in early-phase development for the treatment of COVID-19. Remdesivir, was granted EUA for hospitalized patients with severe COVID-19 on May 1, 2020. Table 2 highlights some of the novel drugs in development for COVID-19. Due to the large number of products being screened for possible use, the table is not intended to be an exhaustive list of potential therapies. Rather, we have highlighted some of the more promising agents progressing through the development process.

Table 2

Drug	Manufacturer	Mechanism	Route	Status
remdesivir	Gilead	Broad-spectrum antiviral	IV infusion (5 or 10 days)	Phase 3*
tradipitant	Vanda Pharmaceuticals	neurokinin-1 receptor antagonist	Oral (twice daily x 14 days)	Phase 3
favipiravir	FujiFilm Toyama Chemical	RNA polymerase antiviral	Oral (twice daily x 7 days)	Phase 3
leronlimab	CytoDyne	CCR5 viral entry inhibitor	Subcutaneous	Phase 3

*EUA = Emergency Use Authorization

Existing Drugs in Development

Several existing medications that are currently approved for other uses are being evaluated for efficacy in the treatment of COVID-19. These drugs may be used alone or in combination with other drugs to treat COVID-19. Table 3 shows some of the existing drugs that are in development for COVID-19. However, the use of these products for COVID-19 is still considered investigational as ongoing clinical trials have yet to demonstrate whether or not the products are proven to be both safe and effective for treating COVID-19.

Table 3

Drug	Manufacturer	Mechanism	Route	Status
tocilizumab (Actemra®)	Genentech	Interleukin-6 inhibitor	IV infusion	Phase 3*
sarilumab (Kevzara®)	Sanofi/Regeneron	Interleukin-6 inhibitor	Subcutaneous	Phase 3*
lopinavir/ritonavir (Kaletra®)	AbbVie	Protease inhibitor/ Booster	Oral	Phase 3
dexamethasone	Generics	Glucocorticoid	Oral or IV	Phase 3

Express Scripts' Recommendations

There are currently no FDA approved therapies for the treatment or prevention of SARS-CoV-2 infections. While a lot of information is surfacing regarding the screening of potential drugs therapies, available data for the treatment and/or prevention of the virus are limited. The Office of Clinical Evaluation and Policy will continue to monitor the evolving literature, track utilization trends, and revise solutions, as needed. Express Scripts created a process for medical director review for medications when coverage is being requested for COVID-19 and developed anti-stockpiling policies. These policies are intended to protect the supply of specific, currently available medicines that may be used off-label to manage COVID-19. As always, the Office of Clinical Evaluation and Policy will continue to monitor this development and provide updates as more information becomes available.

Stay up to date with the latest information regarding COVID-19 infections in the United States at:
https://www.cdc.gov/coronavirus/2019-ncov/index.html
https://www.nih.gov/health-information/coronavirus

Updates

Date	Drug/Vaccine	Comment
3.17.2020	hydroxychloroquine/ azithromycin	An open-label non-randomized clinical trial in France showed that 20 patients treated with hydroxychloroquine had significant COVID-19 viral load reduction and the effects were improved with the addition of azithromycin. https://www.mediterranee-infection.com/wp-content/uploads/2020/03/Hydroxychloroquine_final_DOI_IJAA.pdf However, the regimen has not been proven and additional clinical information is required before routinely used.
3.22.2020	remdesivir	Due to overwhelming demand, Gilead temporarily stopped patient access to its investigational antiviral drug, remdesivir. Exceptions will be made for pregnant women and children younger than 18 years who have severe disease confirmed as COVID-19. Gilead's compassionate use program is becoming expanded access to speed availability for severely ill patients and allow Gilead to collect data on all patients. https://www.statnews.com/2020/03/22/gilead-suspends-access-to-experimental-covid-19-drug-remdesivir/
3.28.2020	chloroquine hydroxychloroquine (EUA)	The FDA issued an Emergency Use Authorization (EUA) to allow chloroquine and hydroxychloroquine products donated to the Strategic National Stockpile (SNS) to be distributed and used for certain hospitalized patients with COVID-19. These drugs will be distributed from the SNS to states for doctors to prescribe to adolescent and adult patients hospitalized with COVID-19, as appropriate, when a clinical trial is not available or feasible. Chloroquine Phosphate Fact Sheet for Healthcare Providers Hydroxychloroquine Phosphate Fact Sheet for Healthcare Providers
4.24.2020	chloroquine hydroxychloroquine	The FDA issued a warning against the use of hydroxychloroquine and chloroquine for treating COVID-19 outside a hospital or clinical trial setting due to the increased risk for heart rhythm issues. These medications have not been shown to be safe and effective for treating or preventing COVID-19. Upon review of case reports and published literature of hydroxychloroquine and chloroquine, either alone or with azithromycin or other medications that can cause QT prolongation, the FDA was concerned about serious heart related side effects and deaths. Prescribers are encouraged to monitor heart function, electrolytes, renal function, and liver tests along with any medications that could potentially cause QT-prolongation while using these products. https://www.fda.gov/media/137250/download

4.29.2020	remdesivir (ACTT)	Preliminary results from the randomized, placebo-controlled Phase 3 Adaptive COVID-19 Treatment Trial, or ACTT, sponsored by the National Institute of Allergy and Infectious Diseases (NIAID), were released. The study of 1,063 hospitalized patients with advanced COVID-19 and lung involvement found that patients treated with remdesivir recovered faster than those receiving placebo (11 days vs. 15 days), a 31% improvement. https://www.niaid.nih.gov/news-events/nih-clinical-trial-shows-remdesivir-accelerates-recovery-advanced-covid-19 While this information looks promising, we caution that the data are unpublished and still requires peer review.
4.29.2020	remdesivir (SIMPLE trial)	Top-line results from the open-label, Phase 3 SIMPLE trial found that 5-day dosing in hospitalized patients with severe manifestations of COVID-19 disease was as effective as 10-day dosing. Remdesivir was generally well-tolerated in both regimens. Grade 3 or higher liver enzyme elevations occurred in 7.3% of patients leading to discontinuation in 3% of patients. https://www.gilead.com/news-and-press/press-room/press-releases/2020/4/gilead-announces-results-from-phase-3-trial-of-investigational-antiviral-remdesivir-in-patients-with-severe-covid-19 This trial could help determine a dosing regimen for remdesivir. Recently, Gilead indicated that 140.000 treatments (assuming a 10 day course) of the drug could be available by the end of May 2020. This study could help maximize the use of available remdesivir supplies. https://www.gilead.com/purpose/advancing-global-health/covid-19/working-to-supply-remdesivir-for-covid-19
05.01.2020	remdesivir (EUA)	The FDA issued Emergency Use Authorization (EUA) for Gilead's remdesivir for hospitalized patients with severe COVID-19 disease. At this time, the medication is on limited supply and will be allocated to maximize access for appropriate patients who have a severe COVID-19 disease. Hospitals with intensive care units and deemed most in need will receive priority. Since the best dosing regimen is still being investigated, both the 5-day and 10-day treatment durations are suggested. The EUA is temporary and does not take place of the new drug application (NDA) or formal approval process. Therefore, it remains an investigational drug that has not been approved by the FDA. Remdesivir is only authorized for use in suspected or laboratory confirmed COVID-19 and severe disease defined as Sp02 ≤ 94% on room air, requiring oxygen supplementation, ventilation, or extracorporeal membrane oxygenation (ECMO) and must be administered intravenously (IV) by a healthcare provider at an in-patient setting. https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-issues-emergency-use-authorization-potential-covid-19-treatment
06.22.2020	Dexamethasone (RECOVERY trial)	Preliminary results from a randomized, controlled, open-label, adaptive study compared a ten day course of dexamethasone 6mg once per day vs. standard hospital care for COVID-19 patients. A total of 6,461 patients were randomly assigned 2:1 to receive either dexamethasone 6mg once per day for ten days or standard hospital supportive care. A total of 21.6% of patients treated with dexamethasone died at 28 days vs. 24.6% of patients who died following standard care. However, dexamethasone did reduce mortality in patients receiving machine-driven ventilated breathing by one third (29% vs. 40.7%). In addition, patients treated with oxygen and no ventilation had a reduction in 28 day death rate by 20%. Patients who did not receive any breathing support, via oxygen or machine driven ventilation, saw no reduction in mortality benefit from dexamethasone. The authors concluded that patients who are suffering from severe respiratory complications due to COVID-19 would see a 28 day mortality reduction by up to 33% when treated with dexamethasone.
08.23.2020	Convalescent plasma (EUA)	The FDA issued an Emergency Use Authorization (EUA) for COVID-19 convalescent plasma (CCP) for the treatment of COVID-19 in hospitalized patients. CCP is a blood product collected from patients who have recovered from COVID-19 with natural antibodies and who meet all blood donor eligibility requirements. The blood is screened and isolated to contain high antibody titers. The EUA gives health care providers the authority to administer CCP to hospitalized patients with suspected

		or confirmed COVID-19. The EUA is temporary and does not take place of the biologics license application (BLA) or the formal approval process. Therefore, it remains an investigational drug that has not been approved by the FDA. The EUA was issued, following several months of data review, indicating the potential benefits of CCP outweigh the risks and it is potentially effective at reducing the severity and duration of COVID-19 in hospitalized patients. Under the terms of the EUA, each health care provider and patient must be given a fact sheet providing dosing, side effects and other important information. Known adverse drug reactions (ADRs) include allergic reactions, transfusion-associated circulatory overload (TACO), transfusion-related acute lung injury (TRALI) and potential for infection transmission. Dosing is based on standard hospital procedures and practices with a considered starting dose of one CCP unit, around 200mL. Each additional unit may be administered based on patient response and professional clinical judgment of the provider. The fact sheet for CCP can be viewed here.
08.28.2020	Remove hydroxychloroquine and chloroquine.	Based on several studies, including a study from the New England Journal of Medicine (NEJM) on June 3, 2020, and the National Institutes of Health (NIH) on June 20, 2020, hydroxychloroquine and chloroquine have been removed from Table 3. Neither study was able to show that hydroxychloroquine provided benefit. The study by the NIH was halted due lack of evidence that it provided benefit to hospitalized patients with COVID-19. The study published in the NEJM, conducted by the University of Minnesota, showed that hydroxychloroquine was not effective at preventing COVID-19 when used as post-exposure prophylaxis. You can read about the NIH study here and the NEJM study here.