Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Regulators split on antimalarials for COVID-19

US and French authorities have authorised the use of chloroquine and hydroxychloroquine, but the EU regulator and WHO say the science doesn't support the decision. Susan Jaffe reports.

With no "adequate, approved and available" alternative, the US Food and Drug Administration (FDA) is allowing the use of the antimalarial drugs hydroxychloroquine and chloroquine to treat coronavirus disease 2019 (COVID-19).

The FDA's emergency use authorisation (EUA) issued last week gives physicians the option to prescribe the drugs, which President Donald Trump has recommended. However, both drugs are unproven and untested for COVID-19, and have rare but potentially deadly side-effects. The decision bypassed the usual drug approval process including double-blind, placebo-controlled clinical trials, stoking a worldwide debate about whether the drugs are appropriate for treating the disease.

"I think it was resorted to more out of a sense of desperation", said Joseph Masci, an infectious disease specialist and director of global health at Elmhurst Hospital in Queens, a borough of New York City, which is at the centre of the epidemic in the USA. "It is just an indication of how sudden and massive this outbreak has been."

In early March, US health authorities reported about 100 cases of COVID-19 and ten deaths. Almost a month later, there are more than 363 000 cases and 10 847 people have died as of April 7, according to state and federal government data compiled by the COVID Tracking Project.

Elmhurst, with 545 beds, is one of 11 hospitals in a network of public hospitals known as the Health and Hospitals Corporation. Masci said hydroxychloroquine, which is more widely used for other diseases and is less toxic than chloroquine, has been administered to some patients with COVID-19 throughout the system, including several hundred at Elmhurst. The course of treatment runs 5 days and, so far, the results have been mixed, he said.

Under the EUA, hydroxychloroquine and chloroquine can be used only in a hospital setting to treat COVID-19 in adults and adolescents who weigh at least 50 kg and are not able to participate in a clinical trial. The drugs must also be obtained from the national stockpile to protect the supply for other patients who have relied on the drugs for years to control autoimmune diseases including lupus and rheumatoid arthritis. But 3 days after the EUA, a surge in demand forced the agency to declare a shortage of both drugs.

So far, France is one of a few countries that also permit the drugs to be used for patients with COVID-19. Opposition has come from the European Medicines Agency, the EU's pharmaceutical regulator, which reiterated earlier this week that studies have not yet documented that the drugs can effectively treat COVID-19.

WHO concurs, citing "insufficient data to assess the efficacy of either of these medicines in treating patients with COVID-19, or in preventing them from contracting the coronavirus".

But in the USA, the FDA's chief scientist Denise Hinton and author of the EUA was less troubled by such concerns. "Based on the totality of scientific evidence available to [the] FDA, it is reasonable to believe that chloroquine phosphate and hydroxychloroquine sulfate may be effective in treating COVID-19", she wrote, without providing references to studies supporting that conclusion.

Although the efficacy of the drugs as a COVID-19 treatment might be uncertain, their side-effects are not.

"What I know for sure as a cardiologist is that these powerful medications have important side-effects including rarely sudden cardiac death", said Michael Ackerman, a genetic cardiologist and director of Mayo Clinic's Windland Smith Rice Genetic Heart Rhythm Clinic. He said that at least 1% of patients will be at increased risk for a hydroxychloroquine or chloroquine QT reaction capable of triggering drug-induced sudden cardiac death (especially if used in combination with azithromycin). Although such reactions are rare, if millions of people receive the drugs, thousands of lives could be at risk from medications that were supposed to help them to recover from the virus, he said. Ackerman believes such dire consequences can be avoided easily if physicians carefully evaluate vulnerable patients.

In New York City, Masci said the patients with COVID-19 at Elmhurst Hospital have not experienced adverse effects from hydroxychloroquine. The hospital is preparing for many new patients and has set up beds in tents in the parking lot. "We are seeing a very rapid rise in patients with [COVID-19], a condition that never existed before and has its own issues in terms of treatment, prevention, and transmission", he said. "It has been a very, very challenging problem and we don't think it has hit the peak yet."

Susan Jaffe

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