

VIEWPOINT

Emergency Use Authorization of Remdesivir

The Need for a Transparent Distribution Process

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On February 4, 2020, the Secretary of the US Department of Health and Human Services (DHHS) determined that there was a public health emergency due to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). On March 27, 2020, the DHHS secretary declared that circumstances existed to justify the authorization of emergency use of drugs and biologics during the coronavirus disease 2019 (COVID-19) outbreak, pursuant to section 564 of the Federal Food, Drug, and Cosmetic Act.¹

To date, 3 medications—chloroquine phosphate, hydroxychloroquine sulfate, and remdesivir—have been granted Emergency Use Authorization (EUA) from the US Food and Drug Administration (FDA) for COVID-19. Since chloroquine and hydroxychloroquine are FDA-approved drugs, clinicians had options for prescribing them outside the EUA mechanisms, and prescribing appears to have been robust.

More detailed and specific description of a transparent allocation process is needed to ensure that allocation is fair and understandable to patients and the clinicians caring for them.

Because remdesivir is not yet FDA-approved, until now, the only way to access this drug was through clinical studies (ClinicalTrials.gov: [NCT04280705](#), [NCT04292899](#), [NCT04292730](#)), expanded access programs (ClinicalTrials.gov: [NCT04323761](#)), and compassionate use programs.² The issuance of an EUA on May 1, 2020, should expand access to remdesivir, yet details about how this drug will become available are opaque and distribution remains limited.³ A clear and transparent process for access to remdesivir through the EUA is needed and is in the best interest of patients.

The authority of the FDA to issue an EUA was granted by Congress through various statutes.¹ An EUA can be issued only after the Secretary of DHHS has declared a public health emergency. The FDA commissioner, in consultation with the DHHS Assistant Secretary for Preparedness and Response, US Centers for Disease Control and Prevention (CDC), and the National Institutes of Health (NIH), can then issue the EUA, if criteria under the statute are met. An EUA is not approval of a drug for sale and has a term of 1 year, which can be renewed, based on the circumstances of the emergency.⁴ Continued clinical studies

are still needed to allow for permanent approval because the EUA is only a temporary means for making a product available.

Other agents have been made available under an EUA, the most relevant recent example was the EUA of intravenous peramivir in 2009-2010 for the influenza A(H1N1) pandemic. In that instance, the CDC was responsible for managing the drug distribution, which was done through an electronic system through which clinicians directly requested peramivir under the EUA.⁴ Only 1200 treatment courses were initially available for distribution through this process. From October 2009 to June 2010, the period that peramivir EUA was available to clinicians, 1371 requests for release of the drug were made, and at least 1274 patients received 1 or more doses.⁵ However, limited data were collected regarding the outcome and adverse effects. Through revisions of the statutes authorizing EUA, more information

is now allowed to be collected about individuals treated under the EUA to better understand safety of drugs issued through the EUA since then. Such data collection remains voluntary and will likely remain incomplete.

The May 1, 2020, EUA for the use of remdesivir³ for the treatment of COVID-19 was based on the following statement.

1. "SARS-CoV-2 can cause a serious or life-threatening disease or condition, including severe respiratory illness, to humans infected by this virus;
2. Based on the totality of scientific evidence available to FDA, it is reasonable to believe that remdesivir may be effective in treating COVID-19, and that, when used under the conditions described in this authorization, the known and potential benefits of remdesivir when used to treat COVID-19 outweigh the known and potential risks of such products; and
3. There is no adequate, approved, and available alternative to the emergency use of remdesivir for the treatment of COVID-19."³

The authorization is limited as follows:

- "Distribution of the authorized remdesivir will be controlled by the United States (U.S.) Government for use consistent with the terms and conditions of this EUA. Gilead will supply remdesivir to authorized distributors, or directly to a U.S. government agency, who will distribute to hospitals and other healthcare facilities as directed by the U.S. Government, in collaboration with state and local government authorities, as needed;

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- The remdesivir covered by this authorization will be used only to treat adults and children with suspected or laboratory confirmed COVID-19 and severe disease defined as $\text{SpO}_2 \leq 94\%$ on room air, requiring supplemental oxygen, mechanical ventilation, or extracorporeal membrane oxygenation (ECMO);
- Remdesivir is administered in an in-patient hospital setting via intravenous (IV) infusion by a health care provider; and
- The use of remdesivir covered by this authorization should be in accordance with the dosing regimens as detailed in the authorized Facts Sheets.”³

Two specific fact sheets, one for clinicians⁶ and one for patients and parents/caregivers, were made available to support this requirement.

Since issuance of the EUA, Gilead initially announced donation of 1.5 million doses of remdesivir to the US government, but the total number of doses available for EUA use was clarified by DHHS when it announced that only 607 000 vials of remdesivir will be made available over the next 6 weeks. This is enough drug to treat an estimated 78 000 hospitalized patients with COVID-19.⁷ This number of doses is not likely to meet demand from the tens of thousands of patients per month who are projected to require hospitalization nationwide due to COVID-19 and meet FDA criteria for remdesivir treatment throughout the summer, but it at least represents a path forward.

On May 9, 2020, DHHS issued additional information about the distribution plan to be made publicly available.⁷ Before the plan was announced, a group of hospitals received allocations of remdesivir by the US government through a process that was unclear. Data about the distribution are only available from an ad hoc, grassroots effort to have hospitals self-identify as having been informed that they will or will not be receiving one of the initial allocations of remdesivir.⁸ Since this is a self-reported survey it is in no way complete, but provides the only available information about allocation decisions to date. Even with the announcement by DHHS confirming that 2 distributions—one allocation of 35 360 doses to Indiana,

Massachusetts, New Jersey, New York, Rhode Island, Tennessee, and Virginia and a second allocation of 10 800 doses to Connecticut, Illinois, Iowa, Maryland, Michigan, and New Jersey—had been made, there remains no information on how these allocations were decided.⁷ Additionally, it is unclear how distributions were made to specific hospitals within those states.

A transparent plan for distributing remdesivir is imperative if a potentially life-saving drug is to be given to the patients in most need. Allocation should be based on hospital, regional, and state COVID-19 infection data with equitable distribution within a region to states and within states to hospitals.⁹ The process should also include a mechanism for redistribution based on the constantly changing endemicity of the outbreak. The plan should ensure appropriate patient access and equitable distribution regardless of race, ethnicity, or socioeconomic status. The plan should be designed to prevent a surge in patients at institutions known or thought to have access to the drug or a large increase in requests to transfer patients to these centers from hospitals that may not have access to remdesivir.

Although the distribution of remdesivir via the EUA is an issue unique to the US, as worldwide demand for the drug increases, the imbalance between drug availability and need will be further exacerbated. Countries, working with the manufacturer, will need to develop a system of distribution.⁹ Not all patients in the world who are eligible may have access to remdesivir, but all patients deserve a fair and transparent allocation process that reflects the rapidly changing epidemiology of the emerging COVID-19 pandemic.

In the US, there is a need for a well-described and transparent process because there will be 2 tiers to the allocation decision: an initial decision to allocate to states by the Office of the Assistant Secretary for Preparedness and Response and a second by state health departments.¹⁰ For now, the agencies responsible for the decisions are known, but how they will make the granular decisions is not known. More detailed and specific description of a transparent allocation process is needed to ensure that allocation is fair and understandable to patients and the clinicians caring for them.

ARTICLE INFORMATION

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