December 7, 2020

Senator Ron Johnson
Chairman, Senate Homeland Security &
Governmental Affairs Committee
340 Dirksen Senate Office Building
Washington, DC 20510

Senator Gary C. Peters
Ranking Member, Senate Homeland Security &
Governmental Affairs Committee
340 Dirksen Senate Office Building
Washington, DC 20510

Dear Chairman Johnson and Ranking Member Peters:

On behalf of the Infectious Diseases Society of America and its HIV Medicine Association, we thank you for scheduling the hearing, "Early Outpatient Treatment: An Essential Part of a COVID-19 Solution, Part II," and for this opportunity to comment. IDSA and HIVMA represent over 12,000 infectious diseases physicians, scientists, public health and other health care professionals on the front lines of the COVID-19 pandemic response. Our members are leading infection prevention and patient management at their institutions, providing direct patient care and treatment, collaborating with state and local health departments on community mitigation measures, and conducting research to increase our understanding of COVID-19 and develop new tools for prevention, diagnosis and treatment. IDSA has developed and continually updated clinical guidelines on the treatment and management of patients with COVID-19, utilizing GRADE (Grading of Recommendations, Assessment, Development and Evaluations), the most widely adopted tool for assessing the certainty in evidence and the strength of recommendations.

We share and appreciate the urgency in expanding therapeutic options for COVID-19 as daily case counts and hospitalization rates reach record levels and continue to surge. Outpatient therapies that can prevent hospitalizations are desperately needed, as many hospitals are quickly reaching or already over capacity. In addition to preventing disease progression, early treatments may help prevent chronic effects of COVID-19 and shorten the period in which individuals are infectious, thereby reducing SARS-CoV-2 transmission.

Although treatments have now emerged for patients hospitalized with severe COVID-19, there is a notable lack of evidence-based treatment options for patients with early or mild disease. Several drugs, including hydroxychloroquine, have failed to show efficacy in rigorous clinical trials, despite early uncontrolled data suggesting positive effects.[1] Studies investigating new treatment options are in development, including assessing repurposed drugs as well as conducting de novo drug trials, such as of monoclonal antibodies. More data are emerging and, as of Dec. 7, the Food and Drug Administration (FDA) has issued Emergency Use Authorizations

[1] Jolkovsky, EL, Biney, BT, et al. Efficacy and Safety of Hydroxychloroquine vs Placebo for Pre-exposure SARS-CoV-2 Prophylaxis Among Health Care Workers: A Randomized Clinical Trial. JAMA Intern Med. Published online Sept 30, 2020. doi:10.1001/jamainternmed.2020.6319

(EUA) for two therapeutics for non-hospitalized patients with mild-to-moderate disease, as detailed below.

It is essential that all new therapeutics be supported by sufficient safety and efficacy data to guide their optimal use. Fair, transparent and equitable distribution strategies are also critical, especially when therapeutics are in limited supply. In the case of outpatient treatments, it is particularly important that they be safe with few adverse effects, easy to administer (unlike current COVID-19 treatments requiring infusion) and widely available at low cost.[2]

Below, we are pleased to share our recommendations regarding the use of existing outpatient therapeutics for COVID-19, and policies to strengthen the study, review and distribution of COVID-19 therapies and medicines for current and future public health emergencies.

Use of Outpatient Therapeutics for COVID-19

Outpatient therapeutic options are limited. As of Dec. 7, 2020, the FDA has issued EUAs for two therapeutics for non-hospitalized patients with mild-to-moderate COVID-19 and high risk for progression to severe disease and hospitalization (bamlanivimab on Nov. 11 and casirivimab and imdevimab on Nov. 21). IDSA updated our clinical guidelines on Dec. 2, 2020 to reflect our assessment of the available data on bamlanivimab. We are currently reviewing the data on casirivimab and imdevimab and plan to update our guidelines in the near future.

IDSA suggests against the routine use of bamlanivimab among ambulatory patients with COVID-19. Our assessment identified only one Phase II randomized control trial that reported on non-hospitalized patients with recently diagnosed mild or moderate COVID-19. In patients at increased risk of progression to severe disease and hospitalization, IDSA notes bamlanivimab is a reasonable treatment option if, after informed decision-making, the patient puts a high value on the uncertain benefits and a low value on uncertain adverse events. Among ambulatory patients, bamlanivimab demonstrated a lower relative risk of hospitalization, which is an important outcome. However, the certainty of the evidence was very low because there were relatively few patients in this early-stage trial and the number of clinical events were very low in both the placebo and antibody groups. As a result, it is not possible to be certain whether the antibody conferred a benefit. More trials are needed to determine definitively whether bamlanivimab confers a clinical benefit and, if it does, which patients are most likely to benefit.

Health Equity and Access

According to the Centers for Disease Control and Prevention, American Indian, Black or African American and Hispanic or Latinx communities continue to experience much higher rates of hospitalizations and death due to COVID-19 than White, non-Hispanic communities.[3] In addition to older Americans, these populations should be prioritized in the study and development of new therapeutics and attention must be given to ensure equitable access to outpatient treatment options available through an EUA or that are approved for commercial use by FDA. The current products

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[2] Kim, PS, Read, SW, Fauci, AS. Therapy for Early COVID-19A Critical Need. JAMA.;324(21):2149-2150. Online at: https://jamanetwork.com/journals/jama/fullarticle/2773058#:~:text=Effective%2C%20early%20treatments%20will%20also,medical%20community%20and%20the%20public.

[3] Centers for Disease Control and Prevention. COVID-19 Hospitalization and Death by Race/Ethnicity. November 30, 2020. Online at: https://www.cdc.gov/coronavirus/2019-ncov/covid-data/investigations-discovery/hospitalization-death-by-race-ethnicity.html.

available through an EUA are in scarce supply and generally require resources or assistance to navigate administrative and logistical issues to secure access.

Policy Recommendations

Strengthening the Emergency Use Authorization Process

In the understandable effort to promote timely access to potentially beneficial treatments, FDA has in some instances issued EUAs before evidence is in a place that supports the routine use of the drugs as standard of care. In addition to potentially promoting widespread use of ineffective or even harmful therapies, issuance of an EUA complicates the ability to complete placebo-controlled clinical trials, thereby undermining the ability to collect the data necessary to evaluate the safety and effectiveness of therapies and determine their optimal clinical use in practice.

IDSA and HIVMA recommend:

- For FDA to establish and publicly communicate benchmarks for COVID-19 therapeutics to receive an EUA, as the agency has done for COVID-19 vaccines.
- For FDA to require the sponsor to have a plan for completing and publishing data from definitive clinical trials necessary to fully evaluate safety and effectiveness to inform optimal use of new therapeutics.

Optimizing the Clinical Trial Infrastructure

There is a critical need for continued research and funding to support the study and development of outpatient treatments. Outpatient clinical trials for COVID-19 therapuetics can be more challenging because they require large numbers of participants and a complex infrastructure to ensure participant and staff safety. In addition, similar to vaccines, the risk-benefit calculus is more complicated in developing treatments for individuals with mild-to-moderate disease because of the greater risk of worsening outcomes than in a patient with severe disease. Treatment for outpatients with mild disease must be safe with few adverse effects, easy to administer, and scalable to reduce health inequities and to realize the population level benefit of preventing disease progression.

Systemic deficiencies within the clinical trials infrastructure limit the speed of rapid innovation in times of need. Within this system, attempting to introduce and systematically study experimental treatments outside of tertiary care academic medical settings is extremely challenging. Optimizing the clinical trial infrastructure should be a key component of pandemic preparedness efforts.

IDSA and HIVMA recommend:

- Increased federal investment in research to study and develop COVID-19 outpatient treatment options and to support clinical trial engagement and outreach to older Americans, communities of color and other populations most heavily impacted by COVID-19.
- For FDA, the National Institutes of Health, and the clinical research community to collaborate to restructure and improve the conduct of rapid evaluation trials by strengthening the clinical trial infrastructure, expanding funding mechanisms, and developing better analytical tools so that the EUA mechanism can be used when strong data are available, and trials can be performed on

larger populations in more settings to increase access to treatments and the ability to gather data.

Improving the Allocation and Distribution of EUA Products

The Assistant Secretary for Preparedness and Response (ASPR) coordinates weekly distributions of all EUA products to states, which then determine allocations to hospitals or other facilities within their borders. ASPR maintains a webpage and holds weekly stakeholder calls and office hours to provide updates on the allocations and respond to questions. These offerings have been helpful and should be maintained but additional steps are needed to improve transparency and the distribution process. In addition, guidance is needed to assist states and facilities with ensuring equitable access to the EUA products for the populations most heavily impacted by COVID-19.

IDSA and HIVMA recommend:

- For ASPR to publicly disclose the data used to make allocation decisions.
- For ASPR to predict allocation decisions further in advance than the current one-week time frame to allow health care facilities to assess their inventory and to prepare the delivery systems, e.g., recently authorized monoclonal antibody products are administered by infusion and require intensive facility and staffing preparation and protocols.
- For the U.S. Department of Health and Human Services (HHS) to develop guidance and best practices for states and facilities to ensure access to outpatient COVID-19 treatment for older Americans, communities of color and other populations most heavily impacted by COVID-19.

Once again, IDSA and HIVMA thank you for your continued attention to the COVID-19 pandemic and would be happy to serve as a resource to you. You may contact us at any time through Amanda Jezek, IDSA Senior Vice President, Public Policy & Advocacy at ajezek@idsociety.org or Andrea Weddle, HIVMA Executive Director at aweddle@hivma.org.

Sincerely,

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