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November 16, 2015

The Honorable Sylvia Mathews Burwell
Secretary
U.S. Department of Health & Human Services
200 Independence Avenue, SW
Washington, D.C. 20201

Dear Secretary Burwell:

On behalf of the Infectious Diseases Society of America (IDSA) and the HIV Medicine Association (HIVMA), thank you for scheduling the Department of Health and Human Services (HHS) Pharmaceutical Forum: *Innovation, Access, Affordability and Better Health* on November 20, 2015. In addition to ensuring patient access to existing therapies for preventing and treating infectious diseases (ID), we also are faced with serious areas of unmet medical need due to emerging infections and increasing antimicrobial resistance in commonly acquired infections that require novel therapies to cure these infections. While we continue to champion federal incentives for innovation to address unmet medical needs, we also strongly support policies that facilitate patient access to available therapies. We look forward to helping the Administration, Congress, and other stakeholders understand the specific ID and HIV patient needs regarding pharmaceutical innovation and accessibility as we all strive to achieve balanced policies that will best serve patients and public health.

In this letter, we describe examples that we believe help illustrate different aspects of the complex issues of pharmaceutical innovation and accessibility: (1) accessibility of older generic medications with little competition; (2) accessibility of novel therapies for hepatitis C virus (HCV); and (3) incentives for new antibiotics to address unmet medical needs. We hope these cases will help federal policymakers better understand and appreciate ID and HIV patient needs. While we appreciate that economic incentives are necessary in some situations to recoup innovation costs for truly novel products that have a significant clinical impact, we believe that checks and balances are necessary to appropriately balance patient access and prevent the inappropriately high prices that severely limit patient access to needed treatments.

Decades-old Generic Drugs Priced Out of Reach

Daraprim: Sudden, Dramatic Price Increase of a 62 Year-Old Drug Severely Hampers

Accessibility: Acquired by Turing Pharmaceuticals in August 2015, Daraprim (pyrimethamine) is part of the first-line treatment regimen for the parasitic disease toxoplasmosis, a serious and potentially life-threatening infection that most commonly affects immune-compromised individuals such as those with HIV. The drug was approved by the FDA in 1953. Shortly after acquiring Daraprim, Turing raised the price of this drug from \$13.50 per tablet to \$750 (Wholesale Acquisition Cost) per tablet. The price increase and a controlled distribution strategy implemented earlier in the summer have left hospitals without the ability to stock the medication, and prompted physicians to prescribe alternative therapies with limited data supporting their use.¹ This has required adding alternative strategies to the federal guidelines for preventing and treating opportunistic infections² for situations where first line agents may not be available.

Under the new price, it is estimated that the annual cost of treatment for toxoplasmosis, for the pyrimethamine component alone, will be \$342,750 for patients who weigh less than 60 kg (or approximately 130 pounds) and \$648,000 for patients who weigh more than 60 kg. Interestingly, the \$342,750 figure is more than quadruple the initial cost of Sovaldi (the first of the new HCV cures whose price came under public criticism) despite the fact that pyrimethamine (the active ingredient in Daraprim) is a decades-old drug that should be available as a generic.

In response to the public outcry concerning the 5000% price hike of Daraprim and resulting significant patient access issues, Turing promised in late September to lower the price of the drug. One month later, no change had been made, prompting more than [150 organizations to urge Turing](#) to take immediate action regarding the Daraprim's price and accessibility. In early November, IDSA and HIVMA joined other HIV advocacy organizations in a meeting with Turing executives. At this meeting, Turing executives described a complex network of assistance programs and suggested making the drug more accessible to hospitals by distributing tablets in 30 rather than 100 tablet bottles in addition to addressing access issues experienced by health care facilities participating in the 340B program. It was subsequently reported that the company intends to modestly lower (by around 10 percent) the price of the drug by the end of the year.³ While these mitigation strategies to address the barriers to accessing Daraprim are urgently needed, they would not be necessary if the new price and distribution strategy were not put into place over the summer.

We remain concerned that a significant disruption in treatment for a life-threatening condition has occurred due to a dramatic price increase of a decades-old drug initiated by a company that had not assumed any of the risk nor provided any of the investment necessary to develop this medication. In addition, the controlled distribution system precludes competition that could result in lower prices and greater accessibility by limiting access to the compounds necessary for other manufacturers to conduct the necessary testing to develop a generic version of this drug. Similar to the situation with cryptococcal meningitis (see below under Flucytosine),

¹ See HIVClinician.Org Access to Daraprim (Pyrimethamine) Blog. Available at <http://hivclinician.org/pyrimethamine/>.

² The Department of Health and Human Services guidelines on the [Prevention and Treatment of Opportunistic Infections in HIV-infected Adults and Adolescents](#) were updated on October 19th to offer guidance on the use of alternative therapies due to limited access to pyrimethamine.

³ *New York Times*. Turing Commits to Modest Price Reduction on a Drug. Nov 3, 2015. Available at: http://www.nytimes.com/2015/11/04/business/turing-commits-to-modest-price-reduction-on-a-drug.html?_r=2&mtref=undefined.

toxoplasmosis is an infection for which effective treatment has been available for decades but has recently been priced out of reach of patients who need it. These are unlike other life-threatening infections caused by multi-drug resistant pathogens for which no effective treatment options are available.

Flucytosine: Significant Price Increase on a Drug Critical in Treating a Serious Infection: In another case that has not received much attention outside of the infectious diseases community, Valeant increased the price of flucytosine from \$10 per 500 mg tablet to \$110 per 500 mg tablet, raising the price of a 100 tablet bottle from \$1000 to \$11,000. Flucytosine was initially approved by the FDA in 1971 and is a key component of the preferred treatment for cryptococcal meningitis – a serious infection of the brain and spinal cord that typically affects patients with compromised immune systems. The price increase also has forced providers to deviate from the preferred treatment for this life-threatening and potentially debilitating infection.

Hepatitis C Virus (HCV): Innovation Victories and Accessibility Challenges

IDSA and HIVMA have been extremely encouraged by the development of new therapies that can cure HCV—a significant clinical advancement over prior HCV therapies. In the U.S., nearly 4 million persons are estimated to be infected with HCV and approximately half are unaware of their status. Approximately 20,000 individuals are newly infected each year.⁴⁵ New cures for this virus, which if not treated can lead to debilitating and costly conditions including cirrhosis, liver cancer, and liver transplants, represent a tremendous scientific advancement with the potential to improve and save the lives of millions of patients. Patient access to these promising new therapies is critical so that scientific advancements can achieve their life-saving potential.

IDSA and HIVMA applaud the Centers for Medicare and Medicaid Services (CMS) for the guidance sent this month to state Medicaid programs and pharmaceutical companies to urge them to improve accessibility to new HCV medications. CMS expressed concern, shared by ID physicians, that many states are limiting access to these drugs only to patients with late stage liver disease, and to those abstinent from drug or alcohol use, and is limiting the types of providers who can prescribe these therapies.

We appreciate that CMS highlighted the IDSA and the American Association for the Study of Liver Diseases (AASLD) guidance in the communication to state Medicaid programs. As you may know, IDSA and AASLD continue to update their guidance at www.HCVguidelines.org, as new therapies and evidence on existing therapies become available. In October 2015, the recommendation for initiating treatment in nearly all patients with hepatitis C was strengthened and the recommendations on how to prioritize patients for treatment were removed based on “real world” experience with the tolerability and efficacy of newer HCV medications.⁶

⁴ Armstrong GL, Wasley A, Simard EP, McQuillan GM, Kuhnert WL, Alter MJ. The prevalence of hepatitis C virus infection in the United States, 1999 through 2002. *Ann Intern Med* 2006;144:705–14.

⁵ CDC. Surveillance for acute viral hepatitis—United States, 2008. Available at: <http://www.cdc.gov/hepatitis/Statistics/2008Surveillance/index.htm>.

⁶ AASLD and IDSA. Hepatitis C Guidance Underscores the Importance of Treating HCV Infection: Panel Recommends Direct-Acting Drugs for Nearly All Patients with Chronic Hepatitis C. October 2015. Available at: <http://hcvguidelines.org/sites/default/files/when-and-in-whom-to-treat-press-release-october-2015.pdf>.

Successful HCV treatment results in sustained virologic response—in other words, cure of the HCV infection—and benefits nearly all of those chronically infected with HCV.

We urge CMS' continued engagement on this important issue, and we look forward to continuing to work with you to ensure appropriate patient access to these important new therapies.

Incentives for New Antibiotics to Address Unmet Medical Needs

Despite tremendous scientific advances in a wide variety of disease areas, there remain some patients—such as those suffering serious or life-threatening infections caused by multi-drug resistant pathogens—who have few or no safe and effective treatment options. The Centers for Disease Control and Prevention (CDC) conservatively estimated in 2013 that at least 2 million individuals in the U.S. are sickened by antibiotic-resistant bacteria every year and that at least 23,000 die as a result. Further, CDC found that resistant infections cost the health care system approximately \$20 billion annually, with a total societal cost of about \$35 billion each year.⁷ IDSA greatly appreciates that the Administration has prioritized this issue through the National Action Plan for Combating Antibiotic Resistant Bacteria (CARB), which includes as one of its five goals accelerating the development of new antibiotics and other therapeutics.

Antibiotic research and development (R&D) has failed to keep pace with increasing patient need due to rising rates of antibiotic resistance. As more and more patients contract and succumb to these serious infections, R&D of new antibiotics to treat these infections has dwindled. Unfortunately, unique significant economic barriers continue to hamper antibiotic R&D. Antibiotics are typically taken for a much shorter course than other drugs, tend to be inexpensive, and are held in reserve to protect their utility from the rapid development of resistance. Combined with high costs for antibiotic R&D, these factors have driven most pharmaceutical companies from antibiotic R&D entirely and left the few who remain struggling to develop the antibiotics that patients need most.

As HHS considers strategies to balance pharmaceutical innovation and accessibility, IDSA urges you to keep in mind those patients who still face significant unmet medical needs, such as those with antibiotic resistant infections. Further, we urge you to consider how new antibiotics to address unmet medical needs can help reduce the significant excess health care costs associated with multidrug resistant infections. New federal incentives are necessary to stimulate the innovation needed to bring forth new life-saving therapies for these patients.

Conclusion

Striking balanced federal policies that provide appropriate patient access to needed treatments and incentivize innovation to address unmet medical needs is a complex endeavor in which many factors must be considered. These factors include: patient access; areas of unmet medical need; barriers to R&D; the role of Medicare, Medicaid, and private payers; and access to generic drugs for uncommon conditions. IDSA and HIVMA are committed partners with the federal government and other stakeholders in examining these issues and considering appropriate policy solutions.

⁷ CDC. Antibiotic Resistance Threats in the United States, 2013. Available at: <http://www.cdc.gov/drugresistance/threat-report-2013/>

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We are committed to continuing to raise awareness regarding both accessibility and innovation to benefit patients with infectious diseases, including HIV and HCV, and to providing feedback on the impact of federal policies and proposals on our patients' needs and the public health.

We welcome the opportunity to discuss these issues with you and your staff and can be reached through the IDSA Vice President for Public Policy and Government Relations Amanda J. Jezek at 703-740-4790 or ajezek@idsociety.org and the HIVMA Executive Director Andrea Weddle at (703) 299-0915 or aweddle@hivma.org.

Sincerely,



Johan Bakken, MD, PhD
President, IDSA Board of Directors



Carlos del Rio, MD
Chair, HIVMA Board of Directors