IDSA Headquarters
1300 Wilson Boulevard
Suite 300
Arlington, VA 22209
TEL: (703) 299-0200
FAX: (703) 299-0204
EMAIL ADDRESS:
info@idsociety.org
WEBSITE:
www.idsociety.org

IDSA
Infectious Diseases Society of America

December 7, 2015

The Honorable Susan Collins
Chairwoman, USSenate Special Committee on Aging
413 Dirksen Senate Office Building
Washington, DC 20510

The Honorable Claire McCaskill
Ranking Member, US Senate Special Committee on Aging
730 Hart Senate Office Building
Washington, DC 20510

Dear Chairwoman Collins and Ranking Member McCaskill:

On behalf of the Infectious Diseases Society of America (IDSA), thank you for scheduling the US Senate Special Committee on Aging Hearing, "Sudden Price Spikes in Off-Patent Drugs: Perspectives From the Front Lines," on December 9, 2015. As you know, patients with serious infections (toxoplasmosis and cryptococcal meningitis) have recently faced serious barriers in accessing their previously affordable, decades-old treatments due to sudden and dramatic price increases. We greatly appreciate the Committee's attention to this serious issue. We hope you also will consider broader, related issues regarding access to existing and new therapies for preventing and treating infectious diseases (ID) as well as serious areas of unmet medical need for which innovation is sorely lacking, such as emerging infections and increasing antimicrobial resistance. We look forward to helping the Committee understand the specific ID patient needs regarding pharmaceutical accessibility and innovation 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 accessibility and innovation: (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 the Committee better understand and appreciate ID 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 Off-Patent 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 infections[2] 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 Daraprim's price and accessibility. In early November, IDSA joined 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] Unfortunately, later in November, Turing reneged on its promise to lower the list price of the drug. Instead, Turing will offer discounts of up to 50% to hospitals. Unfortunately, the reduced hospital pricing is still significantly higher than what hospitals paid for Daraprim prior to Turing's acquisition of the drug and will still present access barriers. Further, patients must typically take Daraprim for 8 to 12 months, most of the time on an outpatient basis. These persisting barriers to accessing Daraprim underscore the need for new options for patients with toxoplasmosis and their medical providers.

IDSA is encouraged by the recent announcement that Express Scripts is working with Imprimis to make its co-formulated compounded version of pyrimethamine and leucovorin more widely available through Express Scripts for $1 per tablet. We are optimistic that this arrangement will

---

[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&mtrref=undefined.

help address the serious cost and access barriers that have prevented or delayed pregnant women, infants, and patients with HIV infection or following transplantation from accessing this lifesaving treatment.

We are, however, very 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), 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 has been extremely encouraged by the development of new therapies that can cure HCV—a significant clinical advancement over prior HCV therapies. In the US, 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.[4,5] 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 new scientific advancement with the potential to improve and save the lives of millions of patients. It is critical that federal policies continue to stimulate this type of innovation, given how it helped fulfill an unmet medical need. It is equally critical that patients be able to have access to these promising new therapies so that scientific advancements can achieve their life-saving potential.

IDSA applauded the Centers for Medicare and Medicaid Services (CMS) for the guidance sent in November 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

[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.

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 our 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] 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 continued engagement from CMS and Congress on this important issue, and we look forward to continuing to work with all stakeholders 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 from 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 infections caused by resistant bacteria 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 Congress has prioritized this issue by enacting the Generating Antibiotic Incentives Now (GAIN) Act as part of the Food and Drug Administration Safety and Innovation Act (FDASIA) in 2012. GAIN provides an additional 5 years of exclusivity for new antibiotics that treat a serious or life-threatening infection and represents a key first step toward addressing the urgent unmet need for new antibiotics. However, experts agree that additional incentives in this space are necessary to bring forth the new antibiotics that patients need.

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

[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.

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

resistance. Antibiotic R&D also faces significant regulatory barriers. Specifically, some of the most highly resistant, most deadly infections are still occurring in a relatively small number of

critically ill patients, making it extremely difficult and in some cases impossible to enroll a sufficient number of these patients in a traditional, large scale clinical trial. Combined with high costs for antibiotic R&D, these factors have driven most pharmaceutical companies away from antibiotic R&D entirely and left the few who remain struggling to develop the antibiotics that patients need most.

Senators Orrin Hatch (R-UT) and Michael Bennet (D-CO) have authored the Promise for Antibiotics and Therapeutics for Health (PATH) Act, which would address a key regulatory barrier to antibiotic R&D by allowing antibiotics that treat a serious or life-threatening infection and address an unmet medical need to be studied in smaller, more rapid clinical trials. New antibiotics studied under PATH would be approved only for the limited populations of patients who need them and would bear distinct "limited population" labeling to alert the healthcare community to the need to use these drugs judiciously. Further, PATH gives the FDA authority to pre-review marketing materials for limited population antibiotics and directs the Department of Health and Human Services (HHS) to monitor the use of these drugs. The House of Representatives included a similar policy in its 21st Century Cures Act (HR 6) which was passed with broad bipartisan support in July. We strongly urge the Senate to advance a similar effort, including the PATH Act. Without this policy, we remain seriously concerned that the antibiotics our patients urgently need will be unable to be developed.

Conclusion

As this Committee investigates recent price spikes of off-patent drugs, we hope you will consider strategies to help prevent future disruptions to care, such as those caused by the sudden and dramatic price increases for Daraprim and flucytosine. We also urge you to balance the need for accessibility for both new and old medications with the need for innovation to help 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 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.

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; defining the 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 is a committed partner with the federal government and other stakeholders in examining these issues and considering appropriate policy solutions. We are committed to continuing to raise awareness regarding both accessibility and innovation to benefit patients with infectious diseases, 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 continue discussing 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.

Sincerely,

Johan S. Bakken MD, PhD

Johan S. Bakken, MD, PhD, FIDSA
IDSA President

About IDSA

IDSA represents over 10,000 infectious diseases physicians and scientists devoted to patient care, disease prevention, public health, education, and research in the area of infectious diseases. Our members care for patients of all ages with serious infections, including meningitis, pneumonia, tuberculosis, HIV/AIDS, antibiotic-resistant bacterial infections such as those caused by methicillin-resistant Staphylococcus aureus (MRSA) vancomycin-resistant enterococci (VRE), and Gram-negative bacterial infections such as Acinetobacter baumannii, Klebsiella pneumoniae, and Pseudomonas aeruginosa, and, finally, emerging infectious syndromes such as Ebola virus fever, enterovirus D68 infection, Middle East Respiratory Syndrome Coronavirus (MERS-CoV), and infections caused by bacteria containing the New Delhi metallo-betalactamase (NDM) enzyme that makes them resistant to a broad range of antibacterial drugs.