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January 9, 2017

The Honorable Lamar Alexander
Chairman
Health, Education, Labor and Pensions
Committee
United States Senate
Washington, DC 20510

The Honorable Patty Murray
Ranking Member
Health, Education, Labor and
Pensions Committee
United States Senate
Washington, DC 20510

RE: New Drug Shortages Survey Data on Anti-Infective Drugs

Dear Chairman Alexander and Ranking Member Murray,

The Infectious Diseases Society of America (IDSAs) applauds the Senate Health, Education, Labor and Pensions Committee's previous efforts to address and prevent drug shortages. Because of your previous work in this area, I write on behalf of IDSAs to share with you new data from a 2016 Emerging Infections Network (EIN) survey on anti-infective drug shortages, as well as to bring your attention to persisting anti-infective drug shortages. The EIN is a flexible sentinel network, funded through a cooperative agreement between the Centers for Disease Control and Prevention (CDC) and IDSAs, composed of over 1,100 infectious disease specialists primarily from North America, with some global members. The overarching goal of the EIN is to assist CDC and other public health authorities with surveillance for emerging infectious diseases and related phenomena.

We greatly appreciate the Committee's past work to help address these issues through hearings as well as through provisions in the Food and Drug Administration Safety and Innovation Act (FDASIA), Public Law 112-144. While the FDA has taken important steps in the past several years to increase its capacity and infrastructure for reporting and monitoring these shortages, as well as prioritizing review of new products (mainly generic sterile injectable drugs), ID physicians remain acutely concerned that the drugs we rely upon to care for patients are still experiencing shortages with alarming frequencies. These shortages have detrimental effects on patient care and public health.

We urge your committee to hold additional hearings on this issue, and to use the upcoming reauthorization of the Prescription Drug User Fee Act (PDUFA) as an opportunity to reexamine the progress that has been made and consider the persisting concerns and needs for additional action. We welcome the opportunity to serve as a resource for you and your staff in order to address the ongoing issues with these anti-infective drug shortages in any capacity.

Scope of Current Drug Shortages Among ID Practitioners

In 2011, the EIN conducted a survey on drug shortages, intending to capture from ID physicians the prevalence of drug shortages and their impacts on patient care. At the time, seventy-eight percent of respondents indicated a need within the past two years to modify their antimicrobial agent of choice because of a drug shortage, while fifty-two percent believed that the resulting change in treatment adversely affected patient care or outcomes.

We appreciate that significant public attention to the issue of drug shortages in 2011 prompted several actions by the FDA and Congress, including new policies to improve notification of drug shortages and prioritize FDA review of new products that can help address shortages. Unfortunately, anti-infective drug shortages continue to persist.

The EIN conducted a [follow-up survey in 2016 on anti-infective shortages](#)¹ to evaluate the impact of policy changes enacted since 2012. The number of physicians reporting shortages had dropped by only eight percent, and sixty percent said that drug shortages had become more common since January of 2013. **Even more startling was the fact that the percent of doctors reporting that a drug shortage affected patient outcomes had ballooned from fifty-two to seventy-three percent.** Of those seventy-three percent, the most common concerns reported were the use of broader spectrum drugs, use of more costly agents, use of less effective therapies or second-line drugs, and use of more toxic antimicrobials. As the threat of antimicrobial resistance grows, the revelation that almost four of five physicians surveyed had to use a broader spectrum drug due to drug shortages is particularly disturbing. A U.S. Government Accountability Office ([GAO](#)) [report on drug shortages released in July 2016](#)² concluded that while the number of total new drug shortages across all classes of drugs has generally decreased since 2011, the number of ongoing shortages remained high.

Impact of Anti-Infective Drug Shortages

Anti-infective drug shortages adversely impact patient care by limiting the availability and choice of antimicrobials. In such situations, ID physicians are forced to choose alternative treatment regimens that often include drugs with higher toxicity, poorer treatment outcomes, or more prolonged and expensive duration of treatment. The problem is even more acute for pediatricians because there are fewer antimicrobials that can be tolerated by infants and children. Drug shortages also exacerbate the serious problem of antimicrobial resistance, as they often limit the physician's ability to provide the appropriate anti-infective with the narrowest spectrum of activity for treating a specific infection. This often results in the use of an otherwise unnecessary broad-spectrum drug, pressuring the microbial flora of patients and institutions into resistant mutations. Patient health also may be compromised when drug shortages force practitioners to use an unfamiliar agent, sometimes at an inappropriate dose and duration (which again favors the development of resistance and toxicity). Shortages further compound the challenges inherent in the treatment of infections caused by multidrug resistant pathogens given the already highly limited treatment options and lack of new antimicrobials in development.

¹ http://www.int-med.uiowa.edu/Research/EIN/FinalReport_DrugShortages2016.pdf

² <http://www.gao.gov/assets/680/678281.pdf>

Drug shortages also hinder broader public health efforts to prevent and control infectious diseases. The CDC found that the national reporting of new syphilis cases was 15% higher in 2014 than 2013 and a further 19% higher in 2015 over 2014. Practitioners are having difficulty obtaining Bicillin-LA, the type of penicillin used to treat syphilis. This shortage is also negatively impacting research on Pre-exposure Prophylaxis (PrEP) for the prevention of HIV infection, as patients with syphilis who are participating in PrEP studies are facing significant barriers obtaining Bicillin-LA.

Recommendations for Potential Solutions to Drug Shortages

The issue of drug shortages is very complex and will likely require a combination of solutions. The [July 2016 GAO report on drug shortages](#), combined with information on specific classes of drugs, such as anti-infectives, that can be provided to medical societies and other stakeholders, contain important data to inform potential solutions. GAO found that recent shortages of sterile injectable anti-infective and cardiovascular drugs were strongly associated with four key factors: 1) a decrease in the number of suppliers; 2) sales of a generic version; 3) the failure of an establishment to make the drug comply with manufacturing standards resulting in a warning letter; and 4) price decline. Relatively low profit margins may cause suppliers to exit the market for less profitable drugs in favor of more profitable ones or may make it unprofitable to increase supply, which could make the market vulnerable to shortages.

Data clearly indicating the persistence of anti-infective drug shortages underscore the need for a more robust response from the federal government to ensure patient access to these life-saving drugs. IDSA is happy to offer the following recommendations:

- Facilitate improved communication between the FDA, the pharmaceutical industry, and health care practitioners to identify actions that can be taken to prevent drug shortages, and to discuss progress. For example, clear communications about ways to extend the shelf life of drugs on a shortage, such as by altering the drug's storage conditions, as well as alternatives or other appropriate options, can all help physicians maintain access to needed drugs and provide high quality patient care.
- Strengthen reporting requirements, established by FDASIA, to provide greater transparency regarding the causes of shortages and potential future shortages.
- Create incentives for manufacturers to perform routine maintenance to production lines to prevent the closures that typically cause shortages; and continue manufacturing drugs during remediation of production line issues and other maintenance to ensure continued supplies.
- Convene a group of federal government, industry, medical, patient, and other relevant stakeholders to analyze the root causes of drug shortages, including the findings in the GAO report; identify current vulnerabilities; and develop solutions.
- The FDA, CDC, and the pharmaceutical industry should develop and implement policies to encourage improvements in manufacturing practices. This includes increasing diversity in manufacturing plant locations, helping ensure multiple manufacturers are not all relying on a single supplier, and increasing transparency regarding manufacturing practices in order to better anticipate future drug shortages.
- Create either incentive strategies to enhance reliable production of critical drugs or a national stockpile similar to the Strategic National Stockpile (SNS) for specified critical drugs.

- Direct the FDA to establish a list of “priority drugs” for medicines that do not have a second line drug or alternative treatment for the FDA and manufacturers to focus on.
- Consider establishing a mechanism for expedited importation of medically necessary drugs that are only available from sources outside the U.S. combined with a stringent quality assessment.

IDSA applauds the HELP Committee for continuing to bring attention to this issue and helping to address several aspects through FDASIA. The 2016 EIN poll indicated that over half of respondents got drug shortage information from the FDA site or an associated source, with over seventy percent saying that current communications about drug shortages are sufficient. Unfortunately, despite recent efforts, the problem of drug shortages continues to persist, and infectious diseases physicians continue to experience shortages in critical anti-infective drugs. At the same time, increasing rates of antimicrobial resistance and a dearth of innovation in new antimicrobial drug developments further limit treatment options. Shortages adversely affect patient care and outcomes through long-term morbidity from inadequate treatment, longer hospitalizations, and sometimes death. Furthermore, the increased use of broad spectrum agents during shortages contributes to increasing antimicrobial resistance. As such, it is imperative to patient care and public health that long-term solutions to drug shortages be identified and implemented.

IDSA stands committed to working with the Senate HELP Committee and other stakeholders to identify long-term solutions to anti-infective drug shortages. Should you have any questions, please do not hesitate to have your staff contact Colin McGoodwin, IDSA’s Program Officer for Public Health Policy at cmcgoodwin@idsociety.org or 703-299-0015.

Sincerely,

A handwritten signature in cursive script that reads "Bill Powderly".

William G. Powderly, MD, FIDSA
President, IDSA

Anti-Infective Shortages with Significant Patient Care and Public Health Impact

The 2016 EIN survey asked respondents to indicate the anti-infective drugs in short supply over the last two years. The following list indicates the anti-infective drugs in the order of frequency mentioned and the number of respondents who indicated they were in shortage:

- Piperacillin-tazobactam (Zosyn), 298: commonly used in hospitals due to its broad coverage
- Ampicillin-sulbactam (Unasyn), 103: spectrum of activity similar to Zosyn but does not cover *Pseudomonas aeruginosa* infections
- Meropenem, 98: a member of the carbapenem class, used for infections caused by multi-drug resistant organisms
- Cefotaxime, 77: commonly used for meningitis and in children
- Cefepime, 63: most often used to treat infections caused by Gram negative bacteria, including *Pseudomonas aeruginosa*
- Trimethoprim-sulfamethoxazole (Bactrim), 56: most commonly used to treat urinary tract infections
- dDoxycycline, 41: used to treat skin, respiratory and tick-borne infections, including Lyme disease
- Imipenem, 40: used for broad spectrum treatment of non MRSA and enterococcus infections, most often for diabetic foot infections
- Acyclovir, 40: anti-viral agent used to treat herpes infections and shingles
- Amikacin, 22: broad spectrum antibiotic often used to treat tuberculosis and related infections
- Pyrimethamine, 18: anti-parasitic medication
- Penicillin, 16: used to treat routine Gram positive bacterial infections
- Cefazolin, 14: Used in surgical prophylaxis and often used for *Staphylococcus* infections
- Vancomycin, 13: used in hospitals and the outpatient setting to treat resistant organisms like MRSA and *Clostridium difficile* infections
- Aztreonam, 11: used to treat certain common infections in patients allergic to beta-lactam class antibiotics
- Tigecycline, 10: last line antibiotic used to treat soft tissue infections and pneumonia