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

November 1, 2019

Seema Verma
Administrator
Centers for Medicare & Medicaid Services
U.S. Department of Health and Human Services
P.O. Box 8013
Baltimore, Maryland 21244-1850

RE: Comments in Consideration for the Fiscal Year 2021 Inpatient Prospective Payment System Proposed Rule

Dear Administrator Verma:

The Infectious Diseases Society of America greatly appreciates the steps taken in the FY 2020 Inpatient Prospective Payment System (IPPS) Rule to improve reimbursement for new antibiotics, as well as the finalization of a new Medicare Condition of Participation requiring hospitals to implement antibiotic stewardship programs. Your recognition of the need for a stronger federal response to the crisis of antibiotic resistance and these specific steps forward represent important progress in the fight against this urgent threat to patient safety, public health and national security. IDSA asserts that additional reimbursement reform is needed to sustain the antibiotic market and support optimal antibiotic use. We welcome this opportunity to offer recommendations and rationale for additional action.

IDSA represents over 12,000 infectious diseases physicians, scientists, public health practitioners and other health care providers. Our members care for patients with a wide variety of infectious diseases, including those caused by multidrug resistant pathogens. They are on the frontlines of the fight against antibiotic resistance leading antibiotic stewardship programs, informing public health responses, and conducting research to deepen our understanding of resistance and develop new tools, including antibiotics, diagnostics and vaccines.

Unique Role of Antibiotics

IDSA recognizes that altering the Medicare reimbursement system to provide separate payments for new antibiotics is a significant change. We gave this issue serious consideration before making our request and believe that antibiotics are fundamentally different from any other class of drugs given their role in underpinning a wide range of medical care as well as their role in protecting our national security. Antibiotics are unique as a class of medicines as they do not directly target the patient but rather a foreign entity, bacteria. Further, bacteria are unique in their ability to mutate and become resistant, and share their resistance genes with other bacteria. Other classes of drugs beyond antimicrobials do not similarly lose their effectiveness over time. As a result, we have a unique,

continuous need for new antibiotics that are effective against the resistant bacteria that develop naturally as a result of antibiotic use. Further, the antibiotic pipeline is approaching collapse, and a lack of rapid federal action is likely to be cause a significant increase in patient morbidity and mortality.

Foundation of Modern Medicine

Antibiotic resistance impacts patients every day and threatens to undo decades of medical progress. Many life-saving procedures—cancer chemotherapy, organ and bone marrow transplants, and other surgeries (joint replacements, Caesarian sections, and many more) are made possible by safe and effective antibiotics. These procedures significantly increase patients' risk of infections by weakening their immune systems or in the case of surgery, allow invasion of bacteria into the wound. We can only manage that risk with antibiotics, but resistance is spreading. Our antibiotic pipeline is dwindling, severely limiting our ability to support this crucial medical care.

We already see patients whose new hips or knees become infected with untreatable infections and who then face amputation or worse. We already see patients whose cancer can be cured, but who ultimately succumb to a multidrug resistant infection. We do not want to lose the ability to perform cancer chemotherapy and other procedures that save lives and enhance the quality of life because we cannot control for risk of infection.

Infections that are not typically life-threatening are also becoming far more difficult to treat as a result of resistance, dramatically increasing health care costs and burdening patients. Consider urinary tract infections, a very common illness among women that were once reliably treated with oral antibiotics. As resistance to all available oral antibiotics has increased, and intravenous antibiotics become the only remaining treatment option for some patients, many more patients are now facing a hospital stay to treat a urinary tract infection.

National Security

Antibiotic resistance poses a significant threat to our national security. Resistant pathogens complicate our soldiers' combat wounds, increasing the risk of limb loss and death, and compromise our military's combat readiness and effectiveness. Between 2004 and 2009, over 3,300 American soldiers in Iraq and Afghanistan became severely ill from a single resistant Gram-negative pathogen—*Acinetobacter*, which has become even more resistant to treatment over time. [1]

Alarmingly, resistant pathogens are also a prime candidate for weaponization by our nation's enemies, both state and non-state actors. The former Soviet Union engineered multidrug-resistant strains of both plague and anthrax.[2] Studies have concluded that the aerosolized release of a weaponized, resistant pathogen in just a single incident of bioterrorism in the Washington, DC

[1] Fighting Superbugs: DoD's Response to Multidrug Resistant Infections in Military Treatment Facilities. Hearing before the Subcommittee on Oversight and Investigations of the Committee on Armed Services. US House of Representatives, September 29, 2010.

[2] Microbial Threats to Health: Emergence, Detection, and Response. Smolinski, M.S., Hamburg, M.A., and Lederberg, J. 2003.

area would result in a death toll of over 3 million.[3] The death toll from a coordinated bioterrorist attack using a weaponized resistant pathogen would be many magnitudes higher. Any mass casualty event is likely to result in severe wounds and burns, which can quickly become infected and further complicated by resistance.

AMR also puts our health security at risk, both within the US and globally. An outbreak of a serious resistant infection with limited or no treatment options could overwhelm health systems, harm economies, and even destabilize communities or entire countries.

Opioid Epidemic

The crisis of antibiotic resistance is converging with the opioid epidemic—which we greatly appreciate is also a high priority for CMS. Even when using a clean syringe, injection drug use can give bacteria on the skin an opportunity to easily cause a variety of serious infections, including endocarditis (a heart valve infection that requires hospitalization), bloodstream infections, bone infections, and skin and soft tissue infections. CDC estimates that in the US, individuals who inject drugs are 16 times more likely to develop an invasive MRSA infection.[4]

Antibiotic Pipeline in Crisis

As the threat of resistance continues to spread and claim lives, our toolbox of antibiotics to treat these infections is shrinking. While the numbers of antibiotics annually approved for marketing in the US has increased in recent years following a decline in the previous decade, significant unmet needs persist, with far too few treatment options available for multidrug-resistant infections.

Nearly all large pharmaceutical companies have left the antibiotic development field. The small companies that are responsible for most of the antibiotic innovation are struggling to stay in business, as the new antibiotics they have developed and launched provide very little opportunity for return on investment. In April 2019, one small antibiotics company—Achaogen—filed for bankruptcy, despite having launched an important new antibiotic plazomicin in 2018. In June 2019, another small antibiotic company—Tetraphase—announced massive layoffs, including eliminating its research function. The few remaining small antibiotics companies face similar fates. Indeed, these companies are struggling financially to manufacture these medicines. These new antibiotics were developed in part with federal taxpayer dollar meant to stimulate research and development of innovative antimicrobials. Yet, after these federal expenses, the drugs developed and FDA-approved may not be available to patients who need them. Further, these companies are unable to conduct necessary post-market studies to support the use of their drugs in precisely the infections for which new therapies are direly needed. And these companies cannot fund continued investment into the development of additional new antibiotics.

There are currently 42 antibiotics in development, 15 in Phase 1 clinical trials, 11 in Phase 2, 13 in Phase 3, and three have had new drug applications submitted. Of these, 16 have the potential

[3] Rosen J et al. Cybercare: A System for Confronting Bioterrorism. National Academy of Engineering. Engineering and Homeland Security, December 3, 2008.

[4] Jackson KA, Bohm MK, Brooks JT, et al. Invasive Methicillin-Resistant Staphylococcus aureus Infections Among Persons Who Inject Drugs — Six Sites, 2005–2016. MMWR Morb Mortal Wkly Rep 2018;67:625–628. DOI: http://dx.doi.org/10.15585/mmwr.mm6722a2external icon

to treat gram-negative infections—which ID physicians consider to be among the worst, most highly resistant, and most difficult to treat threats.[5] It is important to remember that most of these drugs in clinical development do not ultimately achieve FDA approval, and that we need a variety of drugs to address different infectious syndromes, different pathogens, and unique patient needs such as allergies or drug interactions.

The very nature of infectious diseases and antibiotic resistance necessitates a robust and renewable antibiotic pipeline capable of meeting current and future patient, public health and national security needs. New threats continue to emerge, and existing threats continue to evolve. Patients with multidrug-resistant infections often have other health problems which may limit the types of antibiotics that will be safe and effective for them.

Need for Additional Reimbursement Reform

When new antibiotics are brought to the market, they are rarely used. This is due in part to appropriate stewardship policies ensuring that such antibiotics are only used when they are truly needed, and IDSA strongly supports stewardship programs. However, the Medicare reimbursement system can also make it challenging for patients to access new antibiotics even when they are clinically appropriate. The Diagnosis Related Group (DRG) payment is too low to cover the costs of new antibiotics, making it difficult in many instances for new antibiotics to be added to hospital formularies or prescribed even when they are medically the best choice for the patient. In addition to harming patient care, this scenario also makes it extremely difficult for antibiotic developers—primarily small companies—to earn a return on their investment.

A recent study estimated that new antibiotics with activity against a muti-drug resistant bacteria, carbapenem resistant Enterobacteriaceae (CRE), are currently being used to treat 35% of CRE infections in which they were expected to be first-line agents.[6] This uptake is less than what would have been expected. Of concern, antibiotics with high toxicity, such as colistin, are still being used in many cases instead of new antibiotics. Colistin can cause severe kidney damage, sometimes requiring dialysis—which places a significant economic burden on Medicare. Flawed Medicare reimbursement is a key factor in limited uptake of new antibiotics and persistent colistin use.

IDSA greatly appreciates that CMS took important initial steps to improve antibiotic reimbursement in the FY 2020 IPPS rule by increasing New Technology Add On Payments (NTAP) for new antibiotics for serious or life-threatening infections, and by increasing the DRG severity level designation for the diagnosis codes that specify antimicrobial drug resistance. However, the impacts of these changes are limited. NTAP payments only apply for three years, while the need for the new antibiotics persists well beyond that time frame. The increased severity level designation is primarily being applied to codes that are already at the maximum severity level, leaving few instances in which payment would actually be increased as a result of this policy.

---

[5] Tracking the Global Pipeline of Antibiotics in Development. The Pew Charitable Trusts. March, 2019.

[6] Clancy et al. Estimating the Treatment of Carbapenem-Resistant Enterobacteriaceae Infection sin the United States Using Antibiotic Prescription Data. Open Forum Infectious Diseases, Volume 6, Issue 8, August 2019, ofz344, https://doi.org/10.1093/ofid/ofz344 28 July 2019.

IDSA urges CMS to consider carving new antibiotics for serious or life-threatening infections out of the DRG and allowing them to be reimbursed separately. This will help ensure that patients who need these drugs can access them and will help stabilize the precarious antibiotic marketplace for developers.

Stewardship Next Steps

Reimbursement reform or any other policies aimed at incentivizing new antibiotic R&D must be paired with robust stewardship policies to guide appropriate antibiotic use and preserve the effectiveness of new antibiotics, thereby preserving our nation's investment in the discovery and development of those new antibiotics. IDSA applauds the new Medicare Condition of Participation requiring hospitals to implement stewardship programs and looks forward to working closely with CMS on its implementation as well as additional policies and investments to maximize the benefits of stewardship for patients and communities.

IDSA encourages CMS to pair higher reimbursement for antibiotics with a requirement that hospitals report antibiotic use and resistance data to the CDC National Healthcare Safety Network. This mechanism would allow evaluation of the impact of new reimbursement policy on antibiotic utilization and resistance. Additionally, IDSA would greatly appreciate opportunities to work with CMS and other federal agencies to boost resources for stewardship—particularly for hospitals beginning their programs, as initial investments for new stewardship programs are typically higher than ongoing costs. IDSA also looks forward to collaborating with CMS to ensure that infectious diseases physicians leading stewardship programs are appropriately compensated for their contributions.

Once again, IDSA thanks you for your commitment to combating antibiotic resistance and looks forward to our continued partnership.

Sincerely,

Thomas J. File, MD, FIDSA
President, IDSA