Duke | MARGOLIS CENTER for Health Policy

Developing Feasible Payment Reform Pathways for Antibiotics to Meet the Needs of Providers, Payers, and the Populations They Serve

1201 Pennsylvania Ave, NW, Suite 500, Washington, DC 20004
January 29, 2019
9:00am – 3:00pm

Discussion Guide

Introduction

Impact of Antimicrobial Resistance

Serious bacterial infections can result in severe patient morbidity and costly healthcare. These negative consequences are especially prevalent when initial treatments fail and providers must decide how to care for patients with antibiotic resistant infections. In the United States alone, 2 million people suffer from resistant infections every year and 23,000 die as a direct result.[1] In addition, treating resistant infections has been estimated to add an additional $2.2 billion dollars to the yearly cost of healthcare.[2] When antibiotics fail, patients are at risk of severe complications—colitis and toxic megacolon from *Clostridium difficile*, reproductive complications from *Neisseria gonorrhoeae*, paralysis from *Campylobacter*, reactive arthritis from *Shigella*, and others.[3] Even effective antibiotics put patients at risk of serious adverse events—especially patients with complicated resistant infections—who may experience allergic reactions, severe diarrhea, dehydration, or drug interactions that exacerbate routine side effects.[4] Despite intensive treatment, too many patients suffer devastating outcomes. Preventing treatment failure and serious adverse events requires clinicians to provide the right drug to the right patient at the right time. Unfortunately, the prevalence of infections lacking effective therapeutic options and the inappropriate use of antibiotics complicate care. Without novel antibiotics, existing options will likely become less effective as pathogenic organisms continue to evolve and acquire mechanisms of resistance.

Barriers to Developing Treatment

While novel antibiotics are desired, generating return on investment has become especially challenging for innovators. From the outset, clinical development is costly, and is especially so for products with limited patient populations such as those with resistant infections. Further, most antibiotics are approved based on non-inferiority trials that do not demonstrate whether an investigational antibiotic is superior to the standard of care; this both slows the adoption of novel antibiotics over less expensive generics and discourages reimbursement commensurate with innovative development. Finally, when a new antibiotic reaches the market, its utilization is further restricted by stewardship protocols, which guide physicians toward appropriate prescribing practices to avoid enhancing antimicrobial resistance.

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[1] Centers for Disease Control and Prevention. Antibiotic resistance threats in the United States, 2013. CDC website. September 16, 2013. Available at: www.cdc.gov/drugresistance/threat-report-2013.
[2] Thorpe KE, Joski P, Johnston KJ. Antibiotic-Resistant Infection Treatment Costs Have Doubled Since 2002, Now Exceeding $2 Billion Annually. Health Aff (Millwood). 2018;37(4):662-669.
[3] Siemann M, Koch-dörfler M, Rabenhorst G. Clostridium difficile-associated diseases. The clinical courses of 18 fatal cases. Intensive Care Med. 2000;26(4):416-21.
[4] Ibid. at 1

While it is important to keep antibiotic use restricted to maintain effectiveness, this practice results in low volume use, and due to a fee-for-service (FFS) payment structure, limits the revenue that new antibiotics with innovative mechanisms of action will receive. As a result, many developers are leaving the field for more profitable areas, as demonstrated by several recent departures,[5]and strategies are needed to encourage innovators to continue investing in antibiotic research and development.

Global Priorities for Antibiotic Drug Development

New, innovative antibiotics receive little financial support within the current US payment system, and new financing mechanisms that are independent of volume of drug use, are needed. Key actions have been identified that would help to reinvigorate antibiotic development. (For a more detailed summary of proposals and recommendations, please see "Value-based Strategies for Encouraging New Development of Antimicrobial Drugs".[6]) First, there needs to be an increase in funding dedicated to basic and translational research on antimicrobials, which helps to move drugs through preclinical and clinical development. In the US, this type of funding has been supplied through government organizations and public-private partnerships, such as BARDA and CARB-X. Second, implementation of a delinkage mechanism is needed. This type of incentive is provided once an antibiotic has received FDA approval, and it would provide revenue independent of sales volume. To encourage new investment in antimicrobial research and development, a substantial and predictable development reward is needed, such as prize fund or market entry reward. However, it is also necessary to sustain current investment in antibiotic development through more immediate policy changes, which could include reforms to antibiotic payment.

Developing Policy to Improve Treatment Options

To address these financial and health challenges, stakeholders must incentivize the development of novel antibiotics while still advancing antibiotic stewardship. While efforts to implement stewardship programs among hospitals and other care facilities are widespread, dwindling antibiotic research and development threatens the sustainability of these efforts. There are many mechanisms to encourage development, and one of the most important is developing new ways to pay for these drugs. With support from the Wellcome Trust, and guidance from a multi-stakeholder Advisory Committee, the Duke-Margolis Antimicrobial Incentives and Payment Reform project was created to pursue actionable policy recommendations to improve the economic environment supporting antibiotics. Reforming how antibiotics for serious infections are paid for could improve predictability and sustainability of revenue, enabling innovators to remain invested in antibiotic development.

Purpose of this Discussion Guide

The January roundtable is an opportunity to hear from all stakeholders on payment reform options and their potential impact on antibiotic utilization, costs and revenue, and health outcomes. To help facilitate the day's discussion, the guide below will:

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[5] Big pharma backs off superbug: Why 5 drugmakers bailed on antibiotic research. Becker's Hospital Review Available at: https://www.beckershospitalreview.com/pharmacy/big-pharma-backs-off-superbug-why-5-drugmakers-bailed-on-antibiotic-research.html. (Accessed: 7th August 2018)

[6] Daniel, G.W., et al. Value-based Strategies for Encouraging New Development of Antimicrobial Drugs Available at: https://healthpolicy.duke.edu/pave

- Discuss strategies to improve antibiotic reimbursement
- Provide an overview of value-based payment approaches
- Describe how value-based approaches could apply to antibiotics
- Outline the topics to be discussed during the January 29th roundtable

Improving Reimbursement for Antibiotics

In Medicare Part A and the Inpatient Prospective Payment System (IPPS), inpatient-administered drugs are bundled with related hospital services, collectively assigned a diagnosis-related group (DRG), and reimbursed as a global payment. Expensive drugs may exceed the pre-determined DRG reimbursement amount, resulting in losses for the provider. As a result, hospitals may have lower utilization of expensive drugs and patient access to those drugs may be reduced.

To promote uptake and lower the financial burden on hospitals to use innovative, expensive medical products, the Centers for Medicare and Medicaid Services (CMS) introduced the New Technology Add-On Payment (NTAP) in 2000. The NTAP program provides additional reimbursement for new drugs or devices whose cost exceeds the amount covered by the DRG and that demonstrate substantial improvement over existing technologies. Manufacturers must apply for their product to receive the NTAP, and the amount is up to 50% of the cost of the technology not covered by the DRG. A medical product may receive these payments for two to three years, but must apply for renewal each year. As the new technology is adopted among providers during this period, the applicable DRGs adjust by incorporating the cost of the new technology and NTAP eligibility ends.

Legislation has been introduced to allow for add-on payments for antibiotics within a DRG independent of NTAP application. The Developing an Innovative Strategy for Antimicrobial Resistant Microorganisms (DISARM) Act, allows additional payments for antimicrobial drugs that treat infections caused by qualifying pathogens. DISARM was introduced in 2015, and was subsequently included in early versions of the 21st Century Cures Act. Ultimately, DISARM was not included in the bill that passed. However, stakeholder interest in increasing the level of reimbursement remains.

Another proposed mechanism to increase reimbursement for new antibiotics is to carve-out particular antimicrobials from DRGs so that the full cost would be reimbursed. In Medicare, this mechanism would shift antibiotic payments to Part B, where providers would be reimbursed average sales price plus six percent. In commercial settings, the reimbursement amount would vary based on payer. Removing reimbursement of innovative antibiotics from DRGs would allow hospitals to be reimbursed the full purchase price of the antibiotic, mitigating the impact of financial factors on clinical treatment consideration.

While changing the mechanism or amount of reimbursement could bolster novel antibiotic revenue in the short-term, this approach still relies on the volume of the antibiotic that is sold. Novel antibiotics that are used infrequently would not experience significant benefits from these approaches. A transition to value-based payment (VBP) arrangements that delink the payment for antibiotics from the volume of their use could prove more sustainable long-term.

Value-Based Payment Overview

Hospital-administered drugs have traditionally been reimbursed according to FFS schemes, where revenue is tied to the volume of sales, and VBP models represent an opportunity to emphasize and

reward the value that qualified drugs can contribute to high-quality healthcare. VBP arrangements for medical products are intended to align the payment for a drug with the expected or observed value of a drug, based on clinical trials data or evidence generated with post-market use. There are two main categories of VBP: evidence-based pricing and outcomes-based contracts. When setting a payment amount for a product, evidence- or indication-based pricing considers existing evidence, such as that generated through clinical trials. In contrast, outcomes-based contracts rely on evidence generated through real-world use to determine payment for a product. These types of payment contracts may utilize rebates from manufacturers to payers if product use does not result in pre-defined outcomes in a given patient or population. Outcomes-based contracts also include population-based payments, where payment is contingent on the population-level rather than patient-level outcomes. Population-based payments will likely depend on meaningful outcome measures and require greater provider involvement.

Few truly population-based contracts for drugs have been put into place, but stakeholders are beginning to experiment with these formats. The state of Louisiana has recently announced their intention to implement a subscription model for Hepatitis C drugs. In this arrangement, Louisiana's Medicaid program would pay a set fee to the drug manufacturer for unlimited access to the drug. Because the success rate of this drug is very high, outcomes are not being tracked in this arrangement. However, a potential next step for this type of arrangement could incorporate overall patient outcomes, including cure rate, safety measures, or evaluation of the overall cost of care.

Moving to Value-Based Payment for Antibiotics

Why Value-Based Approaches May Be Appropriate for Antibiotics

There are a number of reasons why antibiotics may be appropriate for the application of VBP arrangements. For one, when effective, these drugs have the potential to lower costs through reduced health care utilization and averted additional infections. The main benefits of treatments for antimicrobial resistant bacteria are likely to accrue to the members of a population who never need treatment because the treatment is available and used appropriately in a small number of patients to prevent spread of resistance. VBP arrangements based on population outcomes (e.g., prevention of spread of resistant infections)—or better models where payments are completely de-linked from volume use, could better align drug payments with the population health value of these drugs.

For example, *Clostridium difficile* infection (CDI) is an opportunistic infection, and frequently occurs because of prior broad spectrum antibiotic treatment. As a result, it is difficult to treat, and may recur in 20-30% of patients, with the rate of recurrence increasing to 40-60% after the first repeat event.[7] CDI impacts the elderly at a higher rate than the rest of the population, and it can be costly to treat: expenses are estimated to total $21,448 per patient, with an additional $15,050 spent for each recurrence.[8] The US is estimated to spend over $6 billion on CDI every year, so there are many

[7] Hopkins, R.J. and Wilson, R.B. Treatment of recurrent Clostridium difficile colitis: a narrative review. Gastroenterol Rep (Oxf). 2018 Feb; 6(1): 21–28.

[8] Zhang, S. et al. Cost of hospital management of Clostridium difficile infection in United States—a meta-analysis and modelling study. BMC Infect Dis. 2016; 16(1): 447.; Shah, D.N. et al. Economic burden of primary compared with recurrent Clostridium difficile infection in hospitalized patients: a prospective cohort study. J Hosp Infect. 2016 Jul;93(3):286-9.

opportunities for improved health and averted spending with this type of infection, whether preventing the first infection from occurring, or by preventing recurrent events.[9]

Another potential advantage of VBP arrangements for antibiotics is the potential for better utilization of the drug. Often, limited evidence is generated during antibiotic clinical trials, and improvements in prescribing can be made as additional data is generated over time. New antibiotic approvals trend toward narrower patient populations and their effectiveness across broader and more diverse use cases may be uncertain. As physicians generate more data on a new antibiotic's use, they may gain a better understanding of how and when an antibiotic might be used.

VBP arrangements could also leverage antibiotic stewardship, surveillance, and prevention programs that are already in place. Coordinating antibiotic utilization with more frequent data collection can support both value-based arrangements and appropriate prescribing, simultaneously. Stewardship programs could benefit from more detailed utilization and outcome data and health systems might realize efficiencies in implementing value-based programs where data is already being collected for stewardship purposes.

Incorporating Population Health into Antibiotic Payment Approaches

In June 2018, the Commissioner of Food and Drugs, suggested a model in which CMS would pay a subscription or licensing fee for antibiotic access. Under this proposal, the FDA and CMS would work in coordination to determine eligibility for this new pathway, and drugs in clinical development that meet the criteria could receive subscription payments from CMS after regulatory approval and market entry. Payments to the manufacturer would likely be contingent on certain milestones or outcomes being met, as well as continued availability of the drug.[10]

Details on how this type of model might work are uncertain, and could potentially have different implementation plans in the public and commercial settings. The basics of this model would allow for a regular fee to be paid to the manufacturer in exchange for access to the antibiotics. The amount of the fee would be dependent of certain outcomes or milestones being met. These outcomes could be based on the value that the drug could potentially provide, which might include the types of infections that it is appropriate for, route of administration, and novelty of mechanism, or its impact on cost measures that are important to the health care system, such as readmissions, length of stay, or development of complications. Implementation and enforcement of antibiotic stewardship protocols will also be critical for the success of this type of model, as they will help to ensure that the antibiotic products under subscription payment will continue to be used appropriately. Shifting to payment for hospital-administered antibiotics through subscription arrangements could occur in several ways: the payer could directly contract with the antimicrobial manufacturer; providers could continue to contract with manufacturers, with incentives provided by payers to engage in these non-volume-based contracts; or a third party, such as a group purchasing organization or pharmacy benefit manager, could negotiate directly with manufacturers, with the potential to offer a "bundle" of antibiotics to providers.

[9] Zhang, S. et al. Cost of hospital management of Clostridium difficile infection in United States—a meta-analysis and modelling study. BMC Infect Dis. 2016; 16(1): 447.

[10] Remarks by Scott Gottlieb, M.D., Commissioner of Food and Drugs. Available at: https://www.fda.gov/NewsEvents/Speeches/ucm620495.htm

To be successful, this type of change in payment would likely have to be incremental and build on the current payment reform efforts and other value incentives. There may be many hurdles to implementation in the commercial population, and heterogeneous stakeholder interests and covered populations may be difficult to account for in this model. However, it may be feasible for CMS to set up such a model, where they can provide incentives for provider participation in the form of gain-sharing or bonus payments. Antibiotic use is associated with specific DRGs, and outcomes and associated costs can be measured through claims data. In this way, patient- or population-level outcomes associated with antibiotic use could be measured. The Oncology Care Model is a good example of how CMS was able to change payment and treatment protocols while also collecting outcomes on the impact of care decisions.

Duke-Margolis Roundtable on Antibiotic Payment Reform

Many questions remain about the feasibility of these payment reform approaches within the current healthcare system. During the roundtable, the following topics will be discussed:

The impact of current reimbursement policy on antibiotic utilization and care. A number of factors may affect purchasing and prescribing decisions, including infection incidence rates, available evidence for a particular drug, stewardship protocols, and cost of a drug. This session will focus on the influence of reimbursement policy and how current incentives are viewed. Questions to address may include:

- How do Medicare DRG +/- NTAP and common commercial payer reimbursement policies affect new antibiotic purchasing and use decisions?
- Does current reimbursement policy encourage appropriate antibiotic stewardship? Are there modifications that could improve alignment?
- What are utilization trends for generic vs. brand antibiotics in difficult-to-treat infections?

Potential effects of increasing reimbursement for antibiotics through modifications to DRG payments. Some antibiotic payment reform proposals have focused on increasing reimbursement through available mechanisms, such as increasing the New Technology Add-On Payment (NTAP) add-on amount or carving out antibiotics from the DRG payment. This session will examine the impact of these potential policies on providers and hospitals, and consider other opportunities to improve prescribing and payment practices. Questions to address may include:

- What impacts might policies such as increased add-on or NTAP payments make on brand antibiotic utilization?
- What impacts would a DRG carve-out or full reimbursement of antibiotics make on brand antibiotic utilization?
- Are there payment or policy reforms that would be preferred by providers?

Moving from patient- to population-based payments for antibiotics. There are barriers to implementing a new, non-volume-based payment structure for antibiotics, though some may be more difficult to navigate than others. This session will explore the challenges to implementation of value-based or population-based payment models for antibiotics within the hospital setting, and identify potential opportunities to move these models forward. Questions to address may include:

- What areas represent the biggest challenge for modification to the current payment structure?
- What types of models might work best within the current structure?

- What are the opportunities and limitations for population-based payment models?

Value associated with antibiotics and how to pay for those that are infrequently used. Hospitals and payers encounter a variety of costs for infections, and antibiotic resistance can add a significant amount through treatment time and complications. This session will consider measures that may provide a readout on the most significant costs and patient outcomes associated with infections. Questions to address may include:

- What infection-associated outcomes represent the greatest cost to providers and payers?
- What types of outcomes would reflect the value of antibiotics?
- What characteristics represent priority areas for all stakeholders?